Prediction of Recovery of Left Ventricular Dysfunction After Acute Myocardial Infarction: Comparison Between ^{99m}Tc-Sestamibi Cardiac Tomography and Low-Dose Dobutamine Echocardiography

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The aim of this study was to evaluate the role of ^{99m}Tc-sestamibi cardiac imaging and dobutamine echocardiography in detecting myocardial viability early after acute myocardial infarction. **Methods:** Forty-nine patients (mean age 52 ± 10 y) underwent coronary angiography, low-dose dobutamine echocardiography, radionuclide angiography and rest ^{99m}Tc-sestamibi imaging within 10 d after myocardial infarction. Of these patients, 19 were revascularized and 30 were treated medically. Resting echocardiogram and radionuclide angiography were repeated 8 mo later to evaluate segmental functional recovery and changes in left ventricular (LV) ejection fraction, respectively. **Results:** In revascularized patients, 61 of 108 akinetic or dyskinetic segments showed functional recovery. In these patients, sensitivity in predicting segmental functional recovery was 87% for sestamibi imaging and 66% for dobutamine echocardiography ($P < 0.001$), whereas specificity and accuracy were comparable. Sestamibi activity (≥55% of peak) was the strongest predictor of segmental functional recovery ($P < 0.001$) and of LV ejection fraction improvement ≥5% ($P < 0.01$) after revascularization. In medically treated patients, 60 of 149 akinetic or dyskinetic segments showed functional recovery. In these patients, the majority (94%) of segments with contractile reserve on dobutamine were viable on sestamibi imaging and 86% of them improved function at follow-up. Functional recovery was poor in segments without contractile reserve either with (38%) or without (62%) preserved sestamibi uptake. Inotropic response was the best predictor of segmental ($P < 0.001$) and global ($P < 0.01$) LV functional improvement in medically treated patients. **Conclusion:** Dobutamine echocardiography predicts spontaneous functional recovery after acute myocardial infarction. However, sestamibi imaging is useful to identify patients with dysfunctional myocardium without contractile reserve who may benefit from coronary revascularization.

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A mixture of necrotic, hibernating and stunned myocardium is responsible for the left ventricular (LV) dysfunction observed in patients after acute myocardial infarction (AMI) (*1,2*). Myocardial necrosis induces irreversible damage, whereas hibernation or stunning causes a reversible impairment of myocardial contractility. Various approaches have been proposed to differentiate viable from necrotic myocardium soon after the infarction and to identify the relative prevalence of hibernation and stunning (*1–3*). It should be considered that stunning is often followed by a spontaneous delayed recovery of LV function, whereas hibernation needs prompt revascularization (*4*).

Low-dose dobutamine echocardiography is widely used to detect inotropic reserve of severely dysfunctional myocardium (*5,6*). It is generally accepted that myocardial regions exhibiting improvement in contractile function after inotropic stimulation will recover spontaneously or after coronary revascularization (*7,8*). Several radionuclide imaging techniques have also been proposed to identify viable myocardium. In particular, perfusion imaging at rest is increasingly used to assess myocardial viability and considerable emphasis has been placed on the amount of tracer uptake within dysfunctional regions (*9*). Cardiac imaging with ^{99m}Tc-sestamibi has been demonstrated to correctly differentiate necrotic from hypoperfused but still viable myocardium (*10,11*). However, few data are available regarding the role of sestamibi scintigraphy in detecting residual viability within the infarct region and in predicting late functional improvement in patients recovering from AMI (*11–13*).

In this study, a selected group of AMI patients with available angiographic data underwent low-dose dobutamine echocardiography and sestamibi tomographic imaging at rest before hospital discharge. The purpose was to assess the value of dobutamine echocardiography and sestamibi imaging in predicting recovery of myocardial contractility in AMI patients. Furthermore, we analyzed whether sestamibi imaging provides information incremental to that of dobutamine echocardiography in predicting functional recovery in AMI patients undergoing coronary revascularization procedures.

MATERIALS AND METHODS

Study Population

Between January 1996 and August 1997, 52 patients (46 men, 6 women; mean age 52 ± 10 y) recovering from a first AMI were studied. All patients met the following criteria: first Q-wave myocardial infarction, New York Heart Association functional class I or II, no early postinfarction angina, sinus rhythm and no conduction disturbances, two-dimensional echocardiographic images of adequate quality for quantitative analysis. Patients with history of diabetes, severe hypertension with LV hypertrophy, valvular heart disease or other detectable cardiac disorders or severe concomitant illness were excluded. During the acute phase, 40 patients (77%) who were admitted within 6 h of the onset of symptoms (average, 2.2 ± 1.3 h) received thrombolytic treatment with recombinant tissue-type plasminogen activator (rt-PA). Within 5–12 d after AMI, all patients underwent coronary angiography, low-dose dobutamine echocardiographic stress test, equilibrium radionuclide angiography and rest sestamibi imaging. Echocardiography and radionuclide angiography were repeated 8 mo later under resting conditions to evaluate recovery of contractile function. The study protocol was approved by the local Ethical Committee on Human Research, and written informed consent was obtained from all patients.

^{99m}Tc-Sestamibi Tomography

All patients underwent sestamibi cardiac SPECT on the same day of echocardiographic study. Cardiac medication, except nitrates and antiplatelets drugs, was discontinued at least 48 h before the study. All patients were intravenously injected at rest with 740 MBq ^{99m}Tc-sestamibi. Imaging was performed 60 min after tracer injection as described previously (*14*), using a rotating large-field-of-view gamma camera (Elscint SP4HR; Elscint, Haifa, Israel) equipped with a low-energy, all-purpose, parallel-hole collimator and connected with a dedicated computer system. Thirty-two projections (30 s/projection) were obtained over a semicircular 180° arc, which extended from the 30° right anterior oblique to the left posterior oblique position. A 20% symmetric energy window centered on the 140 keV peak was used. Filtered backprojection was then performed with a low-resolution Butterworth filter with a cutoff frequency of 0.5 cycle per pixel, order 5.0. No attenuation or scatter correction was applied.

In each patient, scintigraphic studies were analyzed by two independent observers who were unaware of angiographic and echocardiographic findings. Regional sestamibi activity was measured on two short-axis tomograms and on the two horizontal and vertical long-axis tomograms selected for analysis, using a semiautomatic, quantitative, circumferential profile method. An operator-defined region of interest was drawn around the LV activity of the short-axis and long-axis tomograms. Each short-axis tomogram was then divided into six sectors of equal arc, starting at the 12 o'clock position and proceeding clockwise, representing the anterolateral, lateral, inferior, posteroseptal, septal and anterior myocardium. To measure apical uptake, vertical and horizontal long-axis tomograms were also divided into six sectors starting at the 9 and 12 o'clock positions, respectively, and proceeding clockwise so that in each case the first and sixth sectors corresponded to the apical segments. Therefore, in each patient, 16 anatomic segments were evaluated (Fig. 1). Regional sestamibi activity was measured in each myocardial sector as mean counts. In each patient, the sector with the maximum mean counts was used as the reference region. Sestamibi uptake in all other sectors was then expressed as the percentage of the activity measured in the reference region. Each myocardial segment was assigned to one of the major vascular territories. Briefly, the left anterior descending coronary artery territory included the anterior wall, septum and apical wall. The right coronary artery was assigned the inferior wall. The left circumflex coronary artery was assigned the lateral wall.

Low-Dose Dobutamine Echocardiography

Patients underwent low-dose dobutamine echocardiography on the same day of sestamibi imaging. Echocardiographic imaging was acquired at rest and during dobutamine infusion. Standard tomographic views of LV were obtained from the parasternal long-axis and short-axis views and from the apical four- and two-chamber views, with particular attention to optimization of regional function. All studies were performed on Hewlett-Packard Sonos 1000 sonography system (Andover, MA), equipped with 2.5 MHz transducer and were recorded on half-inch VHS tape. After rest images were obtained, intravenous dobutamine infusion was performed by means of an infusion pump, starting at a dose of 5 μg/kg/min and increased every 5 min to 7.5 and to 10 μg/kg/min. Three lead electrocardiograms and sphygmomanometer blood pressure were monitored continuously throughout the study and the recovery phase. The test was terminated prematurely if any of the following criteria occurred: angina symptoms, hypotension or significant ventricular arrhythmia. Echocardiograms were analyzed by two independent readers unaware of clinical, angiographic and

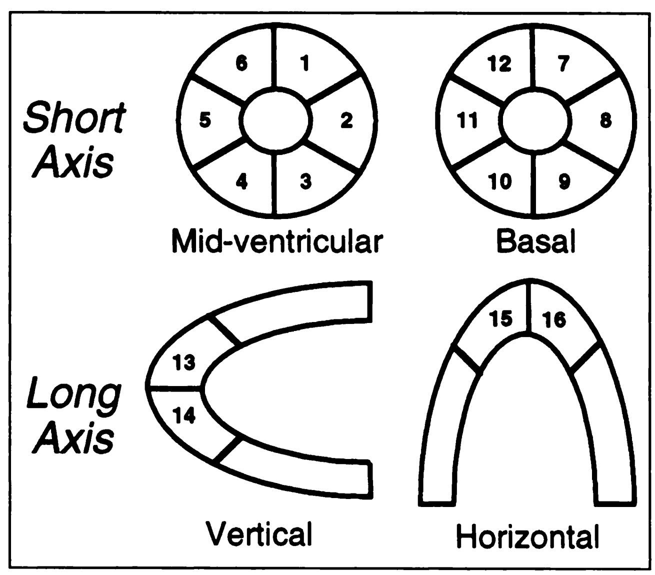

FIGURE 1. Segmentation scheme used for regional analysis of ^{99m}Tc-sestamibi tomography and echocardiography.

scintigraphic data. Discrepancies were resolved by consensus. For analysis of wall motion, the left ventricle was divided into 16 segments corresponding to the scintigraphic regions (Fig. 1). For each segment, wall motion was scored according to the recommendations of the American Society of Echocardiography (*15*) from 1–3, where 1 indicated normal, 2 hypokinesia (reduced wall thickening and inward motion) and 3 akinesia (absence of wall motion and of systolic thickening) or dyskinesia (paradoxical outward motion in systole). For the purpose of this investigation, we focused on akinetic or dyskinetic segments, those that should be evaluated for the assessment of myocardial viability (*16*). A single akinetic or dyskinetic myocardial segment was considered responsive to dobutamine echocardiography if the wall motion score improved by at least 1 point during any stage of dobutamine infusion. All studies were reviewed independently by two experienced observers who were unaware of the clinical, angiographic and scintigraphic data. Interobserver concordance was 92% and discrepancies were resolved by consensus. One observer reviewed all the studies twice, at least 2 wk apart, with an intraobserver concordance of 94%.

Radionuclide Angiography

All patients underwent equilibrium radionuclide angiography within 1 wk from echocardiography and sestamibi imaging. In all patients in vivo labeling of red blood cells was performed with 555 MBq ^{99m}Tc. Radionuclide angiography was performed at rest in the 45° left anterior projection with the patient in supine position. A small-field-of-view gamma camera (Starcam 300 A/M; General Electric, Milwaukee, WI), equipped with a low-energy, all-purpose collimator, was used. Data were recorded at a frame rate of 24 frames per cardiac cycle on a dedicated computer system. Radionuclide angiographic studies were analyzed with a standard commercial software (General Electric). Reproducibility of ejection fraction measurements in our laboratory has been reported previously (*17*). In particular, assessment of the ejection fraction within the same patients under steady-state conditions on different days of observation showed a significant correlation ($r = 0.97$, $P < 0.01$), and the SD of the reproducibility of the measurements was 1.5%.

Coronary Angiography

After intracoronary nitroglycerin administration, selective angiograms were obtained in at least two projections for right coronary artery and at least four for the left coronary artery. The presence of significant (70% coronary diameter reduction) stenosis in the proximal coronary arteries or their major branches was assessed with caliper measurement. The thrombolysis in myocardial infarction (TIMI) flow grade of the infarct-related vessel was assessed (*18*). For statistical analysis, TIMI grades 0 and 1 and TIMI grades 2 and 3, respectively, were combined together.

Functional Outcome

Of the 52 patients enrolled, 21 underwent coronary revascularization (8 coronary bypass grafting and 13 coronary angioplasty with stent implantation) within 2 mo of the acute event. All major epicardial coronary arteries with significant stenosis, including all the infarct-related vessels, were subjected to revascularization procedure. Twelve patients had single-vessel and 1 patient two-vessel coronary angioplasty. Successful dilatation was obtained in all these patients, as defined by a diameter of the residual stenosis of the target vessel not exceeding 30% of luminal diameter. Two patients had two-vessel and 4 patients three-vessel coronary bypass grafting. All attempted coronary bypasses were successful without evidence of postoperative infarction. The remaining 31 patients were treated medically. Patients were not randomly assigned to coronary revascularization or medical therapy. The decision was made by each treating physician, unaware of the results of dobutamine echocardiography and sestamibi imaging, and was based on severity of symptoms, response to therapy, suitability of coronary anatomy for coronary revascularization and patient's preference for one treatment over the other. Eight months after the baseline study, patients repeated the echocardiographic study and radionuclide angiography under control conditions. As for baseline study, cardiac medication, except nitrates and antiplatelets drugs, was withheld 48 h before the study. Baseline akinetic or dyskinetic segments at echocardiography were considered as showing functional recovery when regional wall motion score improved at least 1 point at follow-up. For individual patients, recovery of function was defined as an improvement in LV ejection fraction ≥5% at radionuclide angiography from baseline to follow-up.

Statistical Analysis

Statistical analysis was performed with the SPSS statistical package (SPSS Inc., Chicago, IL) (*19*). Continuous data were expressed as mean ± SD and categorical data as percentage. The unpaired *t* test (for continuous variables) and the chi-square test (for categorical variables) were used as appropriate. A P value < 0.05 was considered statistically significant. The prognostic value in predicting functional outcome of variables considered for the purpose of this study was first assessed by chi-square test, and sensitivity, specificity and accuracy were calculated. To calculate the optimal threshold for sestamibi uptake in predicting segmental functional recovery, a receiver operating characteristic curve was constructed in revascularized patients, resulting in the sensitivity-specificity plot. The optimal cutoff value was defined as that providing the maximal sum of sensitivity and specificity. The independent prognostic value of low-dose dobutamine echocardiographic stress test, sestamibi imaging and TIMI flow grade in predicting functional outcome was assessed by multivariate logistic regression analysis separately in patients who underwent coronary revascularization and in those who were medically treated. The analysis was performed according to the unmodified forward stepwise procedure, and variables were entered into or removed from the model on the basis of a computed significance probability (maximized partial likelihood ratio). To clarify whether sestamibi imaging provides incremental information to those obtained from dobutamine echocardiography, we analyzed the data according to a modified stepwise procedure in which the two techniques were included in the model in hierarchical order. Increments in information on the model at each step were considered significant when the difference in log-likelihood associated with each model, adjusted for differences in degrees of freedom, corresponded to $P < 0.05$. Finally, a separate analysis was performed to assess the value of sestamibi imaging and dobutamine echocardiography in predicting recovery of global LV function. For this purpose, patients were divided according to the presence of two or more akinetic or dyskinetic segments showing contractile reserve at dobutamine echocardiography or evidence of tissue viability at sestamibi imaging, respectively.

RESULTS

Of the 52 patients enrolled, 1 of the revascularized group was lost to follow-up and 2 others died (1 revascularized and 1 not revascularized). Therefore, the final study population comprised 49 patients (44 men, 5 women; mean age 52 ± 10 y). Overall, 784 myocardial segments were analyzed. At baseline echocardiography, 385 segments were normal, 142 hypokinetic and 257 akinetic or dyskinetic. All akinetic or dyskinetic segments were within the infarct-related artery territory. Clinical, baseline echocardiographic, radionuclide angiographic and coronary angiographic data of revascularized patients and of medically treated patients are reported in Table 1. Revascularized patients had a greater prevalence of TIMI score 0 or 1 and a higher number of diseased vessels with ≥70% stenosis.

Segmental Analysis

Patients Undergoing Coronary Revascularization. In revascularized patients, 154 myocardial segments were normal at baseline, 42 hypokinetic and 108 akinetic or dyskinetic. Of these latter segments, 61 (56%) showed functional recovery at follow-up. The receiver operating characteristic curve for sestamibi uptake in predicting functional recovery is reported in Figure 2. A cutoff value of 55% of peak activity maximized the predictive power for recovery of contractility. A regional sestamibi activity above this cutoff was assumed to indicate the presence of dysfunctional but viable myocardium. Sensitivity, specificity, positive and negative predictive values and accuracy for dobutamine echocardiography and sestamibi SPECT in predicting functional recovery after revascularization are reported in Figure 3. Sensitivity of sestamibi imaging was higher compared with dobutamine echocardiography (87% versus 66%, respectively; $P < 0.001$), whereas specificity was not statistically different (74% versus 89%, respectively; P = not significant). Response to dobutamine echocardiography, sestamibi uptake and functional outcome after revascularization in the 108 akinetic or dyskinetic segments at baseline are illustrated in Figure 4. Interestingly, 16 of 23 segments (70%), negative on dobutamine stimulation and viable on sestamibi SPECT, recovered at follow-up. Thirty-five (88%) of the segments without contractile reserve and nonviable on sestamibi imaging showed no functional recovery at follow-up. On multivariate analysis, sestamibi uptake was the strongest predictor of functional recovery after revascularization (Table 2). Moreover, sestamibi imaging provided significant incremental information to dobutamine echocardiographic data, improving the global chi-square of the model from 36.3 to 54.6 ($P < 0.001$).

TABLE 1
Clinical, Echocardiographic, Radionuclide Angiographic and Coronary Angiographic Data of Study Population

	Revascularized patients (n = 19)	Medically treated patients (n = 30)	P
Clinical characteristics			
Age (y)	52 ± 10	52 ± 9	NS
Male (%)	84	93	NS
Female (%)	16	7	
Thrombolysis (%)	79	77	NS
Anterior necrosis (%)	68	70	NS
Baseline echocardiography			
Akinetic or dyskinetic segments	108 (36%)	149 (31%)	NS
Radionuclide angiography			
Left ventricular ejection fraction (%)	42 ± 6	42 ± 8	NS
Coronary angiography			
TIMI grade 0 or 1	18 (95%)	14 (47%)	<0.001
Diseased vessels ≥70% stenosis	1.6 ± 0.8	0.97 ± 0.6	<0.01

TIMI = thrombolysis in myocardial infarction; NS = not significant.

Patients Undergoing Medical Treatment. In medically treated patients, 231 segments were normal, 100 hypokinetic and 149 akinetic or dyskinetic. Response to dobutamine echocardiography, sestamibi activity and functional outcome at follow-up in akinetic or dyskinetic segments are showed in Figure 5. As depicted, the large majority (94%) of segments with contractile reserve had sestamibi uptake ≥ 55% of peak activity, and 86% of them demonstrated functional recovery at follow-up. On the other hand, in segments without contractile reserve, the occurrence of spontaneous functional recovery at follow-up was poor (8%), despite the presence of sestamibi uptake ≥ 55% in 38% of them. On multivariate analysis, the presence of inotropic response to dobutamine infusion was the strongest independent predictor of spontaneous recovery at follow-up (Table 3). Also, TIMI grade 2 or 3 was an independent predictor of functional improvement (Table 3). Noteworthy, of the 60 akinetic or dyskinetic segments recovering at follow-up, 45 (75%) were supplied by coronary arteries with a TIMI grade 2 or 3.

Patient Analysis

No difference in LV ejection fraction between revascularized and medically treated patients was observed either at baseline or at follow-up. In revascularized patients, LV ejection fraction was 42% ± 6% at baseline and increased to 48% ± 7% ($P < 0.001$) after revascularization. In medically treated patients, LV ejection fraction increased from 42% ± 7% at baseline and increased to 46% ± 8% ($P < 0.001$) at follow-up. An increase in LV ejection fraction ≥5% was detectable in 14 (74%) revascularized patients and in 13 (43%) medically treated patients ($P < 0.05$). Sensitivity, specificity and accuracy of dobutamine echocardiography and sestamibi SPECT in predicting improvement of LV ejection fraction after revascularization are reported in Figure 6. Specificity was 40% for both techniques, whereas sensitivity of sestamibi imaging was higher compared with dobutamine echocardiography (100% versus 71%, respectively; $P < 0.01$). Individual characteristics of revascularized patients are reported in Table 4. All 14 patients with LV ejection fraction improvement after revascularization had preserved sestamibi uptake in two or more akinetic or dyskinetic segments. In these patients, a separate analysis

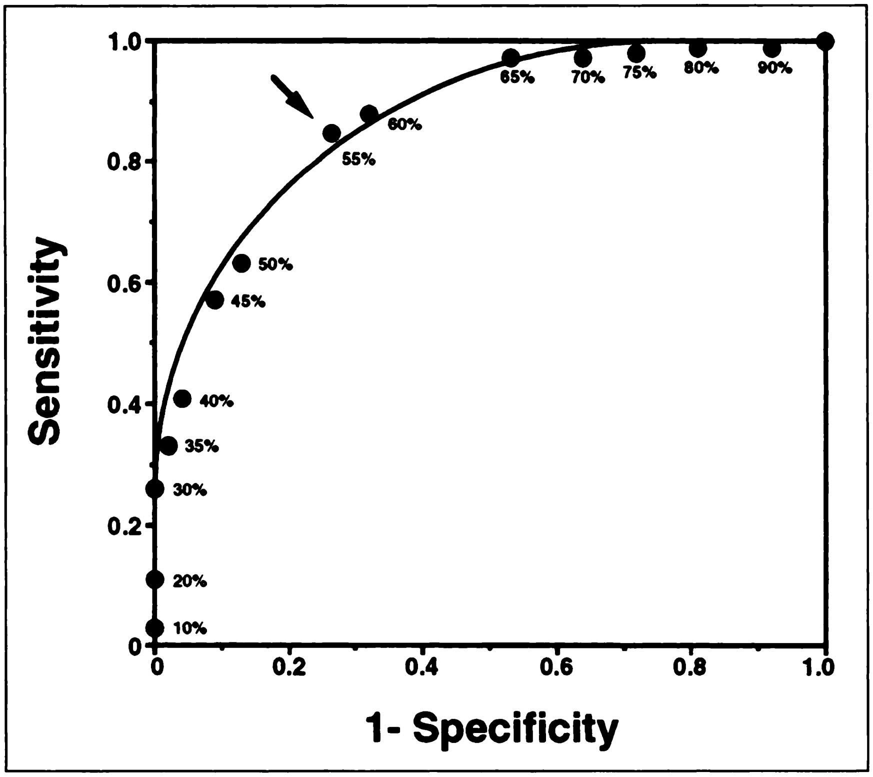

FIGURE 2. Receiver operating characteristic curve shows sensitivity-specificity pairs for different myocardial uptake of ^{99m}Tc-sestamibi for prediction of functional recovery of akinetic or dyskinetic segments in revascularized patients. Arrow indicates operating point associated with best trade-off between sensitivity (86%) and specificity (74%).

was performed to compare those without (n = 4) with those with (n = 10) inotropic response to dobutamine echocardiography. Patients without inotropic response (patients 2, 6, 8 and 13 in Table 4) had more severe stenosis of the infarct-related artery compared with those with contractile reserve at dobutamine echocardiography (97% ± 5% versus 85% ± 10%, respectively; $P < 0.05$), whereas they did not differ with respect to other clinical, baseline echocardiographic and radionuclide angiographic data. At multivariate analysis, the presence of two or more akinetic or dyskinetic segments with sestamibi uptake ≥55% was the only predictor of LV ejection fraction improvement ≥5% after revascularization ($P < 0.01$). On the other hand, the presence of inotropic response to dobutamine infusion in at least two akinetic or dyskinetic segments was the best independent predictor of spontaneous recovery of global LV function at follow-up in medically treated patients ($P < 0.01$).

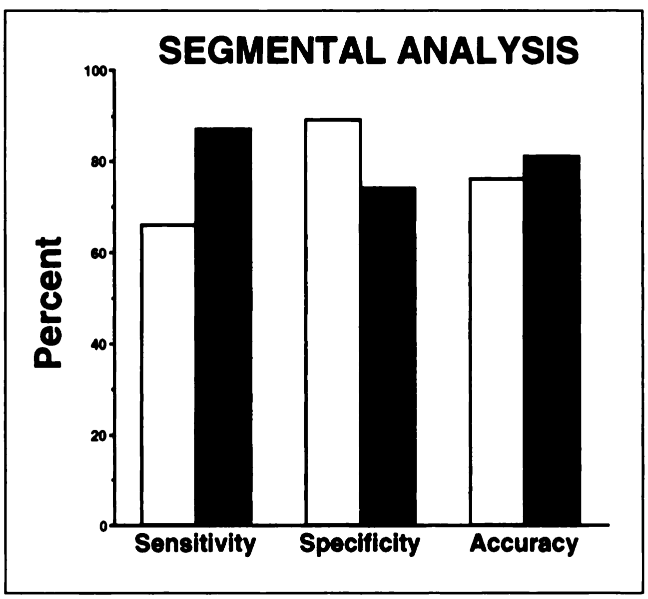

FIGURE 3. Sensitivity, specificity and accuracy of dobutamine echocardiography (white bars) and ^{99m}Tc-sestamibi imaging (black bars) in predicting functional recovery of akinetic or dyskinetic segments in revascularized patients.

DISCUSSION

The results of this study may be useful for clinical decision making in patients with LV dysfunction after AMI. One of the major findings of our study is that akinetic or dyskinetic segments without contractile reserve at dobutamine echocardiography but with preserved sestamibi uptake exhibit functional improvement after coronary revascularization but not after medical treatment. On the other hand, the large majority of dysfunctional segments with a severe reduction of sestamibi uptake did not show contractile reserve at dobutamine echocardiography and did not improve their function either after revascularization or medical treatment.

Dobutamine Echocardiography and Viable Myocardium

In experimental and clinical studies, improvement in wall motion with dobutamine stimulation has been found to be a sensitive indicator of stunned myocardium after restoration

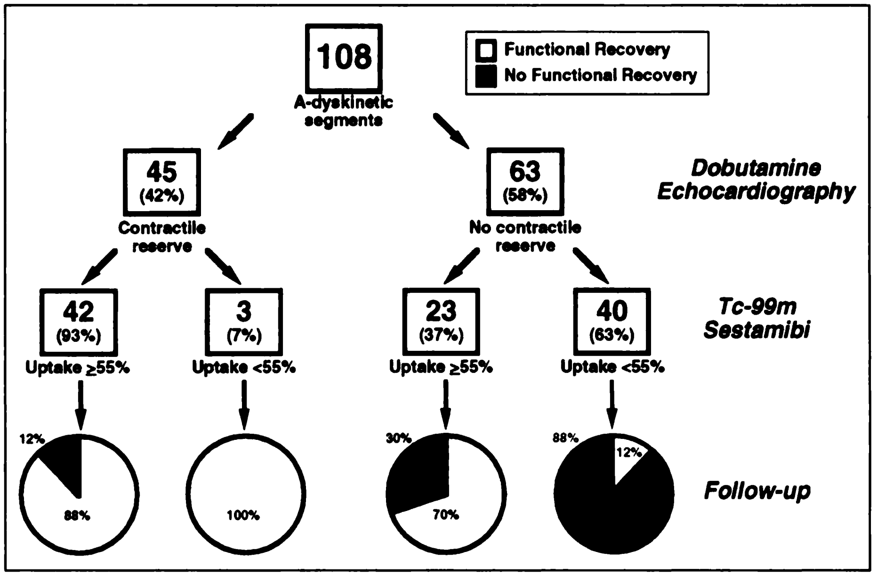

FIGURE 4. Pie charts show functional outcome of akinetic or dyskinetic segments according to dobutamine echocardiography and ^{99m}Tc-sestamibi findings in revascularized patients.

of blood flow after acute ischemic injury (*5,6*). Dobutamine echocardiography also has been used for detection of viable myocardium in patients with advanced coronary artery disease, reduced LV function and chronically dysfunctional areas (*20–22*). However, the results of recent studies suggest that this technique might not reliably detect hibernating segments (*23*). The presence of an exhausted vasodilator reserve in regions with resting hypoperfusion has been proposed to explain the poor results of dobutamine in identifying hibernating myocardium (*23,24*). Recently, Sambuceti et al. (*25*) reported that dobutamine echocardiography improved myocardial function in stunned (55%) more than in hibernating (16%) or necrotic (11%) segments in patients 4 wk after AMI. However, in that study, no follow-up data concerning functional recovery were available.

^{99m}Tc-Sestamibi Imaging and Viable Myocardium

Radionuclide imaging techniques have been used widely to detect viable myocardium in patients with coronary artery disease and LV dysfunction. Viable myocardium can be accurately identified by PET (*26*). However, the cost of the equipment and the on-site production of radiochemical tracers limit the clinical use of this technique. Myocardium viability can be also assessed by ^{201}Tl imaging or ^{99m}Tc-labeled perfusion agents (*4,27–29*). In particular, myocardial perfusion imaging at rest is increasingly used to address this issue, and considerable emphasis has been placed on the amount of tracer uptake within a dysfunctional myocardial region (*9*). Previous studies suggested that sestamibi may overestimate myocardial necrosis compared with PET (*11,12*) and thallium imaging (*30,31*). However, Maes et al. (*11*) demonstrated that quantitative analysis of sestamibi uptake reflects not only flow but also, at least in part, myocardial viability. Therefore, in our study, sestamibi activity was quantitatively assessed on tomographic imaging. Moreover, radionuclide studies were performed in patients on nitrate treatment, and nitrate administration has been reported to improve the accuracy of sestamibi imaging in detecting myocardial viability (*32*). At this time, only few data are available on the role of sestamibi in predicting functional recovery of dysfunctional segments after AMI. Galli et al. (*33*) found that several patients showed improvement of perfusion associated with improvement of contractile function in infarcted area after the first 5 wk, continuing for up to 7 mo, suggesting the presence of hibernating myocardium that may spontaneously improve after the subacute phase. However, in that study, the role of dobutamine stress test in predicting functional recovery was not assessed (*33*).

TABLE 2
Prediction of Segmental Functional Recovery in Revascularized Patients by Multivariate Analysis

Variable	Chi-square	Odds ratio	95% CI	P
Sestamibi uptake ≥ 55%	44.40	9.16	3.1–27.1	<0.001
Contractile reserve on dobutamine	9.41	6.10	1.8–20.1	<0.005

CI = confidence interval.

Functional Recovery After Coronary Revascularization

In our study, in patients undergoing coronary revascularization procedures, the presence of contractile reserve was associated with functional recovery at follow-up. However, the lack of contractile reserve did not preclude the possibility of functional recovery when sestamibi uptake was preserved. In fact, the majority (70%) of segments without inotropic reserve but viable at sestamibi imaging recovered contractility after revascularization. Noteworthy, the presence of preserved sestamibi uptake was the strongest predictor of functional improvement on multivariate analysis. Moreover, the presence of two or more akinetic or

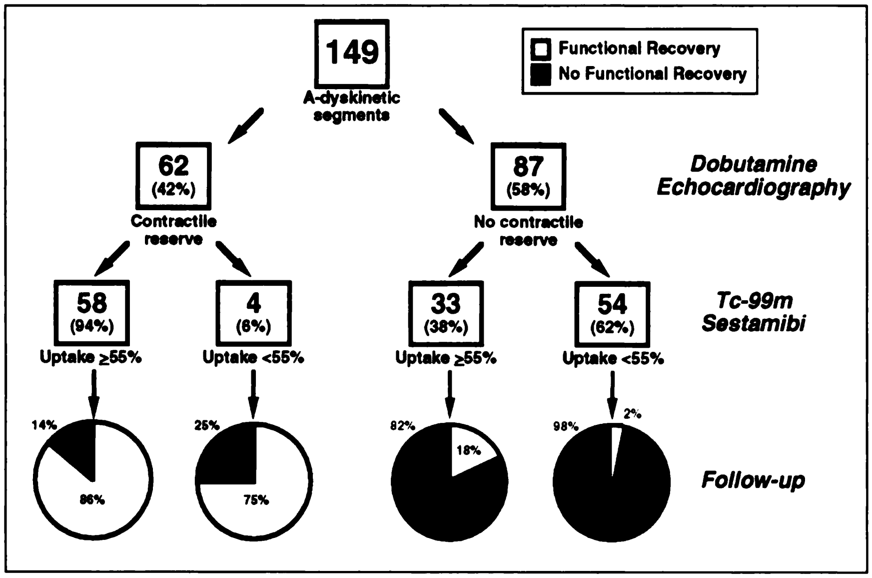

FIGURE 5. Pie charts show functional outcome in akinetic or dyskinetic segments according to dobutamine echocardiography and ^{99m}Tc-sestamibi findings in medically treated patients.

dyskinetic segments with evidence of myocardial viability at sestamibi imaging correctly identified all patients with LV ejection fraction improvement ≥5% after revascularization. On the contrary, dobutamine echocardiography showed a lower sensitivity in predicting improvement of global LV function in such patients. In fact, of 14 patients with functional recovery after revascularization, 4 showed no inotropic response to dobutamine. These latter patients had more severe stenosis of the infarct-related artery compared with those with contractile reserve at dobutamine echocardiography. These findings are in agreement with the concept that, in AMI patients, the response of the postischemic myocardium to dobutamine is influenced by the severity of stenosis of the infarct-related artery (*16*).

Functional Recovery in Medically Treated Patients

A spontaneous recovery in systolic performance of regional LV dysfunction in AMI patients treated with thrombolysis is a well-known phenomenon (*34,35*). In this study, this spontaneous recovery led to an improvement of LV ejection fraction in medically treated patients. Low-dose dobutamine echocardiography accurately predicted the spontaneous recovery of myocardial contractility after infarction.

In fact, the majority (85%) of the akinetic or dyskinetic segments with inotropic reserve at dobutamine echocardiography showed functional recovery at follow-up. On the other hand, most of the segments without inotropic reserve at dobutamine echocardiography did not improve at follow-up, despite the presence of sestamibi uptake ≥ 55% in 38% of them. It should be considered that, as previously described, in patients undergoing revascularization the majority of such segments showed functional recovery at follow-up. Therefore, these segments may represent hibernating myocardium rather than irreversibly necrotic tissue and

TABLE 3
Prediction of Segmental Functional Recovery in Medically Treated Patients by Multivariate Analysis

Variable	Chi-square	Odds ratio	95% CI	*P*
Contractile reserve on dobutamine	100.8	34.01	10.4–97.7	<0.001
TIMI grade 2 or 3	11.65	6.04	1.8–19.4	<0.005
Sestamibi uptake ≥ 55%	4.76	4.78	1.1–20.4	<0.05

CI = confidence interval; TIMI = thrombolysis in myocardial infarction.

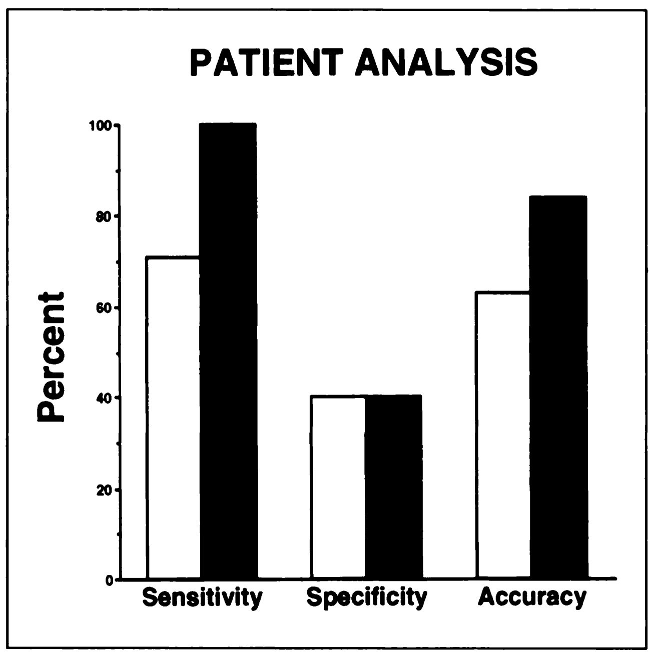

FIGURE 6. Sensitivity, specificity and accuracy of dobutamine echocardiography (white bars) and ^{99m}Tc-sestamibi (black bars) in predicting recovery of global LV ejection fraction in revascularized patients.

TABLE 4
Individual Characteristics of 19 Revascularized Patients

Patient no.	Sex	Site of MI	Akinetic/dyskinetic segments (n)	Diseased vessels (n)	IRA (% of stenosis)	LVEF (%) Baseline	LVEF (%) follow-up	LDDE	Sestamibi imaging
1	M	Anterior	3	1	LAD (80)	40	50	+	+
2	M	Inferior	3	1	RCA (99)	45	55	−	+
3	M	Anterior	8	1	LAD (85)	38	40	+	+
4	M	Anterior	4	1	LAD (80)	48	55	+	+
5	M	Inferior	3	3	RCA (90)	40	42	−	−
6	M	Anterior	7	1	LAD (100)	40	47	−	+
7	M	Inferior	3	1	RCA (75)	45	58	+	+
8	M	Inferior	3	1	RCA (90)	48	53	−	+
9	M	Anterior	9	1	LAD (100)	30	38	+	+
10	F	Inferior	3	1	RCA (90)	52	55	+	+
11	F	Anterior	8	2	LAD (90)	42	48	+	+
12	M	Anterior	9	2	LAD (100)	38	42	+	−
13	M	Anterior	8	3	LAD (100)	33	38	−	+
14	M	Anterior	3	1	LAD (80)	50	55	+	+
15	M	Anterior	7	1	LAD (75)	43	48	+	+
16	M	Anterior	8	3	LAD (100)	35	48	+	+
17	M	Anterior	8	2	LAD (80)	48	55	+	+
18	M	Anterior	7	3	LAD (100)	38	40	−	+
19	F	Inferior	4	1	RCA (95)	37	42	+	+

MI = myocardial infarction; IRA = infarct-related coronary artery; LVEF = left ventricular ejection fraction; LDDE = low-dose dobutamine echocardiography; LAD = left anterior descending coronary artery; RCA = right coronary artery; + indicates presence of inotropic response to LDDE or evidence of viability on sestamibi imaging in more than two akinetic or dyskinetic segments, respectively; − indicates absence of inotropic response or viability in two or more akinetic or dyskinetic segments, respectively.

might exhibit functional recovery after revascularization procedures.

Myocardial Infarction, Hibernation and Stunning

It has been shown that when infarction involves less than 20% of the wall thickness, hypokinesia is noted; on the other hand, when it involves more than 20% of the wall thickness, akinesia or dyskinesia is seen (*36*). Consequently, a reduction in thickening (hypokinesia) indicates that most of the myocardium has escaped necrosis and is hence viable (*16*). Therefore, for the purpose of this study, we focused on akinetic or dyskinetic segments in which the assessment of myocardial viability is clinically relevant (*16*). According to our results, in patients who did not undergo coronary revascularization, many akinetic or dyskinetic segments recovered contractile function spontaneously during follow-up. Interestingly, the large majority of these segments showed contractile reserve at dobutamine echocardiography, had preserved sestamibi activity and were supplied by coronary artery with TIMI grade 2 or 3. Therefore, stunning seems the mechanism underlying the impairment of myocardial contractility in these segments. The high prevalence of myocardial stunning in our patient population may be explained by the early postinfarction phase of the study and by the high percentage of patients treated with systemic thrombolysis.

Myocardial hibernation seems responsible for the dysfunction of the akinetic or dyskinetic segments without contractile reserve at dobutamine echocardiography and viable at sestamibi imaging that did not spontaneously improve at follow-up. In fact, as commonly described for hibernation, a severe impairment of coronary blood flow (TIMI grade 0 or 1) was detectable in most (78%) of these segments. The favorable outcome in 70% of akinetic or dyskinetic segments without contractile reserve and viable at sestamibi SPECT observed in revascularized patients supports the hypothesis of hibernation. It is well-known that hibernating myocardium improves function early after revascularization (*37,38*), while it remains dysfunctional or worsens on medical therapy (*3,39*). These data confirm the accuracy of sestamibi uptake in distinguishing viable myocardium from necrotic tissue and demonstrate that, in hypoperfused but still viable myocardium, the assessment of contractile reserve by inotropic stimulation may underestimate the possibility of functional improvement after revascularization. This phenomenon, already reported in patients with chronic LV dysfunction (*40*), might be related to inadequate interpretation of regional contractility. Alternatively, it might indicate that cellular processes responsible for preserved myocardial contractility require a higher degree of myocyte functional integrity than that required for sestamibi uptake (*25,40*).

The presence of necrotic myocardial tissue seems responsible for LV dysfunction in akinetic or dyskinetic segments without contractile reserve and sestamibi uptake < 55%. As expected, most of these segments did not improve spontane-

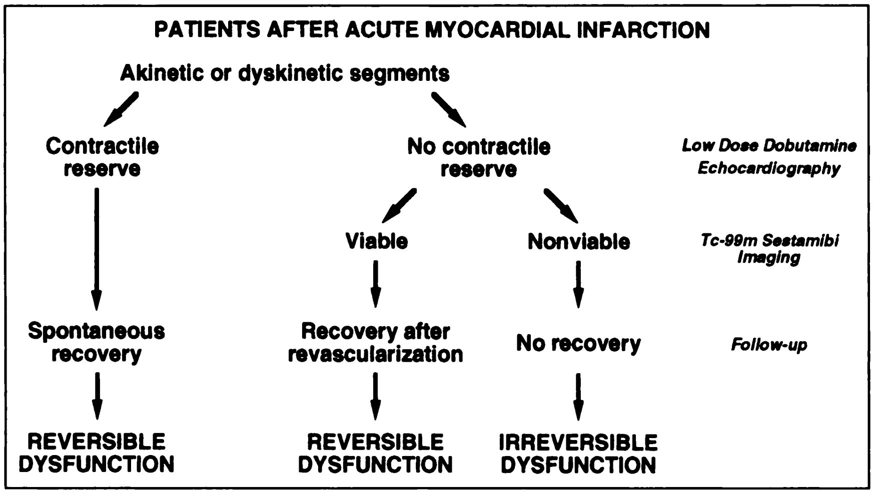

FIGURE 7. Flow diagram proposed to efficiently use low-dose dobutamine echocardiography and sestamibi imaging in patients after AMI to predict recovery of akinetic or dyskinetic segments after medical treatment or coronary revascularization.

ously or after revascularization. It should be considered that the cutoff point ≥55% for myocardial viability was chosen as the best trade-off between sensitivity and specificity. Therefore, the 5 segments without inotropic response to dobutamine and sestamibi uptake < 55% that recovered after revascularization also represent hibernating myocardium rather than necrotic tissue.

Study Limitations

Although extreme care was taken to optimize the proper matching of myocardial segments, the possibility of anatomic misalignment is an intrinsic limitation of studies that attempt to compare different imaging modalities. Patients were not assigned randomly to coronary revascularization or medical therapy. However, it should be considered that the decision was made by treating physicians unaware of the results of dobutamine echocardiography and sestamibi imaging. Furthermore, patients did not undergo coronary angiography at follow-up, therefore, restenosis or graft occlusion in revascularized patients or a progression of coronary impairment cannot be completely excluded. However, all patients were carefully followed-up until the final study, and there was no clinical evidence or electrocardiogram stress test results suggesting recurrent ischemia.

CONCLUSION

The results of this study may be helpful to efficiently use dobutamine echocardiography and myocardial perfusion imaging in patients with LV dysfunction recovering from AMI. As shown in Figure 7, sestamibi imaging seems unnecessary in patients with contractile reserve at dobutamine echocardiography. In fact, the majority of the akinetic or dyskinetic segments with inotropic response to dobutamine exhibit spontaneous functional recovery at follow-up. On the other hand, sestamibi imaging provides important information to identify dysfunctional segments without contractile reserve that will recover contractility after coronary revascularization.

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