Sequential ^{201}Tl Imaging and Dobutamine Echocardiography to Enhance Accuracy of Predicting Improved Left Ventricular Ejection Fraction After Revascularization

Jeroen J. Bax, MD[1]; Jamshid Maddahi, MD[2]; Don Poldermans, MD[3]; Abdou Elhendy, MD[3]; Jan H. Cornel, MD[3]; Eric Boersma, PhD[4]; Jos R.T.C. Roelandt, MD[3]; and Paolo M. Fioretti, MD[3]

[1]Department of Cardiology, University Hospital Leiden, Leiden, The Netherlands; [2]Department of Molecular and Medical Pharmacology (Nuclear Medicine) and Radiological Sciences, UCLA School of Medicine, Los Angeles, California; [3]Department of Cardiology, ThoraxCenter Rotterdam, Rotterdam, The Netherlands; and [4]Department of Clinical Epidemiology/Statistics, ThoraxCenter Rotterdam, Rotterdam, The Netherlands

^{201}Tl imaging and dobutamine echocardiography (DE) can both identify viable myocardium. Prediction of functional outcome after revascularization remains suboptimal with either technique because of the relatively low specificity of ^{201}Tl and low sensitivity of DE. This study was undertaken to develop an optimal testing strategy for prediction of postrevascularization functional outcome. **Methods:** Seventy-three patients (mean [±SD] left ventricular ejection fraction [LVEF], 32% ± 8%) underwent DE and resting ^{201}Tl SPECT (4-h delayed imaging) before surgical revascularization. Dysfunctional segments with ^{201}Tl activity ≥ 50% or with contractile reserve were considered viable. LVEF was assessed before and 3–6 mo after revascularization. **Results:** Analysis of receiver operator characteristic curves showed that the optimum criteria to predict improvement (≥5%) in LVEF after revascularization were ≥6 viable dysfunctional segments (using a 16-segment model) on ^{201}Tl and ≥4 segments on DE. Sensitivity and specificity were 84% and 63% for ^{201}Tl ($P < 0.05$ vs. DE) and 63% and 85% for DE ($P < 0.05$ vs. ^{201}Tl). Changing the ^{201}Tl criteria to improve specificity to 78% (≥8 segments) yielded a low sensitivity of 44%, and changing the DE criteria to improve sensitivity to 84% (≥2 segments) lowered specificity to 56%. Two sequential testing strategies were explored to achieve optimal sensitivity and specificity. In strategy 1, 33 (45%) of 73 patients with an intermediate likelihood of viability by ^{201}Tl (5–8 viable segments) underwent DE. In strategy 2, 31 (42%) of 73 patients with an intermediate likelihood of viability by DE (2–4 viable segments) underwent ^{201}Tl. For strategy 1, sensitivity did not change significantly (69%), whereas specificity was improved significantly (93%, $P < 0.01$ vs. ^{201}Tl). For strategy 2, sensitivity improved significantly (78%, $P < 0.05$ vs. DE) and specificity remained unchanged (80%). **Conclusion:** Sequential testing by ^{201}Tl SPECT and DE in a subgroup of patients with an intermediate likelihood of viability by either test significantly enhanced prediction of postrevascularization improvement of LVEF.

Key Words: ^{201}Tl imaging; dobutamine echocardiography; myocardial viability

Gheorghiade and Bonow (*1*) reported in 1998 that an estimated 4.7 million patients in the United States had chronic heart failure, with 6-y mortality rates between 65% and 80%. The incidence of coronary artery disease in these patients may be as high as 70% (*2*). Therapeutic options for these patients include medical therapy, heart transplantation, and revascularization. Viability assessment may help to guide patient treatment; only in patients with substantial viability can revascularization be considered, because improvement of function and survival may be anticipated in these patients only (*3*). Several techniques have been developed, including ^{18}F-FDG PET (*4*), SPECT with ^{201}Tl (*5,6*) or ^{99m}Tc-labeled tracers (*7*), and dobutamine echocardiography (DE) (*8*). For routine clinical use, ^{201}Tl (using either a rest-redistribution or a reinjection protocol) (*5,6*) and DE (*8*) may be the preferred techniques. However, studies have shown that both techniques may provide suboptimal information concerning identification of viable tissue and prediction of functional outcome after revascularization (*9–11*). ^{201}Tl imaging has an excellent sensitivity but a somewhat lower specificity (*9–11*). Conversely, DE has a high specificity but a relatively lower sensitivity (*9–11*). The likelihood of improvement in left ventricular (LV) function after revascularization relates to the extent of (number of segments with) viability. We hypothesized that in patients with an intermediate likelihood of LV function improvement, as predicted by either test, sequential testing by the second modality may further classify the patient as

having a high or low likelihood of viability. Hence, sequential performance of these tests may result in optimal diagnostic accuracy in patients with an intermediate likelihood of viability. Accordingly, this study was undertaken to develop an optimal testing strategy for prediction of functional outcome after revascularization using ^{201}Tl and DE. All patients presented with depressed LV function, and most had heart failure as the predominant symptom.

MATERIALS AND METHODS

Patients and Study Protocol

Patients were eligible for the study if they had stable, chronic coronary artery disease; had depressed LV function on LV ventriculography; were already scheduled for surgical revascularization (coronary artery bypass grafting); had no significant valvular disease (patients with 3–4+ (moderate to severe) mitral insufficiency were excluded); and had an acoustic window adequate for echocardiographic evaluation (6 patients were excluded because of a suboptimal window).

Within 1 mo before revascularization, radionuclide ventriculography, resting echocardiography, ^{201}Tl imaging, and DE were performed. [201]Tl imaging and DE were performed within 1 wk. β-blockers were withdrawn 36 h before DE; all other cardiac medication was continued during both tests. Three to 6 mo after the revascularization, resting echocardiography and radionuclide ventriculography were repeated. Eighteen patients had been included in previous studies (12). The protocol was approved by the local Medical Ethics Committee, and each patient gave informed consent before inclusion in the study.

Assessment of Baseline Dysfunction and Functional Outcome

Regional LV Function. Regional function was assessed by resting echocardiography before and 3–6 mo after revascularization. A 16-segment model, according to the American Society of Echocardiography (13), was used for the analysis. The LV was divided into 4 apical, 6 distal (anterior, anterolateral, inferolateral, inferior, inferoseptal, and anteroseptal), and 6 basal segments. The segments were classified as normokinetic, mildly hypokinetic, severely hypokinetic, akinetic, or dyskinetic. Previously reported inter- and intraobserver agreements for assessing resting wall motion were 84% and 87%, respectively (14).

Global LV Function. LV ejection fraction (LVEF) (before and 3–6 mo after revascularization) was assessed by radionuclide ventriculography, performed at rest with the patient supine after administration of 740 MBq [99m]Tc. Images were acquired with a small-field-of-view gamma camera (Orbiter; Siemens Corp., Iselin, NJ), oriented in the 45° left anterior oblique position with a 5°–10° caudal tilt. The LVEF was calculated from the 45° left anterior oblique view by an automated technique. Improvement of global function after revascularization was defined as an LVEF increase ≥ 5% (15–17). Thus, the gold standard for viability on a patient basis was considered to be ≥5% improvement of LVEF after revascularization.

[201]Tl Imaging

[201]Tl SPECT was performed as described previously (9–11,18). In short, 111 MBq ^{201}Tl-chloride were injected at rest, and 4-h delayed images were obtained. SPECT was performed on a single-head Orbiter camera. Thirty-two projections were obtained in a

180° orbit extending from the 40° left posterior oblique projection to the right anterior oblique projection, with an acquisition time of 60 s per projection. An energy window of 20% was centered on the 68- to 80-keV peak. Images were stored on a 64 × 64, 16-bit matrix. A Gamma-11 computer system (Compaq Computer Corp., Houston, TX) was used to process the tomographic data. Long- and short-axis tomograms were reconstructed from the 3-dimensional voxel matrix. Circumferential count profiles (60 radii, highest pixel activity per radius) from the ^{201}Tl short-axis slices were generated and displayed in a polar map format. The polar maps were divided into 16 segments, aligning the 16 echocardiographic segments, so that the polar map data could be compared with the echocardiographic data. The polar maps were normalized for peak activity (100%), and segmental activities were expressed as percentage of the maximum. For the classification of viable and nonviable tissue in dysfunctional segments (determined by resting echocardiography), the normalized activity of the 4-h delayed images was used (9–11,18). Segments were considered viable when the activity was ≥50% and nonviable when the activity was <50% (9–11,18). The criteria for viability on a patient basis (how many dysfunctional but viable segments were needed to classify a patient as having viable myocardium) were determined by receiver operating characteristic (ROC) curve analysis.

DE

DE (low-dose protocol) was performed as described previously (14). First a 2-dimensional transthoracic echocardiogram in the standard apical and parasternal views and a 12-lead electrocardiogram were recorded at rest. Dobutamine was infused through an antecubital vein at dosages of 5 and 10 μg/kg/min for 5 min at each dose. Continuous monitoring of the echocardiogram was obtained during the test and recorded on videotape at the last minute of both stages. The echocardiographic images were also digitized on an optical disk (CFM 800; Vingmed, Horten, Norway) or on a floppy disk (SIM 7000; Esaote Biomedica, Munich, Germany) and displayed side by side in a cine-loop format to facilitate the comparison of the rest and dobutamine images. A 3-lead electrocardiogram was continuously monitored, and a 12-lead electrocardiogram was recorded every minute. Blood pressure was measured by sphygmomanometry at each stage. Two experienced observers (in cases of disagreement, 3 observers) who were unaware of the clinical data, ^{201}Tl results, and outcome data interpreted the echocardiograms. The DE studies were analyzed using the digitized rest and low-dose (5 and 10 μg/kg/min) dobutamine images, displayed in a cine-loop format, and also by reviewing the images recorded on the videotape. Myocardium was judged to be viable when dysfunctional segments improved during dobutamine stimulation (improvement from dyskinesia to akinesia was not considered to indicate viability). Dysfunctional segments without improvement were considered nonviable. Inter- and intraobserver agreements of 92% and 94% for the analysis of DE studies were reported previously (14). The criteria for viability on a patient basis (how many dysfunctional but viable segments were needed to classify myocardium as viable) were determined by ROC curve analysis.

Statistical Analysis

Continuous data were expressed as mean ± SD and compared using the Student *t* test for paired and unpaired data when appropriate. Univariate analysis for categoric variables was performed using the χ^2 test with Yates correction. The optimal number of viable segments on ^{201}Tl or DE (discriminating between patients

with and without improvement of LVEF after revascularization) was determined by ROC curve analysis. The optimal cutoff value (number of segments) was defined as that providing the maximal sum of sensitivity and specificity. Sensitivity and specificity were based on their standard definitions. Differences between sensitivities and specificities (of the different modalities or sequential approaches) were determined by McNemar testing. For all tests, a probability value < 0.05 was considered significant.

RESULTS

Study Population

Seventy-three patients (68 men, 5 women; age range, 45–80 y; mean age, 61 y) with coronary artery disease and depressed LV function (mean LVEF, 32% ± 8%) who were scheduled for surgical revascularization were enrolled in the study. The reasons for revascularization were heart failure in 56 patients and angina pectoris in 17. Seventy-one patients (97%) had a previous infarction (>1 mo before entrance into the study), and 58 exhibited pathologic Q waves on the electrocardiogram. All patients had significant coronary artery disease on angiography (>50% reduction in luminal diameter of at least 1 major epicardial coronary artery). They had an average of 2.5 ± 0.7 stenosed vessels. All patients were stable during the study; none had unstable angina or myocardial infarction between revascularization and scintigraphy or after the intervention.

Baseline Function Versus Functional Outcome

A total of 1,168 segments were analyzed (in 73 patients), with 571 (49%) showing abnormal wall motion. Baseline dysfunction included dyskinesia in 20 segments (4%), akinesia in 264 (46%), severe hypokinesia in 106 (19%), and mild hypokinesia in 181 (32%). Wall motion improved in 201 segments (35%), including 67 that were mildly hypokinetic, 51 that were severely hypokinetic, and 83 that were akinetic or dyskinetic. Baseline LVEF ranged from 13% to 48%. In the entire group, LVEF improved modestly but significantly (32% ± 8% vs. 36% ± 10%, $P < 0.05$). The LVEFs before and after revascularization of the individual patients are shown in Figure 1. Thirty-two patients (44%) improved ≥5% in LVEF after the revascularization (from 31% ± 8% to 41% ± 9%). In 41 patients, LVEF did not improve ≥5% (33% ± 8% vs. 33% ± 8%). The characteristics of the patients with and without improvement are shown in Table 1; no significant differences were observed between the 2 groups, only the number of viable segments on ^{201}Tl and DE was significantly higher in the patients with improved LVEF than in the patients without LVEF. Of interest, significantly more dysfunctional segments were classified as viable by ^{201}Tl than by DE, both in the entire population (6.2 ± 3.6 vs. 2.9 ± 2.7, $P < 0.01$) and in the subgroups with and without improvement of LVEF (Table 1).

[201]Tl Imaging

ROC curve analysis showed that a cutoff value of 6 dysfunctional but viable segments yielded the highest sensitivity and specificity (Fig. 2; area under the curve, 0.76); 27 of 32 patients with an improvement of LVEF after the revascularization had at least 6 viable segments, and 26 of 41 patients with fewer than 6 viable segments did not improve. Using this cutoff level, ^{201}Tl had a sensitivity of 84% and a specificity of 63%. When specificity was improved to 78% (by shifting the optimal cutoff value to at least 8 viable segments), the sensitivity declined to 44%.

An intermediate likelihood of viability was defined as 5–8 dysfunctional but viable segments on ^{201}Tl; this range was determined on the basis of the ROC curve (Fig. 2). Twenty-six patients (36%) had 4 or fewer viable segments on ^{201}Tl and were classified as low likelihood; only 4 patients (15%) showed improvement of LVEF. Fourteen
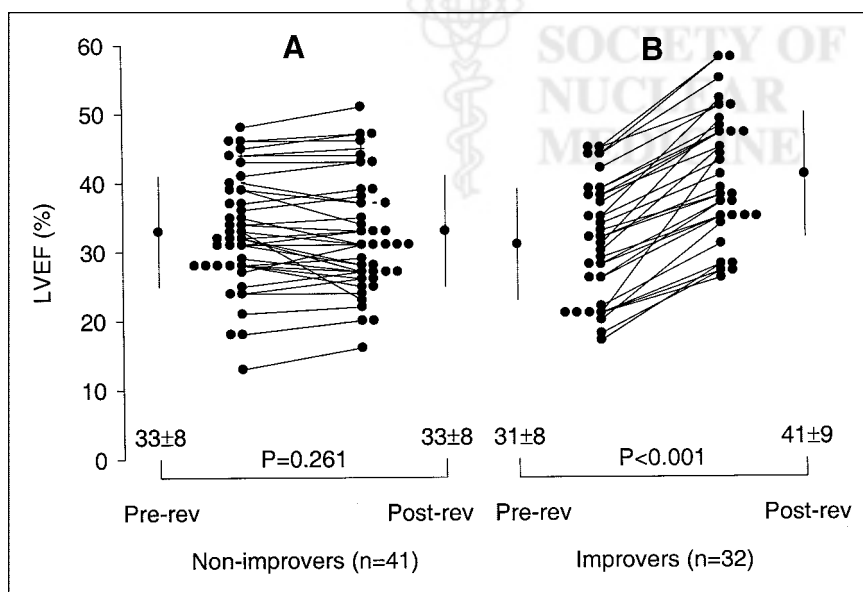

FIGURE 1. Individual LVEFs before and after revascularization (rev) in patients without ≥5% improvement of LVEF (A) and with ≥5% improvement of LVEF (B).

TABLE 1
Clinical Data Before Revascularization, Grouped by LVEF Status After Revascularization

Parameter	Patients with improvement ($n = 32$)	Patients without improvement ($n = 41$)	P
Age (y)	62 ± 9	61 ± 9	NS
Sex (M/F)	3/29	4/37	NS
Q wave myocardial infarction	27 (84%)	31 (76%)	NS
Reason for revascularization (AP/HF)	6/26	11/30	NS
AP (CCS)	3.0 ± 0	3.2 ± 0.4	NS
HF (NYHA)	3.0 ± 0.5	3.2 ± 0.4	NS
Vessel disease	2.4 ± 0.8	2.6 ± 0.7	NS
LVEF	31 ± 8	33 ± 8	NS
No. of viable segments on ^{201}Tl	$8.2 \pm 3.7^*$	$4.7 \pm 2.7^*$	<0.01
No. of viable segments on DE	4.5 ± 3.0	1.6 ± 1.5	<0.01

$^*P < 0.01$ vs. DE.

AP = angina pectoris; HF = heart failure; CCS = Canadian Cardiovascular Society; NYHA = New York Heart Association functional class.

(19%) of the patients had at least 9 viable segments and were classified as high likelihood, with LVEF improving in 10 patients (71%). The remaining 33 patients had 5–8 viable segments, with LVEF improving in 17; these were classified as intermediate likelihood and were referred for DE.
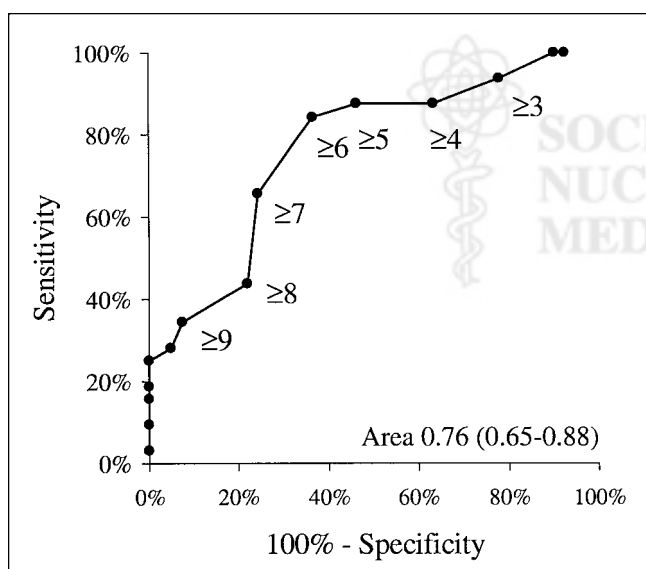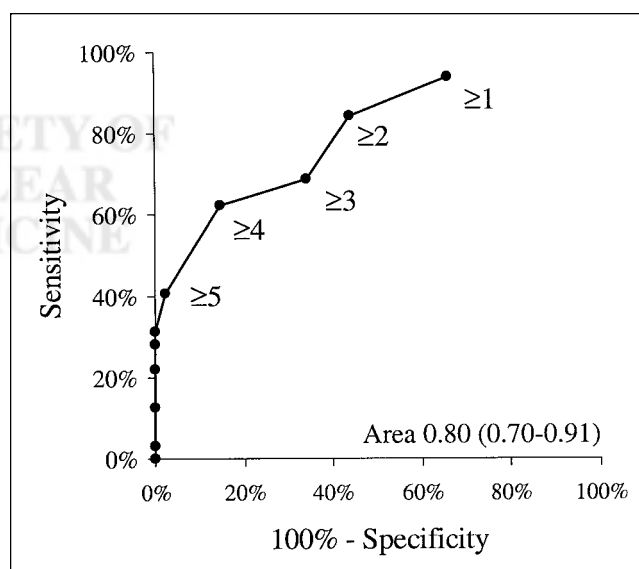
DE

ROC curve analysis showed that a cutoff value of 4 dysfunctional but viable segments yielded the highest sensitivity and specificity (Fig. 3; area under the curve, 0.80); 20 of 31 patients with an improved LVEF after revascularization had at least 4 viable segments, and 35 of 41 patients with fewer than 4 viable segments did not improve. Using this cutoff level, DE had a sensitivity of 63% ($P < 0.05$ vs. ^{201}Tl) and a specificity of 85% ($P < 0.05$ vs. ^{201}Tl). When sensitivity was improved to 84% (by shifting the optimal cutoff value to at least 2 viable segments), the specificity was lowered to 56%.

An intermediate likelihood of viability was defined as 2–4 dysfunctional but viable segments on DE; this range was based on the ROC curve (Fig. 3). Twenty-eight patients (38%) had fewer than 2 viable segments on DE and were classified as low likelihood; only 5 patients (18%) had improved LVEF. Fourteen (19%) of the patients had at least 5 viable segments and were classified as high likelihood, with 13 patients (93%) showing improved LVEF. The remaining 31 patients had 2–4 viable segments, with LVEF improving in 14; these were classified as intermediate likelihood and were referred for ^{201}Tl.

Sequential Testing, Strategy 1

For strategy 1, ^{201}Tl was performed as the initial test and DE was performed as an additional test on the patients with an intermediate likelihood of viability on ^{201}Tl. Hence, in 33 (45%) of 73 patients, an additional test was needed to further assess the likelihood of improvement in LVEF (Fig. 4).

Twenty-two (67%) of these patients had fewer than 4 viable segments on DE and were subsequently classified as

FIGURE 2. ROC curve analysis of ^{201}Tl data shows that cutoff value of 6 dysfunctional but viable segments yielded highest sensitivity and specificity for predicting improved LVEF after revascularization.

FIGURE 3. ROC curve analysis of dobutamine echocardiographic data shows that cutoff value of 4 dysfunctional but viable segments yielded highest sensitivity and specificity for predicting improved LVEF after revascularization.
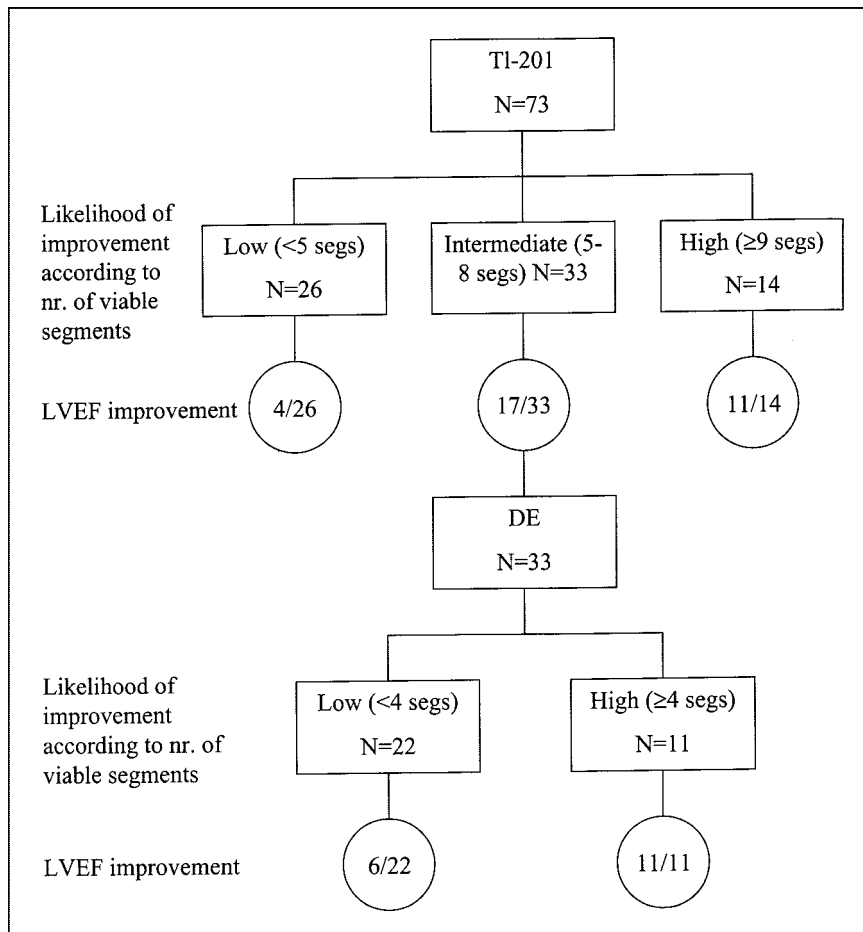
FIGURE 4. Flow chart of characterization (and outcome) of patients according to strategy 1 (²⁰¹Tl was performed as initial test, and DE was performed as additional test on patients with intermediate likelihood of viability on ²⁰¹Tl). nr. = number; segs = segments.

low likelihood; LVEF improved in 6 (27%) of them. The remaining 11 patients had at least 4 viable segments on DE and were classified as high likelihood; all (100%) exhibited improved LVEF after revascularization (Fig. 4).

Thus, sequential testing correctly identified 22 of 32 patients with improvement of LVEF and 38 of 41 patients without improvement of LVEF, resulting in a sensitivity of 69% and a specificity of 93% (Fig. 5). Sequential testing according to strategy 1 improved specificity significantly compared with ²⁰¹Tl alone ($P < 0.05$, Fig. 5). Moreover, the specificity of strategy 1 was not significantly different from that of DE alone or of strategy 2 (Fig. 5). Finally, the sensitivity of strategy 1 was not significantly different from that of ²⁰¹Tl alone ($P = 0.07$) or of strategy 2 (Fig. 5).

Sequential Testing, Strategy 2

For strategy 2, DE was performed as the initial test and ²⁰¹Tl was performed as an additional test on the patients with an intermediate likelihood of viability on DE. Hence, in 31 (42%) of 73 patients, an additional test was needed to further assess the likelihood of improvement in LVEF (Fig. 6). Twelve (39%) of these patients had fewer than 6 viable segments on ²⁰¹Tl and were subsequently classified as low likelihood; LVEF improved in 2 (17%) of them. The remaining 19 patients had at least 6 viable segments on ²⁰¹Tl

and were classified as high likelihood; 12 (63%) exhibited improved LVEF after revascularization (Fig. 6).

Thus, sequential testing correctly identified 25 of 32 patients with improvement of LVEF and 33 of 41 patients without improvement of LVEF, resulting in a sensitivity of 78% and a specificity of 80% (Fig. 5). Sequential testing according to strategy 2 improved sensitivity compared with DE alone ($P < 0.05$, Fig. 5). Moreover, the sensitivity of strategy 2 was not significantly different from that of ²⁰¹Tl alone or of strategy 1 (Fig. 5). Finally, the specificity of strategy 2 was not significantly different from that of DE alone or of strategy 1 (Fig. 5).

DISCUSSION

With the increasing number of patients presenting with heart failure (secondary to ischemic heart disease), assessment of myocardial viability has become more relevant for routine patient management (*1–3,6,8*). Many noninvasive tests have been developed for this purpose over the past 10–15 y (*3,6,8*). For clinical routine, ²⁰¹Tl imaging and DE are used most frequently (*5,6,8*). However, both tests have proven suboptimal for the preoperative prediction of functional improvement (*9–11*). In the current study, we explored whether sequential use of these techniques (in a
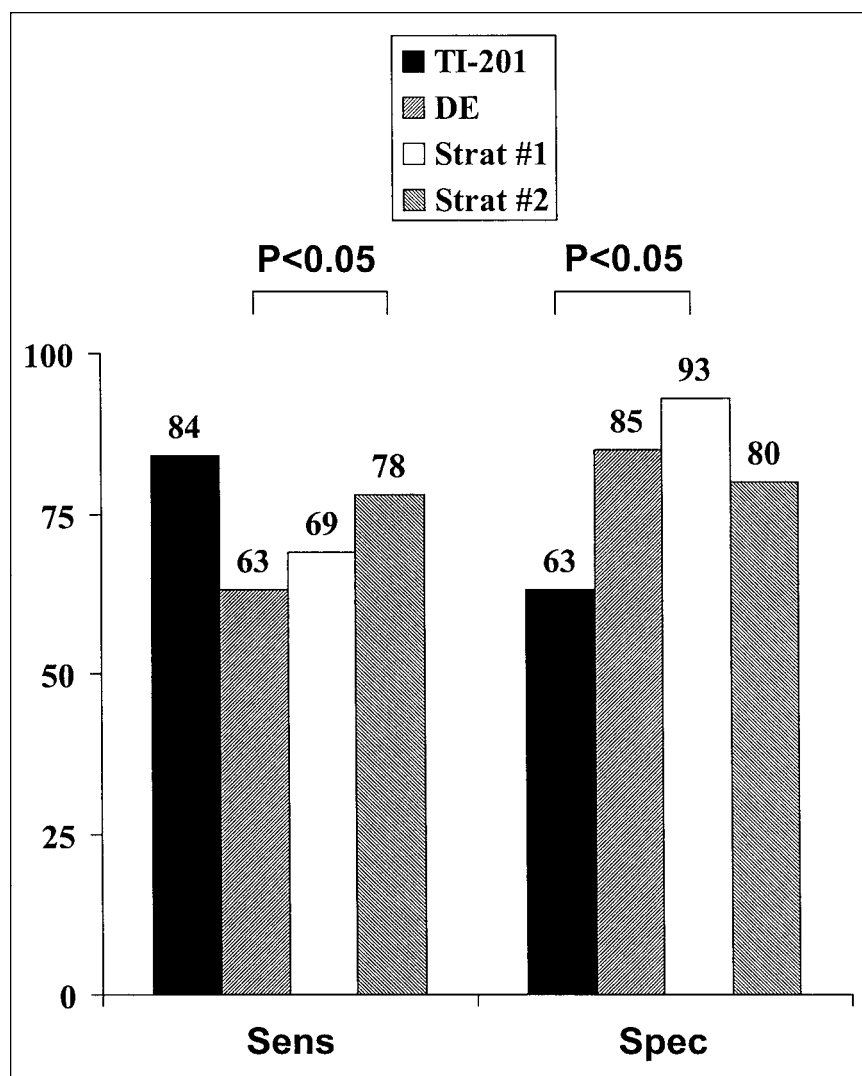
FIGURE 5. Bar graph shows sensitivities and specificities of ^{201}Tl, DE, and sequential strategies (strategy 1: ^{201}Tl was initial test, and DE was additional test; strategy 2: DE was initial test, and ^{201}Tl was additional test) for predicting improved LVEF after revascularization. Sens = sensitivity; spec = specificity; strat = strategy.

subset of patients with an intermediate likelihood of viability) enhanced the accuracy of predicting improved function.

The hallmark of viability for ^{201}Tl SPECT is tracer retention on 4-h delayed images (5,6). Segments were classified as viable when the ^{201}Tl activity was ≥50% (normalized to maximum tracer uptake), as was used in most of the ^{201}Tl studies (9–11,18). Because the amount of viable tissue needed to predict improvement of LVEF after revascularization is unknown, ROC curve analysis was used to identify the number of viable segments best discriminating between patients with and without recovery of LVEF.

The optimal cutoff value was determined to be 6 dysfunctional segments containing ≥50% activity. Hence, at least 38% of the LV (6/16 segments) had to be viable on 4-h delayed ^{201}Tl images to result in improvement of LVEF. At this cutoff level, a sensitivity of 84% was obtained at the cost of a somewhat lower specificity (63%), in line with the literature (9–11).

Identification of tissue viability with DE is based on demonstration of contractile reserve during infusion of do-

butamine (8). A shortcoming of the technique is that a substantial percentage of the patients may have a suboptimal acoustic window. Dysfunctional segments were classified as viable when wall motion improved during the infusion of low-dose dobutamine. Myocardium was classified as viable using ROC curve analysis; the best trade-off between sensitivity and specificity was found at a cutoff level of 4 dysfunctional segments showing contractile reserve, in line with previous work from our laboratory in a different patient population (12). In other words, ≥25% of the LV (4/16 segments) had to be viable on DE to result in improvement of LVEF. Using this cutoff criterion, a high specificity (85%) was obtained at the cost of a lower sensitivity (69%), in line with the literature (9–11).

Attempts to improve the sensitivity of DE resulted in a loss of specificity because of the shape of the ROC curve (Fig. 3). Similarly, improving the specificity of ^{201}Tl imaging resulted in a decline of sensitivity (Fig. 2). Thus, either modality alone could not provide optimal accuracy for predicting improved LVEF. Direct comparative studies be-
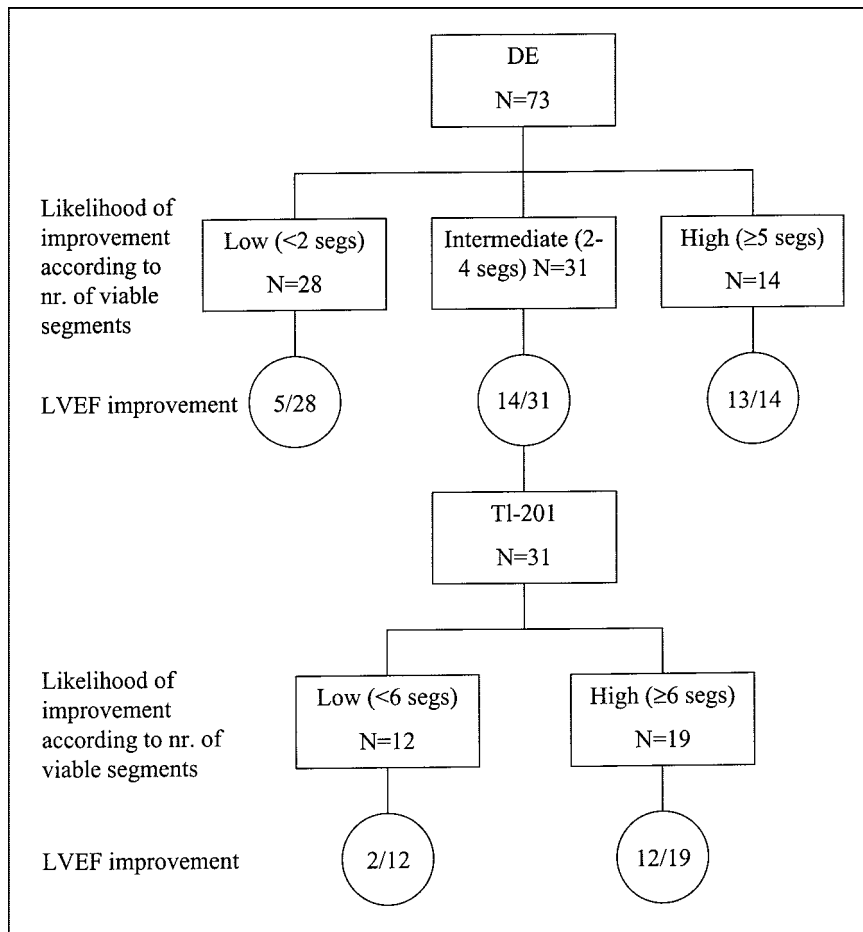
FIGURE 6. Flow chart of characterization (and outcome) of patients according to strategy 2 (DE was performed as initial test, and ^{201}Tl was performed as additional test on patients with intermediate likelihood of viability on DE). nr. = number; segs = segments.

tween ^{201}Tl and DE confirmed our findings (although these studies were performed on a segmental basis) (Table 2).

In the current study, we evaluated the use of sequential testing to increase the accuracy of predicting improved LVEF after revascularization. In the first strategy, ^{201}Tl was performed as the initial test. On the basis of the ROC curve analysis, patients with at least 9 viable segments on ^{201}Tl were considered to have viable myocardium and patients with 4 or fewer viable segments were considered to have nonviable myocardium. For these patients, no additional test was performed. For the 33 patients (45% of the population) with an intermediate likelihood of viability (5–8 viable segments), DE was performed to enhance diagnostic accuracy. Accordingly, sensitivity did not change significantly (69%), whereas specificity improved significantly (93%, $P < 0.05$ vs. [201]Tl alone) (Fig. 5).

TABLE 2
Direct Comparisons Between Resting [201]Tl Imaging and DE (166 Patients, 8 Studies)

Study	Sensitivity (%)		Specificity (%)	
	[201]Tl	DE	[201]Tl	DE
Qureshi et al. (9)	90 (38/42)	76 (32/42)	56 (59/106)	82 (87/106)
Nagueh et al. (10)	76 (42/46)	92 (23/25)	43 (27/63)	71 (25/35)
Perrone-Filardi et al. (11)	100 (73/73)	79 (58/73)	22 (8/36)	83 (30/36)
Marzullo et al. (19)	86 (42/49)	82 (40/49)	92 (24/26)	92 (24/26)
Alfieri et al. (20)	94 (92/98)	91 (85/93)	64 (14/22)	78 (25/32)
Charney et al. (21)	91 (19/20)	70 (22/31)	85 (11/13)	93 (25/27)
Pace et al. (22)	91 (35/46)	52 (24/46)	74 (34/46)	87 (40/46)
Senior et al. (23)	92 (108/118)	78 (39/50)	87 (103/118)	82 (41/50)
Weighted mean	91 (449/492)	79 (323/409)	65 (280/430)	83 (297/358)

Data in parentheses are numbers of segments.

In the second strategy, DE was performed as the initial test. On the basis of ROC curve analysis, ^{201}Tl was required for 31 patients (42% of the population). Use of sequential testing enhanced sensitivity significantly (78%, $P < 0.05$ vs. DE alone), whereas specificity remained unchanged (80%) (Fig. 5).

Hence, the strategies better predicted improved LVEF when applied together than when applied separately. The sensitivity and specificity of the 2 strategies were not significantly different, suggesting that the order of testing did not influence the results. The choice of the first test can therefore best be determined by local expertise and experience.

This study had several limitations. The first was that low-dose DE was performed. Recent data indicate that the use of combined low- and high-dose DE resulted in higher diagnostic accuracy for predicting functional recovery, with the higher accuracy being ascribed to integration of information about both viability and stress-induced ischemia (12,24). In the current study, however, the nuclear technique was resting ^{201}Tl imaging, which also takes only viability (and not stress-induced ischemia) into account.

A second study limitation was that the ^{201}Tl data were analyzed according to ^{201}Tl activity on the delayed image; using redistribution as an additional criterion might have improved specificity. Alignment between scintigraphic and echocardiographic imaging modalities remains difficult, although much experience has been obtained in previous studies (14,15).

Finally, follow-up was 3–6 mo after revascularization; a longer time may be needed for the function of severely damaged myocardium to improve after revascularization. In particular, segments with ^{201}Tl uptake without contractile reserve may need a longer time to improve in function.

CONCLUSION

The results of the current study indicated that sequential testing by ^{201}Tl SPECT and DE on a subgroup of patients with an intermediate likelihood of myocardial viability by either test alone significantly enhanced prediction of post-revascularization improvement of LVEF. Sequential testing may be the method of choice for optimal assessment of myocardial viability and prediction of improved LVEF after revascularization.

REFERENCES

1. Gheorghiade M, Bonow RO. Chronic heart failure in the United States: a manifestation of coronary artery disease. *Circulation.* 1998;97:282–289.
2. Challapalli S, Hendel RC, Bonow RO. Clinical profile of patients with congestive heart failure due to coronary artery disease: stunned/hibernating myocardium, ischemia, scar. *Coron Artery Dis.* 1998;9:629–644.
3. Wijns W, Vatner SF, Camici PG. Hibernating myocardium. *N Engl J Med.* 1998;339:173–181.
4. 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.
5. Bonow RO, Dilsizian V. Assessing viable myocardium with thallium-201. *Am J Cardiol.* 1992;70:10E–17E.
6. Beller GA. Assessment of myocardial viability. *Curr Opin Cardiol.* 1997;12:459–467.
7. Udelson JE, Coleman PS, Metherall J, et al. Predicting recovery of severe regional ventricular dysfunction: comparison of resting scintigraphy with ^{201}Tl and ^{99}Tc-sestamibi. *Circulation.* 1994;89:2552–2561.
8. Marwick TH. The viable myocardium: epidemiology, detection, and clinical implications. *Lancet.* 1998;351:815–819.
9. Qureshi U, Nagueh SF, Afridi I, et al. Dobutamine echocardiography and quantitative rest-redistribution ^{201}Tl tomography in myocardial hibernation: relation of contractile reserve to ^{201}Tl uptake and comparative prediction of recovery of function. *Circulation.* 1997;95:626–635.
10. Nagueh SF, Vaduganathan P, Ali N, et al. Identification of hibernating myocardium: comparative accuracy of myocardial contrast echocardiography, rest-redistribution thallium-201 tomography and dobutamine echocardiography. *J Am Coll Cardiol.* 1997;29:985–993.
11. Perrone-Filardi P, Pace L, Prastaro M, et al. Assessment of myocardial viability in patients with chronic coronary artery disease: rest-4-hour-24-hour ^{201}Tl tomography versus dobutamine echocardiography. *Circulation.* 1996;94:2712–2719.
12. Bax JJ, Poldermans D, Elhendy A, et al. Improvement of left ventricular ejection fraction, heart failure symptoms and prognosis after revascularization in patients with chronic coronary artery disease and viable myocardium detected by dobutamine stress echocardiography. *J Am Coll Cardiol.* 1999;34:163–169.
13. Schiller NB, Shah PM, Crawford M, et al. Recommendation for quantification of the left ventricle by two-dimensional echocardiography. *J Am Soc Echocardiogr.* 1989;2:358–367.
14. Arnese M, Cornel JH, Salustri A, et al. Prediction of improvement of regional left ventricular function after surgical revascularization: a comparison of low-dose dobutamine echocardiography with 201-Tl SPECT. *Circulation.* 1995;91:2748–2752.
15. Bax JJ, Cornel JH, Visser FC, et al. Prediction of improvement of contractile function in patients with ischemic ventricular dysfunction after revascularization by F18-fluorodeoxyglucose SPECT. *J Am Coll Cardiol.* 1997;30:377–384.
16. Vom Dahl J, Eitzman DT, Al-Aouar ZR, et al. Relation of regional function, perfusion and metabolism in patients with advanced coronary artery disease undergoing surgical revascularization. *Circulation.* 1994;90:2356–2366.
17. Vanoverschelde J-LJ, D'Hondt A-M, Marwick T, et al. Head-to-head comparison of exercise-redistribution-reinjection thallium single-photon emission computed tomography and low dose dobutamine echocardiography for prediction of reversibility of chronic left ventricular ischemic dysfunction. *J Am Coll Cardiol.* 1996;28:432–442.
18. Ragosta M, Beller GA, Watson DD, Kaul S, Gimple LW. Quantitative planar rest-redistribution ^{201}Tl imaging in 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.
19. Marzullo P, Parodi O, Reisenhofer B, et al. Value of rest thallium-201/technetium-99m sestamibi and dobutamine echocardiography for detecting myocardial viability. *Am J Cardiol.* 1993;71:166–172.
20. Alfieri O, La Canna G, Giubbini R, et al. Recovery of myocardial function: the ultimate target of coronary revascularization. *Eur J Cardiothorac Surg.* 1993;7:325–330.
21. Charney R, Schwinger ME, Chun J, et al. Dobutamine echocardiography and resting-redistribution thallium-201 scintigraphy predicts recovery of hibernating myocardium after coronary revascularization. *Am Heart J.* 1994;128:864–869.
22. Pace L, Perrone-Filardi P, Mainenti P, et al. Combined evaluation of rest-redistribution thallium-201 tomography and low-dose dobutamine echocardiography enhances the identification of viable myocardium in patients with chronic coronary artery disease. *Eur J Nucl Med.* 1998;25:744–750.
23. Senior R, Glenville B, Basu S, et al. Dobutamine echocardiography and thallium-201 imaging predict functional improvement after revascularization in severe ischaemic left ventricular dysfunction. *Br Heart J.* 1995;74:358–364.
24. Afridi I, Kleiman NS, Raizner AE, Zoghbi WA. Dobutamine echocardiography in myocardial hibernation: optimal dose and accuracy in predicting recovery of ventricular function after coronary angioplasty. *Circulation.* 1995;91:663–670.