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Accuracy of Currently Available Techniques for Prediction of Functional Recovery After Revascularization in Patients With Left Ventricular Dysfunction Due to Chronic Coronary Artery Disease: Comparison of Pooled Data

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Objectives. **This study evaluated the relative merits of the most frequently used techniques for predicting improvement in regional contractile function after coronary revascularization in patients with left ventricular dysfunction due to chronic coronary artery disease.**

Background. **Several techniques have been proposed for predicting improvement in regional contractile function after revascularization, including thallium-201 (Tl-201) stress–redistribution–reinjection, Tl-201 rest–redistribution, fluorine-18 fluorodeoxyglucose with positron emission tomography, technetium-99m sestamibi imaging and low dose dobutamine echocardiography (LDDE).**

Methods. **A systematic review of all reports on prediction of functional recovery after revascularization in patients with chronic coronary artery disease (published between 1980 and March 1997) revealed 37 with sufficient details for calculating the sensitivity and specificity of each imaging modality. From the pooled data, 95% and 99% confidence intervals were also calculated.**

Results. **Sensitivity for predicting regional functional recovery after revascularization was high for all techniques. The specificity of both Tl-201 protocols was significantly lower ($p < 0.05$) and LDDE significantly higher ($p < 0.01$) than that of the other techniques.**

Conclusions. **Pooled analysis of 37 studies showed that although all techniques accurately identify segments with improved contractile function after revascularization, the Tl-201 protocols may overestimate functional recovery. The evidence available thus far indicates that LDDE appears to have the highest predictive accuracy.**

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The awareness that even severely dyssynergic myocardium in patients with chronic coronary artery disease (CAD) may show an improvement in functional state after revascularization (1,2) has resulted in a search for the optimal diagnostic approach to identify areas with recoverable dysfunction (3). Reversal of myocardial dysfunction is particularly relevant in patients with depressed ventricular function because surgical revascularization improves long-term survival in such patients (4,5). However, surgical intervention is associated with a higher risk for perioperative complications and mortality in the same patient subset (6). Thus, it becomes critical to identify and select those patients who may benefit from a revascularization procedure. The morphologic characterization of the dysfunctional myocardium (7–9) has led to further insights into the mechanisms that determine the presence or absence of functional recovery after revascularization. Contractile dysfunction may be caused by necrotic myocardium or by jeopardized but viable myocardium. If the dysfunction is due to fibrosis, no recovery can be expected after revascularization; if the dysfunction is due to jeopardized but viable myocardium, recovery can occur in some patients (9–11). Although the exact pathophysiology of dysfunctional but viable myocardium remains controversial (1,2,11,12), the potential for functional recovery has clinical relevance. Indeed, whatever the exact mechanism of reversible dysfunction, revascularization is required for functional recovery.

Several techniques have been developed to identify dysfunctional but viable myocardium, including positron emission tomography (PET) with fluorine-18 fluorodeoxyglucose (F-18 FDG), thallium (Tl)-201 stress–redistribution–reinjection, Tl-201 rest–redistribution, single-photon emission computed to-

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Abbreviations and Acronyms

CAD	=	coronary artery disease
CI	=	confidence interval
F-18 FDG	=	fluorine-18 fluorodeoxyglucose
LDDE	=	low dose dobutamine echocardiography (echocardiographic)
LV	=	left ventricular
LVEF	=	left ventricular ejection fraction
PET	=	positron emission tomography (tomographic)
SPECT	=	single-photon emission computed tomography (tomographic)
Tc-99m MIBI	=	technetium-99m sestamibi
Tl-201	=	thallium-201

mography (SPECT) with technetium-99m sestamibi (Tc-99m MIBI) and low dose dobutamine echocardiography (LDDE). However, the relative merits of the various techniques in the prediction of functional recovery after revascularization remain a matter of debate. To provide more insight into this issue, we performed a pooled analysis of the presently available data supporting the use of the aforementioned imaging modalities for the prediction of functional recovery.

Methods

Review of published reports. The objective of the current analysis was to evaluate the available published reports on the relative merits of F-18 FDG PET, Tl-201 stress–redistribution–reinjection, Tl-201 rest–redistribution, Tc-99m MIBI and LDDE for prediction of recovery of regional left ventricular (LV) function after revascularization. The studies were identified by means of several combined search strategies: 1) A search of the MEDLINE data base (January 1980 to December 1996) was conducted using the following key words: Tl-201 rest–redistribution, Tl-201 reinjection, Tc-99m MIBI, dobutamine echocardiography, F-18 FDG and myocardial viability. 2) A manual search of eight cardiology and nuclear medicine journals (*American Heart Journal*, *American Journal of Cardiology*, *British Heart Journal*/*Heart*, *Circulation*, *European Heart Journal*, *European Journal of Nuclear Medicine*, *Journal of the American College of Cardiology* and *Journal of Nuclear Medicine*) from January 1980 to March 1997 was carried out. 3) The reference lists of the reports obtained through these searches were screened for additional articles that might have been missed. 4) The list of articles was then reviewed by the co-investigators, all of whom are active in the field. Only articles in English were considered, and reviews or abstracts were disregarded.

Inclusion criteria. For inclusion in the analysis, the following criteria had to be met: 1) the study was prospective and evaluated one or more of the aforementioned five techniques; 2) the technique was tested for predictive accuracy versus functional outcome after revascularization, assessed during follow-up; 3) the study evaluated only patients with chronic, stable LV dysfunction; 4) the study contained sufficient details so that the sensitivity and specificity for predicting improvement in regional LV function could be calculated. In cases where these details were not readily available, a co-investigator of that particular study was approached to supply the relevant information.

Exclusion criteria. Exclusion criteria were 1) studies assessing viability with any of the techniques but without functional follow-up after revascularization; and 2) studies in patients with acute ischemic syndromes (including viability assessment within 1 month after infarction).

From the pooled data, weighted sensitivities (number of viable segments divided by the number of segments with improved function after revascularization) and specificities (number of nonviable segments divided by the number of segments without improved function after revascularization) were calculated. The 95% confidence intervals (CIs) of the weighted sensitivities and specificities were also calculated from the following formula: $p \pm 1.96 \times \sqrt{\{p \times (1 - p)/n\}}$, where p = the number of viable segments divided by the number of segments with improved function after revascularization or the number of nonviable segments divided by the number of segments without improvement after revascularization; and n = the total population. For example, if sensitivity is 80% and the total number of segments is 100, the 95% CI is calculated as follows: $0.80 \pm 1.96 \times \sqrt{\{0.80 \times (1 - 80)/100\}}$. Similarly, the 99% CIs were calculated using the following formula: $p \pm 2.575 \times \sqrt{\{p \times (1 - p)/n\}}$. The 95% and 99% CIs were calculated for each technique, and the individual intervals were compared. Differences between techniques were considered significant at the 0.05 level when 95% CI did not overlap and significant at the 0.01 level when 99% CIs did not overlap.

The majority of the studies in patients undergoing revascularization concentrated on changes in regional contraction. For the individual patient, improvement in global LV function is the most clinically relevant factor. When available, these data are included and discussed for each technique anecdotally. Because of the limited data available for prediction of global LV improvement and their descriptive nature, it was not possible to assess pooled sensitivity/specificity figures.

Results

A total of 396 reports were identified by means of the different search strategies, with only 37 fulfilling the inclusion criteria. The reasons for exclusion were: 1) absence of revascularization (275 reports); 2) experimental studies (animal models, 43 reports); 3) revascularization in patients with acute ischemic syndromes (21 reports); 4) insufficient information for calculation of sensitivity and specificity on a segmental basis (3 reports); and 5) study design not allowing calculation of sensitivity and specificity (17 studies in which the preoperative viability test results were given for patients with and without functional recovery as determined postoperatively, emphasizing the pathophysiologic differences between patients with and without viable myocardium; these data do not permit calculation of sensitivity and specificity). The results of the pooled

Table 1. Sensitivity and Specificity of Fluorine-18 Fluorodeoxyglucose Positron Emission Tomography for Detection of Improved Regional Contractile Function After Revascularization

Study (ref no.)	No. of Pts	Male (%)	Mean Age (yr)	Mean LVEF (SD) (%)	Pts With MVD (%)	Pts With Prev MI (%)	Segs With Recovery (%)	Technique Assessing RWM After Revasc	Sens (%) (no. of segs)	Spec (%) (no. of segs)
Marwick et al. (16)	16	88	NA	NA	44	100	41	Echo	71 (25/35)	76 (38/50)
Gerber et al. (17)	39	87	60	33 (±10)	85	59	62	Echo	75 (18/24)	67 (10/15)
Tamaki et al. (18)	22	91	57	NA	NA	77	50	RNV	78 (18/23)	78 (18/23)
Gropler et al. (19)	34	76	60	NA	76	62	40	Echo/RNV	83 (38/46)	50 (35/70)
Maes et al. (20)	23	NA	NA	41 (±13)	NA	NA	52	RNV	83 (10/12)	91 (10/11)
Tamaki et al. (21)	43	95	58	41 (NA)	NA	100	39	CV/RNV	88 (45/51)	82 (65/79)
Knuuti et al. (22)	48	96	54	53 (±11)	85	100	30	Echo	92 (23/25)	85 (50/59)
Baer et al. (23)	42	90	59	40 (±13)	74	100	62	Echo	92 (24/26)	88 (14/16)
Lucignani et al. (24)	14	86	61	38 (±5)	93	NA	74	RNV	93 (37/40)	86 (12/14)
Carrel et al. (25)	23	91	56	34 (±14)	NA	100	74	Echo	94 (16/17)	50 (3/6)
Tillisch et al. (26)	17	94	NA	32 (±14)	NA	94	55	CV/RNV	95 (35/37)	80 (24/30)
Tamaki et al. (27)	11	NA	NA	NA	NA	NA	71	RNV	100 (40/40)	38 (6/16)
Average	28	90	58	40	78	88	51			
Weighted mean									88 (329/376)	73 (285/390)

CV = contrast ventriculography; Echo = echocardiography; LVEF = left ventricular ejection fraction; MI = myocardial infarction; MVD = multivessel disease; NA = not available; Prev = previous; Pts = patients; ref = reference; Revasc = revascularization; RNV = radionuclide ventriculography; RWM = regional wall motion; Segs = segments; Sens = sensitivity; Spec = specificity.

analysis of the 37 remaining studies are discussed in detail for each technique.

Metabolic imaging with F-18 FDG and PET. Since the original observation by Marshall et al. (13) in 1981, considerable evidence has accumulated to show that F-18 FDG in combination with PET can detect viable myocardium (14,15). F-18 FDG is a glucose analogue that traces exogenous glucose uptake by the myocardium. Viable myocardium is characterized by preserved F-18 FDG uptake.

Diagnostic accuracy for prediction of regional improvement. Many studies have used F-18 FDG PET to predict functional recovery in patients undergoing revascularization (16–27). The results from these studies are summarized in Table 1. Reanalysis of the original data (obtained in 332 patients) showed that the sensitivity ranged from 71% to 100%, with a weighted mean of 88%. Specificity ranged from 38% to 91%, with a weighted mean of 73%.

Diagnostic accuracy for prediction of global improvement. Revascularization in patients with preserved F-18 FDG uptake was shown to result in improved LV ejection fraction (LVEF) (9–11,17,25,26,28–32). In the study by Tillisch et al. (26), LVEF improved from 30 ± 11% to 45 ± 14% (mean ± SD) in the patients with two or more viable, dysfunctional segments on F-18 FDG PET, whereas LVEF did not improve in the patients with one or less viable, dysfunctional segment. Comparable findings have been recently reported (10,28,29).

Areas of ongoing research. On the basis of F-18 FDG PET results, several reports have recently evaluated the feasibility of cardiac F-18 FDG imaging with SPECT cameras equipped with 511-keV collimators to allow F-18 FDG imaging in centers without PET facilities (33,34).

Tl-201 scintigraphy. The initial uptake of Tl-201 by myocytes is mainly determined by regional perfusion, whereas the integrity of the cell membrane is predominantly important for delayed imaging of tracer retention. Although different Tl-201 protocols have been described (3), both Tl-201 stress–redistribution–reinjection and Tl-201 rest–redistribution are currently used for prediction of functional recovery.

Tl-201 stress–redistribution–reinjection imaging. *Diagnostic accuracy for prediction of regional improvement.* Several studies have shown (35–37) that reinjection of 1 mCi of Tl-201 after 3- to 4-h redistribution imaging detects viability in 31% to 49% of segments deemed irreversibly damaged because they showed a fixed defect on conventional stress–redistribution Tl-201 imaging. Bonow et al. (38) showed concordance between Tl-201 stress–redistribution–reinjection and F-18 FDG PET for the presence or absence of viable myocardium in 88% of segments; however, postrevascularization results were not reported.

It also appears that semiquantitation of Tl-201 activity is important. The majority of mild to moderate (Tl-201 activity ≥50% of normal) fixed defects on redistribution (38) and reinjection images (39) are viable on F-18 FDG PET.

Seven studies (27,34,35,37,40–42) have evaluated the diagnostic accuracy of Tl-201 stress–redistribution–reinjection for assessing improvement in regional function after revascularization. Reanalysis of the available data revealed that Tl-201 stress–redistribution–reinjection imaging has a high sensitivity (average 86%) but a relatively low specificity (average 47%) (Table 2). These results suggest an overestimation of potential recovery by Tl-201 stress–redistribution–reinjection imaging.

Table 2. Sensitivity and Specificity of Thallium-201 Reinjection Imaging for Detection of Improved Regional Contractile Function After Revascularization

Study (ref no.)	No. of Pts	Male (%)	Mean Age (yr)	Mean LVEF (SD) (%)	Pts With MVD (%)	Pts With Prev MI (%)	Segs With Recovery	Technique Assessing RWM After Revasc	Sens (%) (no. of segs)	Spec (%) (no. of segs)
Vanoverschelde et al. (42)	73	85	59	36 (±12)	79	68	38	Echo/RNV	80 (213/267)	47 (198/425)
Ohtani et al. (37)	24	75	62	NA	100	58	61	RNV	89 (33/37)	50 (12/24)
Arnese et al. (40)	38	68	59	31 (NA)	92	100	22	Echo	89 (34/38)	48 (63/132)
Bax et al. (34)	17	82	57	36 (±11)	100	100	29	Echo	93 (25/27)	43 (28/65)
Tamaki et al. (27)	11	NA	NA	NA	NA	NA	71	RNV	95 (38/40)	38 (6/16)
Dilsizian et al. (35)	20	88	58	NA	61	NA	57	RNV	95 (35/37)	80 (8/10)
Haque et al. (41)	26	81	55	43 (±14)	56	88	77	Echo	100 (33/33)	40 (4/10)
Average	30	80	59	36	81	79	45			
Weighted mean									86 (411/479)	47 (319/682)

Abbreviations as in Table 1.

Diagnostic accuracy for prediction of global improvement. Bax et al. (34) evaluated 17 patients with Tl-201 reinjection imaging to assess improvement of global function after revascularization. Tl-201 reinjection identified five of six patients who demonstrated improvement in LVEF of at least 5%. Of the 11 patients with no improvement in global function, Tl-201 reinjection identified nonviable myocardium in six. Vanoverschelde et al. (42) recently reported a sensitivity of 72% and a specificity of 73% for Tl-201 reinjection imaging in predicting improved global LV function.

Tl-201 rest–redistribution imaging. *Diagnostic accuracy for prediction of regional improvement.* Whereas Tl-201 stress–redistribution–reinjection scintigraphy provides information on both exercise-induced ischemia and viability, Tl-201 rest–redistribution provides information on viability only. Two studies (43,44) compared Tl-201 stress–redistribution–reinjection with Tl-201 rest–redistribution imaging and showed a concordance between the two techniques of 80%, at least when defect reversibility was considered an indicator of viability. When the severity of Tl-201 activity in irreversible defects was considered, the concordance increased to 94% (43). In addition, Dilsizian et al. (43) showed that F-18 FDG PET and Tl-201 rest–redistribution imaging yielded comparable information regarding viability when the Tl-201 rest–redistribution studies were analyzed semiquantitatively.

Eight studies (45–52) evaluated the use of Tl-201 rest–redistribution imaging to predict improvement of regional contractility after revascularization. In these studies the average sensitivity and specificity were 90% and 54% (Table 3), also suggesting some overestimation of recovery by Tl-201 rest–redistribution imaging.

Diagnostic accuracy for prediction of global improvement. Iskandrian et al. (53) studied 26 patients and showed that Tl-201 rest–redistribution identified 12 of 14 patients who demonstrated improvement in LVEF of at least 5% after revascularization. In contrast, Tl-201 rest–redistribution identified 8 of 12 patients with no improvement. Comparable results were reported in other studies (45,48).

Tc-99m MIBI. Myocardial uptake of Tc-99m MIBI parallels regional perfusion and provides adequate information for

Table 3. Sensitivity and Specificity of Thallium-201 Rest–Redistribution Imaging for Detection of Improved Regional Contractile Function After Revascularization

Study (ref no.)	No. of Pts	Male (%)	Mean Age (yr)	Mean LVEF (SD) (%)	Pts With MVD (%)	Pts With Prev MI (%)	Segs With Recovery	Technique Assessing RWM After Revasc	Sens (%) (no. of segs)	Spec (%) (no. of segs)
Mori et al. (45)	17	82	62	37 (±7)	52	100	51	RNV	44 (11/25)	88 (23/26)
Marzullo et al. (46)	14	79	54	39 (±7)	93	100	65	Echo	86 (42/49)	92 (24/26)
Udelson et al. (47)	18	72	67	34 (±10)	NA	100	37	Echo	88 (15/17)	83 (24/29)
Qureshi et al. (52)	34	NA	61	39 (±14)	76	56	28	Echo	90 (38/42)	56 (59/106)
Ragosta et al. (48)	21	86	64	27 (±5)	100	76	51	RNV	93 (81/89)	31 (27/87)
Alfieri et al. (49)	13	100	52	35 (±8)	NA	NA	82	Echo	94 (92/98)	64 (14/22)
Charney et al. (50)	10	NA	NA	NA	NA	NA	61	Echo	95 (19/20)	85 (11/13)
Perrone-Filardi et al. (51)	18	NA	NA	NA	NA	NA	69	Echo	100 (73/73)	22 (8/36)
Average	18	83	61	35	80	81	51			
Weighted mean									90 (371/413)	54 (188/345)

Abbreviations as in Table 1.

Table 4. Sensitivity and Specificity for Technetium-99m Sestamibi Scintigraphy With and Without Addition of Nitrates for Detection of Functional Recovery After Revascularization

Study (ref no.)	No. of Pts	Male (%)	Mean Age (yr)	Mean LVEF (SD) (%)	Pts With MVD (%)	Pts With Prev MI (%)	Segs With Recovery (%)	Technique Assessing RWM After Revasc	Sens (%) (no. of segs)	Spec (%) (no. of segs)
Technetium-99m Sestamibi Scintigraphy Without Addition of Nitrates										
Marzullo et al. (70)	22	86	57	44 (±13)	91	100	56	Echo	73 (40/55)	54 (27/50)
Marzullo et al. (46)	14	79	54	39 (±7)	93	100	65	Echo	75 (37/49)	84 (22/26)
Gonzalez et al. (71)	36	89	57	52 (±15)	72	86	43	Echo	80 (30/39)	35 (18/51)
Marzullo et al. (72)	14	93	55	43 (±9)	93	100	57	Echo	83 (35/42)	68 (21/31)
Maes et al. (20)	23	NA	NA	40 (±13)	NA	NA	57	RNV	92 (12/13)	60 (6/10)
Udelson et al. (47)	18	72	67	34 (±10)	NA	100	37	Echo	94 (16/17)	86 (25/29)
Maublant et al. (73)	25	92	62	52 (±15)	60	NA	78	CV	100 (21/21)	67 (4/6)
Average	22	86	59	45	78	95	55			
Weighted mean									81 (191/236)	60 (122/203)
Technetium-99m Sestamibi Scintigraphy With Addition of Nitrates										
Maurea et al. (74)	8	NA	NA	NA	NA	100	48	Echo	88 (22/25)	89 (24/27)
Bisi et al. (75)	19	89	57	35 (±10)	84	100	24	Echo	91 (10/11)	88 (30/34)
Bisi et al. (76)	28	86	57	36 (±10)	61	100	43	RNV	95 (18/19)	88 (22/25)
Average	18	87	57	36	70	100	37			
Weighted mean									91 (50/55)	88 (76/86)

Abbreviations as in Table 1.

the detection of CAD (54). The uptake and retention of Tc-99m MIBI is also dependent on cell membrane integrity and mitochondrial function (membrane potential) (55–57) and thus may reflect cellular viability. Many studies have compared Tc-99m MIBI imaging with other scintigraphic modalities, including Tl-201 stress–redistribution–reinjection (58,59), Tl-201 rest (46,47,60,61), Tl-201 rest–redistribution (60,62–64) and F-18 FDG PET (20,63,65–69). These concordance studies were consistent in showing that Tc-99m MIBI was less accurate in the detection of myocardial viability.

Diagnostic accuracy for prediction of regional improvement. The results of studies that evaluated Tc-99m MIBI imaging with regard to functional outcome after revascularization are summarized in Table 4 (20,46,47,70–73). All studies reported a high sensitivity, whereas specificity varied considerably from 35% to 86%. Recently, the administration of nitrates before Tc-99m MIBI imaging has been described (74–76). Three studies that have used this approach suggest an improved specificity (Table 4).

Diagnostic accuracy for prediction of global improvement. At present, no published data are available on the diagnostic accuracy of Tc-99m MIBI imaging for predicting improvement of global function.

Areas of ongoing research. Several approaches can potentially improve the diagnostic accuracy of Tc-99m MIBI, including stress–rest imaging (71), gated SPECT (71,77), semiquantitative analysis (47,59) and delayed imaging after tracer administration (59).

LDDE. Echocardiography during the infusion of low dose dobutamine (5 to 15 μg/kg body weight per min) has been proposed as an alternative method for assessing myocardial viability in patients with chronic ischemic heart disease (78). The hallmark of viability is improved contraction of a dyssynergic segment after adrenergic stimulation. Several studies have compared LDDE with other imaging modalities to assess viability, including F-18 FDG PET (17,23,79), Tl-201 stress–redistribution–reinjection (34,40–42,80,81), Tl-201 rest–redistribution (46,49–52) and Tc-99m MIBI (46), showing good agreement in most studies.

Diagnostic accuracy for prediction of regional improvement. The available studies that have evaluated LDDE for detecting functional recovery after revascularization in patients with chronic CAD are summarized in Table 5 (17,23,34,40–42,46,49–52,79,82–86). The results indicate that LDDE adequately detects recovery of contractile function after revascularization, with a mean sensitivity of 84% and a mean specificity of 81%. It is worth mentioning that all studies with low dose dobutamine have used echocardiography, rather than an independent technique, to assess improvement of regional wall motion.

Diagnostic accuracy for prediction of global improvement. Meluzin et al. (87) showed that LVEF increased from 38 ± 5% to 42 ± 5% after revascularization in patients with contractile reserve but did not improve in patients without contractile reserve. Moreover, the improvement in LVEF was linearly related to the number of segments with contractile reserve on LDDE, indicating that the amount of jeopardized but viable tissue determines the magnitude of improvement of LV function (87). Several studies (34,42,84) have now confirmed these findings.

Table 5. Sensitivity and Specificity for Low Dose Dobutamine Echocardiography for Detection of Improved Regional Contractile Function After Revascularization

Study (ref no.)	No. of Pts	Male (%)	Mean Age (yr)	Mean LVEF (SD) (%)	Pts With MVD (%)	Pts With Prev MI (%)	Segs With Recovery (%)	Technique Assessing RWM After Revasc	Sens (%) (no. of segs)	Spec (%) (no. of segs)
Gerber et al. (7)	39	87	60	33 (±10)	85	59	62	Echo	71 (17/24)	89 (13/15)
Charney et al. (50)	17	59	63	46 (±9)	76	65	53	Echo	71 (22/31)	93 (25/27)
Arnese et al. (40)	38	68	59	31 (NA)	92	100	22	Echo	74 (28/38)	96 (127/132)
Perrone-Filardi et al. (51)	34	NA	NA	39 (±14)	NA	NA	28	Echo	74 (31/42)	89 (94/106)
Afridi et al. (82)	20	85	60	NA	40	55	33	Echo	76 (29/38)	74 (56/76)
Vanoverschelde et al. (42)	73	85	59	36 (±12)	79	68	38	Echo/RNV	79 (211/267)	80 (340/425)
Qureshi et al. (52)	18	NA	61	NA	76	56	69	Echo	79 (58/73)	83 (30/36)
Marzullo et al. (46)	14	79	54	39 (±7)	93	100	65	Echo	82 (40/49)	94 (24/26)
Bax et al. (34)	17	82	57	36 (±11)	100	100	29	Echo	85 (23/27)	63 (41/65)
Senior et al. (83)	22	95	61	26 (±8)	86	NA	70	Echo	87 (103/118)	82 (41/50)
Perrone-Filardi et al. (84)	18	94	59	43 (±12)	50	89	61	Echo	88 (42/48)	87 (27/31)
Alfieri et al. (49)	14	100	52	35 (±8)	NA	NA	82	Echo	91 (85/93)	78 (25/32)
La Canna et al. (85)	33	97	56	33 (±8)	94	70	65	Echo	92 (164/179)	75 (101/135)
Haque et al. (41)	26	81	55	43 (±14)	56	88	77	Echo	94 (31/33)	80 (8/10)
Baer et al. (23)	42	90	59	40 (±13)	74	100	62	Echo	96 (25/26)	69 (11/16)
DeFilippi et al. (86)	23	100	NA	38 (±10)	NA	NA	61	Echo	97 (94/97)	75 (41/55)
Average	28	86	58	36	78	78	52			
Weighted mean									84 (909/1086)	81 (963/1182)

Abbreviations as in Table 1.

Areas of ongoing research. It was recently suggested that analysis of the response to high dose dobutamine in addition to low dose dobutamine (82) or a combination of dobutamine infusion with dipyridamole (0.28 mg/kg body weight over 4 min) (88) might further improve the results. To overcome the limitations of transthoracic echocardiography, in terms of patient-dependent image quality, several studies have demonstrated the feasibility of transesophageal LDDE (23,79,80, 89,90).

Relative merits of the imaging techniques. The results of the pooled analysis are summarized in Table 6. All techniques have a high sensitivity for predicting recovery of rest regional function. LDDE has a higher specificity than all other methods ($p < 0.01$), and both Tl-201 approaches have significantly less specificity than LDDE ($p < 0.01$), F-18 FDG PET ($p < 0.01$) or Tc-99m MIBI SPECT ($p < 0.05$). As illustrated in Figure 1, LDDE has the highest predictive accuracy.

Discussion

The current study revealed that sensitivity for predicting improved regional contractile function after revascularization is high for all techniques analyzed; however specificity varied greatly for all techniques and was lowest for Tl-201 stress–redistribution–reinjection and Tl-201 rest–redistribution. We chose to present the data in terms of sensitivity and specificity because the proportion of segments showing functional recovery varied greatly from one study to another, and sensitivity and specificity are less dependent than predictive values on the prevalence of recovery or no recovery of rest function. There

Table 6. Sensitivity and Specificity for the Different Imaging Techniques (based on weighted mean values from available studies)

	No. of Pts	Sens (%)	95% CI	99% CI	Spec (%)	95% CI	99% CI
Tc-99m MIBI	207	83	78–87	77–89	69	63–74	61–76
LDDE	448	84	82–86	81–87	81	79–84	79–84
Tl-201 reinjection	209	86	83–89	82–90	47	43–51	42–52
F-18 FDG PET	332	88	84–91	83–92	73	69–77	69–77
Tl-201 rest–redistribution	145	90	87–93	86–94	54	49–60	48–61

CI = confidence interval; F-18 FDG = fluorine-18 fluorodeoxyglucose; LDDE = low dose dobutamine echocardiography; Tc-99m MIBI = technetium-99m sestamibi; Tl-201 = thallium-201; other abbreviations as in Table 1.

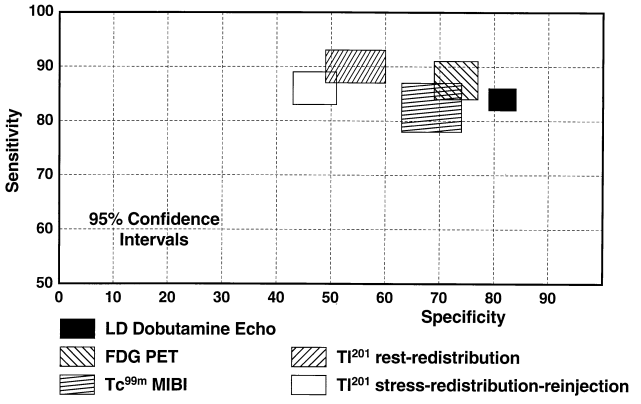

Figure 1. Receiver operating characteristic display, indicating 95% confidence intervals for each technique. The most effective modalities are located closer to the **upper right corner** of the graph. In this display, the smaller the **square,** the better the technique. A **square** (as opposed to a **rectangle**) indicates a good balance between sensitivity and specificity. A **small symbol** reflects narrow confidence intervals. LD = low dose.

are data supporting the value of each diagnostic test discussed here (with exception of Tc-99m MIBI) for predicting improvement in global rest function; however, the number of available studies remains too small to compare their respective accuracy. On the basis of the search strategies that we used, we believe that all available data as of March 1997 are included in the present analysis. Given the relatively small sample size of the individual studies and the lack of randomized data, it was not possible to perform a formal meta-analysis that included the assessment of the effect of variation in study validity and the effect of variation in patient characteristics (91). However, by restricting our analysis to patients with chronic LV dysfunction, a relatively homogenous study group was defined. Moreover, the study populations did not differ substantially (Tables 1 to 5). Still, some variation in the quality of the data is possible despite our attempts to reduce it by setting narrow inclusion criteria. It should be acknowledged that variations between the studies may still occur from the use of different criteria for defining a positive or negative test result; for instance, many different viability criteria and analytical procedures have been described for Tl-201 and F-18 FDG imaging.

In practice, the choice between imaging modalities also depends on local availability and expertise, which is particularly critical for the acquisition and interpretation of LDDE. Of the nuclear techniques, it appears that the Tl-201 stress–redistribution–reinjection approach is the least effective. Because most tests do not have equivalent performance characteristics, complementary techniques could be combined to obtain an optimal balance between sensitivity and specificity. Strategies can be developed for a more cost-effective use of tests in a sequential manner, as preliminary data suggest (92).

Limitations of the available data and new areas of research. This analysis of the published data reveals some of the weaknesses of the currently available evidence. The inclusion criteria may vary considerably from one study to the other, particularly with respect to the severity of baseline dysfunction. Ideally, only patients with a global ejection fraction <35% should be studied because these patients are both likely to benefit from and to have a greater risk during a revascularization procedure. Most studies included only a limited number of patients. Information about patients lost to follow-up is rarely given, and partial data duplication seems likely in a few reports. The majority of studies do not provide evidence of vessel or graft patency; reocclusion may prohibit viable segments from recovering, thereby underestimating the true specificity of all techniques. The optimal moment for the assessment of functional follow-up after revascularization is uncertain. Currently, follow-up is frequently performed 3 months after revascularization. However, preliminary data (93) have demonstrated that full recovery should not be expected to occur before 6 or even 12 months after revascularization.

Importantly, global and regional function should be evaluated by an independent technique. Studies of LDDE have invariably used echocardiograms to evaluate the effect of revascularization. The use of an internally consistent standard may contribute in part to the excellent predictive value of this technique. In addition, the acquisition and interpretation of echocardiograms strongly depends on operator experience. Although variability in interpretation of stress echocardiograms between institutions has been reported for the diagnosis of CAD (94), no such data are available for the detection of contractile reserve in dysfunctional areas (95).

Finally, it should be acknowledged that a prospective, long-term evaluation of patients with severe dysfunction with and without revascularization is still awaited. The presence of viable myocardium may have implications and long-term effects on prognosis that are independent from the rest functional state of the left ventricle (96–98). Therefore, additional end points, such as the response during stress (99), exercise capacity (100) and quality of life (101), should be prospectively evaluated in a large patient cohort.

Conclusions. The current analysis of pooled data showed that sensitivity for prediction of functional recovery after revascularization is high for all techniques reviewed here. Specificity is highest for LDDE and lowest for Tl-201 stress–redistribution–reinjection and Tl-201 rest–redistribution. Thus, the available evidence favors the use of LDDE as the technique of first choice for prediction of regional functional recovery in patients with chronic ischemic LV dysfunction for whom revascularization is contemplated.

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