

# **Current Problems in Cardiology<sup>®</sup>**

Volume 26 Number 2 February 2001

## **Sensitivity, Specificity, and Predictive Accuracies of Various Noninvasive Techniques for Detecting Hibernating Myocardium**

---

**Jeroen J. Bax, MD, PhD**

Department of Cardiology  
Leiden University Medical Center  
Leiden, The Netherlands

**Don Poldermans, MD, PhD  
Abdou Elhendy, MD, PhD**

The ThoraxCenter  
Rotterdam, The Netherlands

**Eric Boersma, PhD**

Department of Epidemiology and Medical Statistics  
Rotterdam University  
Rotterdam, The Netherlands

**Shahbudin H. Rahimtoola, MB, FRCP, MACP, MACC**

Keck School of Medicine  
University of Southern California  
Los Angeles, California

 **Mosby**

# Current Problems in Cardiology®

## Information for Readers

*Current Problems in Cardiology* (ISSN 0146-2806) is published monthly by Mosby. Corporate and editorial offices: 11830 Westline Industrial Drive, St. Louis, MO 63146-3318. Accounting and circulation offices: Mosby, 6277 Sea Harbor Drive, Orlando, FL 32887-4800. Periodicals postage paid at Orlando, FL 32862, and at additional mailing offices. POSTMASTER: Send address changes to *Current Problems in Cardiology*, Mosby, Periodicals Department, 6277 Sea Harbor Dr, Orlando, FL 32887.

Visit our Web site at [www.mosby.com/cpcardiol](http://www.mosby.com/cpcardiol).

**Subscription Orders/Inquiries and Back Issues:** Subscriptions may begin at any time. To enter a subscription to *Current Problems in Cardiology*, call 800-654-2452 or 407-345-4000; fax 407-363-9661; or e-mail [periodical.service@mosby.com](mailto:periodical.service@mosby.com). Remittances made by check, draft, post office, or express money order should be in US funds, drawn through a US bank, made payable to this Journal, and sent to Mosby, Subscription Customer Service, 6277 Sea Harbor Dr, Orlando, FL 32887, USA.

2001 US subscription rates: individual, \$115.00; institution, \$186.00; student and resident, \$56.00; single issue, \$18.00. Outside of the US and possessions: individual, \$139.00; institution, \$210.00; student and resident, \$80.00; surface delivery, no additional charge. Airmail delivery to Canada and Mexico, add \$18.00; for all other international, add \$22.00. Canadian customers, please add 7% GST to international prices. Prices subject to change without notice. Subscription rates include supplements. To receive student/resident rate, orders must be accompanied by name of affiliated institution, date of term, and the signature of program/residency coordinator on institution letterhead. Orders will be billed at individual rate until proof of status is received.

Single-copy prices will be charged on missing issues older than 3 months (6 months international) from mail date. Back issues generally are available for the previous 5 years.

**Copyright.** Copyright © 2001 by Mosby, Inc. All rights reserved. No part of this publication may be reproduced, stored in a retrieval system, or transmitted in any form or by any means—electronic, mechanical, photocopying, recording, or otherwise—without prior written permission from the publisher, except in cases described below.

This journal has been registered with the Copyright Clearance Center, Inc., 222 Rosewood Drive, Danvers, MA 01923. Consent is given for the copying of articles for personal or internal use of specific clients. This consent is given on the condition that the copier pay directly to the CCC the base fee of \$35.00 per article for copying beyond that permitted by U.S. Copyright Law: 0146-2806/2001 \$35.00. This consent does not extend to other kinds of copying, such as for general distribution, resale, advertising, and promotional purposes or for creating new collective works. All inquiries regarding copyrighted material from this publication other than those that can be handled through the CCC should be directed, in writing, to Journals Permission Department, Mosby, 6277 Sea Harbor Dr, Orlando, FL 32887; fax (407) 345-4058.

**Indexing.** *Current Problems in Cardiology* is listed in *Index Medicus*, *Current Contents/Clinical Medicine*, and *SCI*.

**Disclaimer.** Statements and opinions expressed herein are those of the author(s) and not necessarily those of the editor(s) or publisher. The editor(s) and publisher disclaim any responsibility or liability for such material and do not guarantee, warrant, or endorse any product or service advertised in this publication, nor do they guarantee any claim made by the manufacturer of such product or service.

# Current Problems in Cardiology®

## Sensitivity, Specificity, and Predictive Accuracies of Various Noninvasive Techniques for Detecting Hibernating Myocardium

---

<b>Foreword</b>	144
<b>Introduction</b>	147
<b>Methods</b>	148
<b>Results</b>	151
Dobutamine Echocardiography	151
<sup>201</sup> Tl Imaging	152
<sup>99m</sup> Tc-labeled Tracers	155
FDG PET	155
Direct Comparisons Between Nuclear Imaging and DE	156
Comparison of the Techniques	157
<b>Discussion</b>	158
Lower PPVs and Specificities	159
<b>Features of the Different Viability Tests</b>	163
Nuclear Imaging Versus DE	167
Unresolved Issues	168
Limitations of Pooled Analysis	169
<b>Conclusion</b>	171
<b>Addendum</b>	172
<b>References</b>	173

---

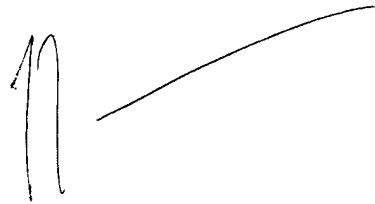
■

## Foreword

In the February 2001 issue of *Current Problems in Cardiology*, Dr Jeroen J. Bax and his colleagues in the Netherlands provide a comprehensive discussion of sensitivity, specificity, and predictive accuracy of various noninvasive tests for detecting hibernating myocardium, a condition originally described by the Senior Author, Dr Shahbudin H. Rahimtoola. This is the most complete discussion of the use of noninvasive tests for identifying viable myocardium in patients with coronary artery disease that has ever been written.

The editorial board of *Current Problems in Cardiology* is most grateful to Dr Bax and his coauthors for their extensive review of the relevant literature concerning this important topic.

*Robert A. O'Rourke, MD, FACC, MACP*  
*Editor in Chief*



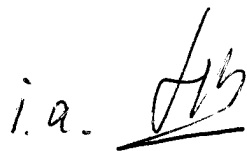
Jeroen J. Bax, MD, PhD, is a resident in Cardiology at the Leiden University Medical Center, The Netherlands. He earned his doctorate in the use of single photon emission computed tomographic imaging with 511 keV collimators to evaluate myocardial uptake of F18-fluorodeoxyglucose (Free University Hospital Amsterdam, The Netherlands, 1996). His main research activities involve the use of noninvasive imaging (nuclear imaging, [stress-] echocardiography and magnetic resonance imaging) to evaluate the different aspects of coronary artery disease.

Free University Hospital Amsterdam, The Netherlands, 1996). His main research activities involve the use of noninvasive imaging (nuclear imaging, [stress-] echocardiography and magnetic resonance imaging) to evaluate the different aspects of coronary artery disease.



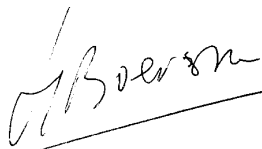
Don Poldermans, MD, PhD, has been a consultant in Internal Medicine at the University Hospital Rotterdam, The Netherlands, since 1989. He graduated from Erasmus University Rotterdam, The Netherlands. He completed general medicine, infectious disease, and intensive care medicine residencies at the Erasmus Medical Center Rotterdam, The Netherlands. His primary research interests are cardiovascular risk stratification, hypertension, and echocardiography.

He completed general medicine, infectious disease, and intensive care medicine residencies at the Erasmus Medical Center Rotterdam, The Netherlands. His primary research interests are cardiovascular risk stratification, hypertension, and echocardiography.



Abdou Elhendy, MD, PhD, received his medical degree and performed his training in cardiology at Cairo University Hospital, Egypt. He worked for 3 years at the ThoraxCenter Rotterdam, The Netherlands, as a research fellow in the field of stress echocardiography. He earned his doctorate at Erasmus University Rotterdam, The Netherlands, in 1996. He is a lecturer in cardiology at Cairo University Hospital, Egypt. He is currently working at the Mayo Clinics, Rochester, Minn, as a research fellow at the Department of Medicine. His major interests are stress echocardiography and myocardial perfusion imaging in coronary artery disease.

He earned his doctorate at Erasmus University Rotterdam, The Netherlands, in 1996. He is a lecturer in cardiology at Cairo University Hospital, Egypt. He is currently working at the Mayo Clinics, Rochester, Minn, as a research fellow at the Department of Medicine. His major interests are stress echocardiography and myocardial perfusion imaging in coronary artery disease.



Eric Boersma, MSc, PhD, has been head of the Department of Clinical Epidemiology, ThoraxCenter Cardiology at the University Hospital Rotterdam, The Netherlands, since 1997. He received master's degrees in mathematics and statistics from the University of Delft, The Netherlands, and in epidemiology at the University of Rotterdam, The Netherlands. He defended a doctoral thesis on decision making in myocardial infarction in 1998. His primary research interests are cardiovascular epidemiology and cardiac risk stratification.

He defended a doctoral thesis on decision making in myocardial infarction in 1998. His primary research interests are cardiovascular epidemiology and cardiac risk stratification.



Shahbudin H. Rahimtoola, MB, FRCP, received his MRCP from the Royal College of Physicians of Edinburgh in 1963 and was awarded the fellowship in 1972.

Since 1980 he has been a Professor of Medicine, University of Southern California. He was chief of the Division of Cardiology, University of Southern California and LAC+USC Medical Center, from 1980 to 1992. In 1984 he was appointed the first George C. Griffith Professor of Cardiology, which is funded in part by the American Heart Association—Greater Los Angeles Affiliate. In 1993, Dr Rahimtoola was awarded the title of Distinguished Professor, University of Southern California. In 1996, he was awarded Master of the American College of Physicians. In 1999, he was awarded Master of the American College of Cardiology. He is a past chairman of the Council on Clinical Cardiology, American Heart Association, and a past trustee of the American College of Cardiology. Dr Rahimtoola serves on the editorial boards of *Circulation* and numerous other journals. He has received numerous awards and citations, including the Gifted Teacher Award from the American College of Cardiology in 1986 and the James B. Herrick Award from the American Heart Association/Council on Clinical Cardiology in 1989. He received the Distinguished Alumnus Award from the Mayo Foundation in 1998. Dr Rahimtoola's research interests are broad and extensive. He is best known for his work in valvular heart disease, coronary artery disease, results of cardiac surgery, arrhythmias, heart failure, cardiomyopathy, and congenital heart disease.

---

# Sensitivity, Specificity, and Predictive Accuracies of Various Noninvasive Techniques for Detecting Hibernating Myocardium

## Introduction

**D**ata from large clinical trials have indicated that improvement in survival after revascularization occurs in subgroups of patients presenting with multivessel coronary artery disease (CAD) and left ventricular (LV) dysfunction.<sup>1,2</sup> However, it is not known if this is a result of improvement or normalization of LV dysfunction present at rest, from reduction of ischemia and subsequent myocardial infarction, or both mechanisms.<sup>3</sup> It is estimated that 25% to 40% of the patients with ischemic LV dysfunction may have improved LV ejection fraction (LVEF) after revascularization.<sup>4</sup> Improvement of LV systolic dysfunction is clinically important because LVEF is a major determinant of survival in patients with CAD, in particular in patients with severely depressed LVEF.<sup>5</sup> On the other hand, these patients are at high risk for events during or after the revascularization procedure.<sup>6</sup> Thus accurate identification of patients with potentially reversible LV dysfunction is important in the clinical decision making to recommend revascularization.

Several noninvasive techniques have been developed to identify viable myocardium in the dysfunctional segments.<sup>7-11</sup> Each of these techniques focuses on a different aspect of viable myocardium. Most experience has been obtained with dobutamine echocardiography (DE) and radionuclide imaging using fluorine 18 deoxyglucose (FDG), thallium 201 chloride, or technetium 99m-labeled tracers.<sup>7-11</sup> The sensitivities/specificities of these different modalities are useful in deciding which test(s) should be obtained. On the other hand, the predictive accuracies of a positive and negative test result are of value in deciding whether to recommend revascularization after the results of these tests are available. Accordingly, the aim of the present analysis was to perform a pooled analysis of the currently available studies in the literature to determine and compare the sensitivities, specificities, positive predictive value (PPV), and negative predictive value (NPV) to predict improvement of regional LV function after revascularization) of the 5 most frequently used techniques, namely DE, single photon

**TABLE 1a.** Studies that used improvement of wall motion during low-dose DE as criterion for viability.

Reference	No. of Patients	% Male	Mean age (y)	Mean LVEF (%) (SD)
Gerber et al <sup>12</sup>	39	87	60	33 (±10)
Charney et al <sup>13</sup>	17	59	63	46 (±9)
Arnese et al <sup>14</sup>	38	68	59	31 (NA)
Perrone-Filardi et al <sup>15</sup>	18	NA	NA	NA
Vanoverschelde et al <sup>16</sup>	73	85	59	36 (±12)
Marzullo et al <sup>17</sup>	14	79	54	39 (±7)
Bax et al <sup>18</sup>	17	82	57	36 (±11)
Senior et al <sup>19</sup>	22	95	61	26 (±8)
Perrone-Firaldi <sup>20</sup>	18	94	59	43 (±12)
Alfieri et al <sup>21</sup>	14	100	52	35 (±8)
La Canna et al <sup>22</sup>	33	97	56	33 (±8)
Haque et al <sup>23</sup>	26	81	55	43 (±14)
Baer et al <sup>24</sup>	42	90	59	40 (± 13)
DeFilippi et al <sup>25</sup>	23	100	NA	38 (±10)
Elhendy et al <sup>26</sup>	42	79	59	39 (± 14)
Kostopoulos et al <sup>27</sup>	31	84	48	41 (± 6)
Cornel et al <sup>28</sup>	30	83	61	35 (±10)
Sconamiglio et al <sup>29</sup>	60	90	58	48 (±10)
Pagano et al <sup>30</sup>	30	87	57	25 (±7)
Baer et al <sup>31*</sup>	43	93	58	42 (± 10)
Voci et al <sup>32</sup>	30	93	56	NA
Picano et al <sup>33†</sup>	34	88	55	43 (± 12)
Elhendy et al <sup>34</sup>	28	NA	NA	NA
Cornel et al <sup>35</sup>	91	80	60	32 (±11)
Pace et al <sup>36</sup>	46	97	59	40 (±11)
Sayad et al <sup>37*</sup>	10	70	NA	NA
Sicari <sup>38†</sup>	57	89	60	31 (±11)
Gunning et al <sup>39*‡</sup>	30	90	61	24 (±8)

CABG, Coronary artery bypass grafting; MI, myocardial infarction; MRI, magnetic resonance imaging; MVD, multivessel disease; PTCA, percutaneous transluminal coronary angioplasty; RNV, radionuclide ventriculography; RWM, regional wall motion; NA, not available.

\*Magnetic resonance imaging instead of echocardiography.

†Thirty patients with follow-up/revascularization.

‡Twenty-three patients completed the study.

emission computed tomography (SPECT) using <sup>201</sup>Tl RR or <sup>201</sup>Tl RI, <sup>99m</sup>Tc-labeled sestamibi (MIBI), and positron emission tomography (PET) with FDG.

## Methods

A MEDLINE search (1980 through January 2000) was performed using the search term “myocardial viability” in combination with a set of terms for the techniques: “Thallium-201 rest-redistribution,” “Thallium-201 reinjection,” “technetium-99m Sestamibi,” “technetium-99m Tetrofos-

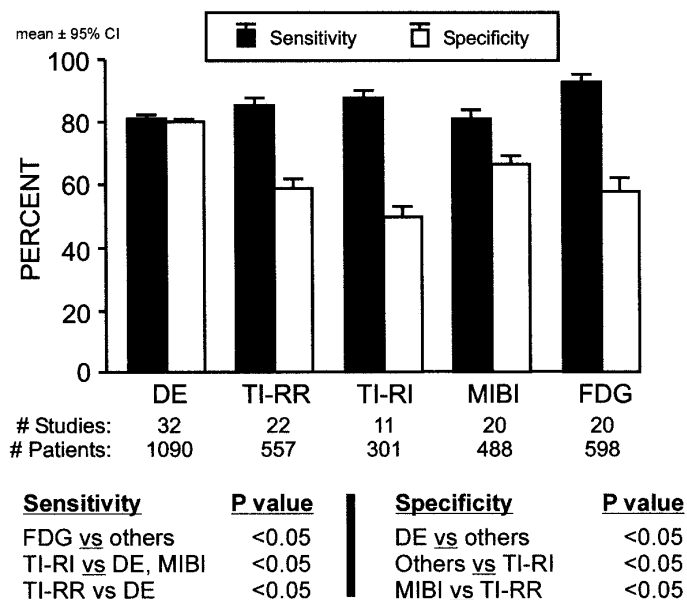
(%) Patients with MVD	PTCA/ CABG	Patients with MI (%)	Segments with recovery (%)	Technique to assess RWM after revascularization
85	0/100	59	62	Echo, 5 ± 1.9 mo
76	29/71	65	53	Echo, 7 ± 3 d
92	0/100	100	22	Echo, 3 mo
NA	61/39	NA	69	Echo, 43 ± 39 d
79	30/70	68	38	Echo/RNV, 5.5 ± 2.5 mo
93	36/64	100	65	Echo, 11 ± 2 wk
100	0/100	100	29	Echo, 3 mo
86	14/86	NA	70	Echo, 9 ± 1 wk
50	61/39	89	61	Echo, 34 ± 10 d
NA	0/100	NA	82	Echo, 12 mo
94	0/100	70	65	Echo, 3 mo
56	96/4	88	77	Echo, 3 mo
74	48/52	100	62	Echo, 4-6 mo
NA	43/57	NA	61	Echo, 30-60 d
86	0/100	100	16	Echo, 3 mo
NA	39/61	100	45	Echo, 97 ± 12 d
77	0/100	100	37	Echo, 3 mo
100	0/100	58	54	Echo, 4-6 wk
100	0/100	100	57	Echo, 6 mo
70	51/49	100	46	MRI, 4-6 mo
100	0/100	60	NA	Echo, 1 mo
47	74/26	100	57	Echo, 7 ± 4 wk
NA	0/100	100	23	Echo, 3 mo
91	8/92	100	28	Echo, 3 mo
65	46/54	97	50	Echo, 40 ± 10 d
NA	NA	NA	65	MRI, 4-8 wk
89	73/27	88	56	Echo, 7 ± 3 wk
100	0/100	100	40	MRI, 3-6 mo

min,” “Dobutamine echocardiography,” and “FDG.” Next, referenced studies used by the selected articles and a hand search of 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, Journal of Nuclear Medicine, and the Journal of Nuclear Cardiology*) from 1980 through January 2000 was performed to ensure that all relevant studies were included. All articles were reviewed. The following criteria were used for inclusion in the pooled data: (1)

**TABLE 1b.** Sensitivity, specificity, PPV, and NPV for low-dose DE to detect functional recovery after revascularization (925 patients, 28 studies)

Reference	Sensitivity (%) (segments)	Specificity (%) (segments)	PPV (%) (segments)	NPV (%) (segments)
Gerber et al <sup>12</sup>	71 (17/24)	89 (13/15)	89 (17/19)	65 (13/20)
Charney et al <sup>13</sup>	71 (22/31)	93 (25/27)	92 (22/24)	74 (25/34)
Arnese et al <sup>14</sup>	74 (28/38)	96 (127/132)	85 (28/33)	93 (127/137)
Perrone-Filardi et al <sup>15</sup>	79 (58/73)	83 (30/36)	91 (58/64)	67 (30/45)
Vanoverschelde et al <sup>16</sup>	79 (211/267)	80 (340/425)	71 (211/296)	86 (340/396)
Marzullo et al <sup>17</sup>	82 (40/49)	94 (24/26)	95 (40/42)	73 (24/33)
Bax et al <sup>18</sup>	85 (23/27)	63 (41/65)	49 (23/47)	91 (41/45)
Senior et al <sup>19</sup>	87 (103/118)	82 (41/50)	92 (103/112)	73 (41/56)
Perrone-Filardi <sup>20</sup>	88 (42/48)	87 (27/31)	88 (42/48)	87 (27/31)
Alferi et al <sup>21</sup>	91 (85/93)	78 (25/32)	92 (85/92)	76 (25/33)
La Canna et al <sup>22</sup>	92 (164/179)	75 (101/135)	87 (164/188)	87 (101/116)
Haque et al <sup>23</sup>	94 (31/33)	80 (8/10)	94 (31/33)	80 (8/10)
Baer et al <sup>24</sup>	96 (25/26)	69 (11/16)	83 (25/30)	92 (11/12)
DeFilippi et al <sup>25</sup>	97 (94/97)	75 (41/55)	87 (94/108)	93 (41/44)
Elhendy et al <sup>26</sup>	58 (15/26)	94 (130/138)	65 (15/23)	92 (130/141)
Kostopoulos et al <sup>27</sup>	86 (64/74)	94 (85/90)	93 (64/69)	89 (85/95)
Cornel et al <sup>28</sup>	89 (55/62)	82 (87/106)	74 (55/74)	93 (87/94)
Sconamiglio et al <sup>29</sup>	84 (348/414)	81 (279/345)	84 (348/414)	81 (279/345)
Pagano et al <sup>30</sup>	61 (117/192)	63 (90/144)	68 (117/171)	55 (90/165)
Baer et al <sup>31</sup>	82 (155/188)	81 (177/219)	79 (155/197)	84 (177/210)
Voci et al <sup>32</sup>	91 (NA)	93 (NA)	97 (NA)	79 (NA)
Picano et al <sup>33</sup>	95 (59/62)	92 (58/63)	92 (59/64)	95 (58/61)
Elhendy et al <sup>34</sup>	71 (30/42)	90 (130/144)	68 (30/44)	92 (130/142)
Cornel et al <sup>35</sup>	92 (159/173)	62 (278/449)	8 (159/330)	5 (278/292)
Pace et al <sup>36</sup>	52 (24/46)	87 (40/46)	80 (24/30)	65 (40/62)
Sayad et al <sup>37</sup>	89 (25/28)	93 (14/15)	96 (25/26)	82 (14/17)
Sicari et al <sup>38</sup>	82 (103/126)	93 (92/99)	94 (103/110)	80 (92/115)
Gunning et al <sup>39</sup>	50 (41/82)	81 (101/125)	63 (41/65)	71 (101/142)
Weighted mean	82 (2138/2618)	79 (2415/3038)	78 (2138/2753)	83 (2415/2893)

prospective studies in patients with chronic CAD who underwent revascularization, (2)  $\geq 1$  of the 5 aforementioned techniques had to be evaluated, and (3) the results had to allow assessment of the sensitivity, specificity, PPV, and NPV of the technique(s) tested. Studies were excluded if they (1) evaluated  $\geq 1$  of the 5 aforementioned techniques in patients who did not undergo revascularization; (2) included patients with acute ischemic coronary syndromes (unstable angina or acute myocardial infarction); and (3) did not allow assessment of the sensitivity, specificity, PPV, and NPV to predict improvement of regional LV function after revascularization. From the pooled data, weighted sensi-



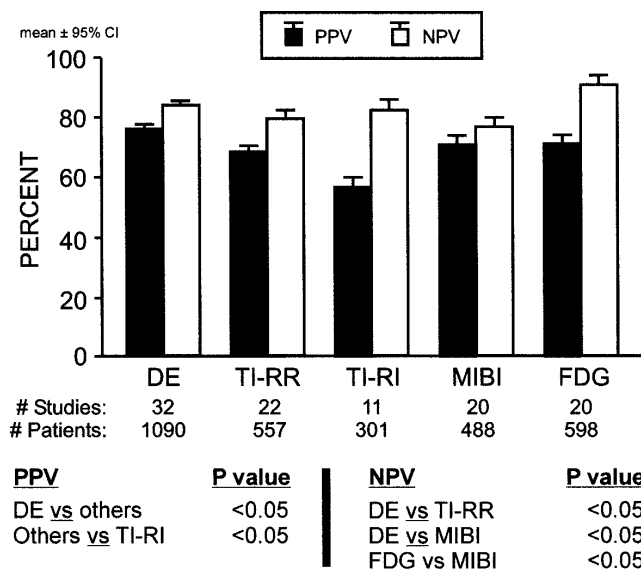
**FIG 1.** The sensitivities (black bars) and specificities (white bars) of the different techniques, presented with their 95% CIs.

tivities (test-viable segments/segments with recovery after revascularization), specificities (test-nonviable segments/segments without recovery after revascularization), PPV (segments with recovery after revascularization/test-viable segments), and NPV (segments without recovery after revascularization/test-nonviable segments) were calculated. The 95% confidence intervals (CIs) were also calculated ( $p \pm 1.96 \times \sqrt{\{p \times (1-p)/n\}}$ , with  $p$  representing the fraction and  $n$  representing the total population). The 95% CIs for the different techniques were compared and differences between techniques were considered significant ( $P < .05$ ) when the 95% CIs did not overlap.

## Results

A total of 850 references were identified using the different search strategies, with only 77 articles meeting the inclusion/exclusion criteria. The results of the pooled analysis of these 77 studies are shown in Figures 1 to 4 and are summarized in Tables 1 to 10; other details of the studies regarding protocol, criteria of viability, and analyses are shown in Appendices 1 to 5. In addition to the data from these studies, many other aspects of the different studies are also presented.

**Dobutamine echocardiography.** Twenty-nine studies used DE and 3 used

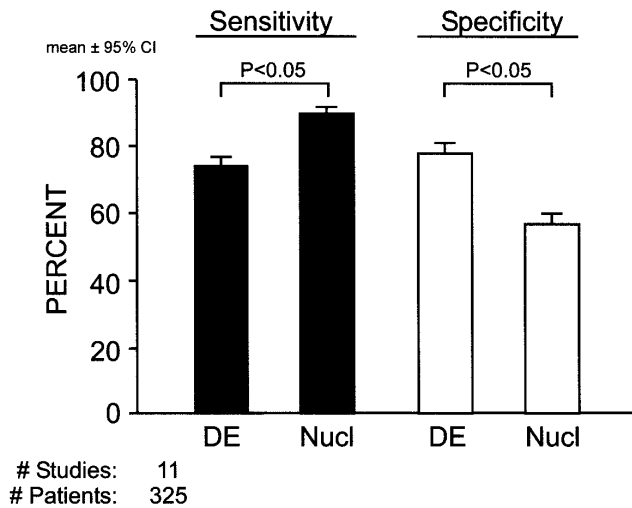


**FIG 2.** The positive (PPV, black bars) and negative predictive values (NPV, white bars) of the different techniques, presented with their 95% CIs.

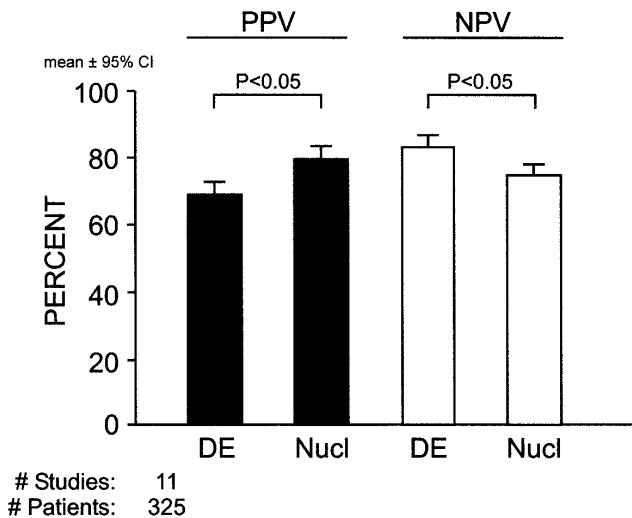
dobutamine magnetic resonance imaging to predict functional outcome after revascularization (total of 1090 patients; Tables 1a, 1b, 2a, and 2b). In these studies, the mean sensitivity and specificity were 81% and 80%, whereas the PPV and NPV were 77% and 85%. The exact protocols (infusion steps, stage duration, image analysis) varied among the different studies and some of the details of each study are summarized in Appendix 1.

In 28 studies the presence of contractile reserve (improvement of wall motion and/or thickening at low-dose DE) was used to assess myocardial viability (1 of these studies used a combination infusion of low-dose and dipyridamole 0.28 mg/kg over 4 minutes). Four studies used a high-dose dobutamine protocol. With this protocol 4 response patterns of wall motion can be observed: (1) biphasic response (initial improvement followed by worsening of wall motion), (2) worsening (immediate deterioration of wall motion without initial improvement), (3) sustained improvement (improvement during dobutamine infusion without subsequent worsening), and (4) no change (unchanged wall motion abnormalities during the entire test). Two studies considered the biphasic response and worsening as indicators of viable myocardium, whereas 2 studies considered the biphasic response as the single marker for viability.

**<sup>201</sup>Tl imaging.** Twenty-two studies (557 patients) in which a <sup>201</sup>Tl RR protocol were selected (Tables 3a and 3b, Appendix 2). The mean sensi-



**FIG 3.** The sensitivities and specificities of dobutamine echocardiography (DE) and nuclear techniques (Nucl) in studies that have performed a direct comparison in the same patients.



**FIG 4.** The positive (PPV) and negative predictive values (NPV) of dobutamine echocardiography (DE) and nuclear techniques (Nucl) in studies that have performed a direct comparison in the same patients.

tivity and specificity were 86% and 59%; the mean PPV and NPV were 69% and 80%. Four studies used planar imaging, 15 SPECT, and 1 study used planar imaging and SPECT; in 2 studies the camera system was not described. Twenty studies used the conventional rest and 3- to 4-hour delayed protocol; 2 studies used 24-hour delayed imaging. Two studies

**TABLE 2a.** Studies that used HDDE to assess viability

Reference	No. of patients	% Male	Mean age (y)	Mean LVEF (%) (SD)
Afridi et al <sup>40</sup>	20	85	60	NA
Qureshi et al <sup>41</sup>	34	NA	61	NA
Nagueh et al <sup>42*</sup>	19	NA	57	38 (± 13)
Cornel et al <sup>43</sup>	61	80	61	33 (NA)

LDDE, Low-dose dobutamine echocardiography; HDDE, high-dose dobutamine echocardiography; all other abbreviations as in Table 1a.

\*Eighteen patients underwent revascularization.

**TABLE 2b.** Sensitivity, specificity, PPV, and NPV for HDDE to detect functional recovery after revascularization (134 patients, 4 studies)

Reference	Sensitivity (%) (segments)	Specificity (%) (segments)	PPV (%) (segments)	NPV (%) (segments)
Afridi et al <sup>40</sup>	76 (29/38)	74 (56/76)	59 (29/49)	86 (56/65)
Qureshi et al <sup>41</sup>	76 (32/42)	82 (87/106)	63 (32/51)	90 (87/97)
Nagueh et al <sup>42*</sup>	68 (23/34)	83 (49/59)	70 (23/33)	82 (49/60)
Cornel et al <sup>43</sup>	83 (140/169)	89 (322/362)	75 (140/186)	92 (322/351)
Weighted mean	79 (244/283)	85 (514/603)	70 (224/319)	90 (514/573)
Weighted mean for all DE (LDDE + HDDE) studies	81 (2362/2901)	80 (2929/3641)	77 (2362/3072)	85 (2929/3466)

LDDE, Low-dose dobutamine echocardiography; HDDE, high-dose dobutamine echocardiography.

\*Eighteen patients underwent revascularization.

used visual analysis, and the remaining 20 studies used a semiquantitative approach, with 3 using normal reference values and the other studies using normalization to the segment with maximum <sup>201</sup>Tl uptake.

The viability criteria were as follows: 2 studies used defect reversibility (redistribution) as the indicator of viable myocardium, 11 studies used a cutoff level of <sup>201</sup>Tl activity (varying from 50% to 75%) on the delayed image, and 9 studies used the combination of reversibility, a cutoff level of <sup>201</sup>Tl activity on the delayed image, or both.

Eleven studies (301 patients) using a reinjection (RI) protocol fulfilled the inclusion/exclusion criteria (Tables 4a and 4b, Appendix 3). The mean sensitivity and specificity were 88% and 50%, and the mean PPV and NPV were 57% and 83%. All but one study used SPECT for the image acquisition. Eight studies used the <sup>201</sup>Tl RI protocol, while 3 studies used a stress-RI protocol (thus omitting the redistribution acquisition). Three studies used visual analysis, and the remaining 8 studies used a semiquantitative approach, with 7 using normalization to maximum tracer uptake and 1 using normal reference values.

The viability criteria were as follows: 4 studies used defect reversibility

No. of patients with MVD	PTCA/CABG	No. of patients with MI	Segments with recovery (%)	Technique to assess RWM after revascularization
40	100/0	55	33	Echo, 7 ± 2 wk
76	82/18	56	69	Echo, >6 wk
42	89/11	58	42	Echo, >6 wk
97	0/100	97	46	RNV, 14 mo

(redistribution) as a marker of viable tissue, and 7 used the combination of the activity on the (redistribution or) RI image and/or the presence of reversibility as the criterium for viable tissue.

**<sup>99m</sup>Tc-labeled tracers.** Twenty studies (488 patients) using <sup>99m</sup>Tc-ses-tamibi were selected (3 of these studies used <sup>99m</sup>Tc-tetrofosmin) (Tables 5a, 5b, 6a, and 6b; Appendix 4). The mean sensitivity and specificity were 81% and 66%, and the mean PPV and NPV were 71% and 77%. Three studies used planar imaging and 17 used SPECT. Thirteen studies were performed without the addition of nitrates; 11 of these studies used a resting study and 2 used the combination of a rest and a stress study (1-day rest/stress and 2-day stress/rest protocol).

Seven studies were performed with the addition of nitrates (intravenous or orally). Five studies used visual analysis and 15 used a semiquantitative approach (with normalization to the segment with maximum tracer uptake).

The viability criteria on the 13 studies without nitrates were as follows: 1 study used reversibility (redistribution) as a marker of viable tissue, and 12 used a cutoff level of activity on the resting image (varying from 50% to 65%). On the 7 studies with nitrates the viability criteria were reversibility on the “nitrate image” or decrease of defect extent/severity on the “nitrate image” in 4, activity on the “nitrate image” in 1, and a combination of both criteria in 2 studies.

**FDG PET.** Twenty studies fulfilling the inclusion criteria were selected. These studies included a total of 598 patients. The details of the studies are presented in Tables 7a and 7b and Appendix 5. The mean sensitivity and specificity were 93% and 58%, and the mean PPV and NPV were 71% and 86%.

The metabolic circumstances varied in the different studies. Nine studies were performed after oral glucose loading, 5 during hyperinsulinemic euglycemic clamping, and 5 with patients in the fasting state.

Different protocols were used: 4 studies used FDG alone without a flow

**TABLE 3a.** Studies that used rest-redistribution to assess viability

Reference	No. of patients	% Male	Mean age (y)	Mean LVEF (%) (SD)
Mori et al <sup>44</sup>	17	82	62	37 (±7)
Marzullo et al <sup>17</sup>	14	79	54	39 (±7)
Udelson et al <sup>45</sup>	18	72	67	34 (±10)
Qureshi et al <sup>41</sup>	34	NA	61	39 (±14)
Ragosta et al <sup>46</sup>	21	86	64	27 (±5)
Alfieri et al <sup>21</sup>	13	100	52	35 (±8)
Charney et al <sup>13</sup>	14	NA	NA	NA
Perrone-Filardi <sup>15</sup>	18	NA	NA	NA
Nagueh et al <sup>42*</sup>	19	NA	57	38 (±13)
Matsunari et al <sup>47</sup>	25	NA	NA	42 (±8)
Cuocolo et al <sup>48</sup>	38	92	56	39 (±9)
Bax et al <sup>49</sup>	32	84	65	42 (±14)
Sciagra et al <sup>50</sup>	35	94	58	36 (±8)
Marzullo et al <sup>51</sup>	22	86	57	44 (±13)
Matsunari et al <sup>52</sup>	14	NA	64	41 (±8)
Sciagra et al <sup>53</sup>	29	93	60	35 (±7)
Bax et al <sup>54</sup>	24	88	65	45 (±14)
Pace et al <sup>36</sup>	46	96	59	40 (±11)
Senior et al <sup>19</sup>	22	95	61	26 (±8)
Gunning et al <sup>39†</sup>	30	90	61	24 (±8)
Gunning et al <sup>55</sup>	15	93	61	23 (±8)
Sicari et al <sup>38‡</sup>	57	89	60	31 (±11)

See Table 1a for abbreviations.

\*Eighteen patients underwent revascularization.

†Twenty-three patients completed the study.

‡Thirty patients underwent revascularization.

tracer, and the remaining studies compared the FDG data with myocardial blood flow (assessed by <sup>13</sup>N-ammonia in 8 studies, rubidium 82 in 2, and <sup>201</sup>Tl or <sup>99m</sup>Tc-sestamibi (SPECT tracers) in 4 studies. Absolute quantitation was used in 5 studies, semiquantitative analysis in 11, and visual analysis in 3.

The criteria for viability were a mismatch pattern in 15 studies, normal perfusion in 5 studies, and a cutoff level of regional myocardial glucose utilization/percentage FDG uptake in 7.

**Direct comparisons between nuclear imaging and DE.** A total of 18 studies, including 563 patients, performed a direct comparison between a nuclear technique and low-dose DE (Tables 8a and 8b). In 3 studies FDG PET was compared with DE, and in the remaining studies <sup>201</sup>Tl imaging (RI protocol in 5, rest/redistribution [RR] protocol in 10) was compared with DE (low-/high-dose protocol in 2 studies). The pooled results indicate that the nuclear techniques had a higher sensitivity and NPV, whereas

<b>Patients with MVD (%)</b>	<b>PTCA/CABG</b>	<b>No. of patients with MI</b>	<b>% of segments with recovery</b>	<b>Technique to assess after revascularization</b>
52	71/29	100	51	RNV, 1.5 mo
93	36/63	100	65	Echo, 11 ± 2 wk
NA	33/67	100	37	Echo, 20 ± 16 d
76	82/18	56	28	Echo, >6 wk
100	0/100	76	51	RNV, 64 ± 23 d
NA	0/100	NA	82	Echo, 12 mo
NA	29/71	NA	61	Echo, 7 ± 3 d
NA	61/39	NA	69	Echo, 43 ± 39 d
42	89/11	58	42	Echo, >6 wk
NA	36/64	NA	62	RNV, 24-135 d
92	39/61	100	63	RNV/echo, 14 ± 4 mo
88	31/69	91	37	Echo, 3 mo
71	54/46	100	54	Echo, 1-3 mo
91	41/59	100	56	Echo, 11 ± 2 wk
NA	14/86	71	53	RNV, 8 wk
62	66/34	100	54	Echo, 1-3 mo
88	29/71	88	34	Echo, 3 mo
65	46/54	85	50	Echo, 40 ± 20 d
86	14/86	NA	70	Echo, 9 ± 1 wk
100	0/100	100	40	MRI, 3-6 mo
100	0/100	100	42	MRI, 3-6 mo
89	73/27	88	56	Echo, 7 ± 3 wk

DE had a higher specificity and PPV.

The analysis of the findings between nuclear imaging and DE was repeated when the nuclear studies with a stress component ( $^{201}\text{Tl}$  RI studies) were deleted (because they combine information on viability and stress-induced ischemia) and the low-/high-dose dobutamine studies were deleted (because they also combine information on viability and stress-induced ischemia). By restricting the analysis, the sensitivities of DE and nuclear imaging were 74% and 90% ( $P < .05$ ), and the specificities were 57% and 80% ( $P < 0.05$ , Figure 3); and the PPV of DE and nuclear imaging were 84% and 75% ( $P < .05$ ), respectively; and the NPV of DE and nuclear imaging were 69% and 80% ( $P < .05$ ), respectively (Figure 4).

**Comparison of the techniques.** The sensitivities, specificities, PPV, and NPV with their 95% CIs for the different techniques are summarized in Tables 9 and 10 and Figures 1 and 2. FDG PET had the highest sensitivity ( $P < .05$  vs other techniques), followed by the other nuclear techniques

**TABLE 3b.** Sensitivity, specificity, PPV, and NPV of <sup>201</sup>Tl rest-redistribution imaging to detect improvement in regional contractile function after revascularization (557 patients, 22 studies)

Reference	Sensitivity (%) (segments)	Specificity (%) (segments)	PPV (%) (segments)	NPV (%) (segments)
Mori et al <sup>44</sup>	44 (11/25)	88 (23/26)	79 (11/14)	62 (23/37)
Marzullo et al <sup>17</sup>	86 (42/49)	92 (24/26)	95 (42/44)	77 (24/31)
Udelson et al <sup>45</sup>	88 (15/17)	83 (24/29)	75 (15/20)	92 (24/26)
Qureshi et al <sup>41</sup>	90 (38/42)	56 (59/106)	45 (38/85)	94 (59/63)
Ragosta et al <sup>46</sup>	93 (81/89)	31 (27/87)	57 (81/141)	77 (27/35)
Alfieri et al <sup>21</sup>	94 (92/98)	64 (14/22)	92 (92/100)	70 (14/20)
Charney et al <sup>13</sup>	95 (19/20)	85 (11/13)	90 (19/21)	92 (11/12)
Perrone-Filardi et al <sup>15</sup>	100 (73/73)	22 (8/36)	72 (73/101)	100 (8/8)
Nagueh et al <sup>42</sup>	91 (42/46)	43 (27/63)	54 (42/78)	87 (27/31)
Matsunari et al <sup>47</sup>	92 (45/49)	33 (10/30)	69 (45/65)	71 (10/14)
Cuocolo et al <sup>48</sup>	94 (116/124)	48 (35/73)	75 (116/154)	81 (35/43)
Bax et al <sup>49</sup>	89 (51/57)	56 (55/99)	49 (51/105)	90 (55/61)
Sciagra et al <sup>50</sup>	70 (21/30)	65 (17/26)	70 (21/30)	65 (17/26)
Marzullo et al <sup>51</sup>	91 (50/55)	74 (37/50)	79 (50/63)	88 (37/42)
Matsunari et al <sup>52</sup>	93 (25/27)	54 (13/24)	69 (25/36)	87 (13/15)
Sciagra et al <sup>53</sup>	78 (90/115)	58 (57/99)	68 (90/132)	70 (57/82)
Bax et al <sup>54</sup>	67 (24/36)	79 (55/70)	62 (24/39)	82 (55/67)
Pace et al <sup>36</sup>	76 (35/46)	74 (34/46)	74 (35/47)	76 (34/45)
Senior et al <sup>19</sup>	92 (108/118)	78 (39/50)	91 (108/119)	80 (39/49)
Gunning et al <sup>39</sup>	72 (59/82)	58 (73/125)	53 (59/111)	76 (73/96)
Gunning et al <sup>55</sup>	71 (39/55)	64 (49/77)	58 (39/67)	75 (49/65)
Sicari et al <sup>38</sup>	87 (110/126)	61 (60/99)	74 (110/149)	79 (60/76)
Weighted mean	86 (1186/1379)	59 (751/1276)	69 (1186/1730)	80 (751/944)

(<sup>201</sup>Tl RR, <sup>201</sup>Tl RI, MIBI), whereas DE had the lowest sensitivity ( $P < .05$  vs other techniques, except MIBI). The highest NPV was observed for FDG PET, followed by DE, followed by the other nuclear imaging techniques. Specificity was highest for DE ( $P < .05$  vs other techniques), followed by FDG PET, <sup>201</sup>Tl RR, and MIBI; the lowest specificity was observed for <sup>201</sup>Tl RI ( $P < .05$  vs other techniques). The highest PPV was observed for DE ( $P < .05$  vs other techniques), followed by FDG PET, <sup>201</sup>Tl RR, and MIBI, and the lowest PPV was observed for <sup>201</sup>Tl RI ( $P < .05$  vs other techniques).

## Discussion

The current analysis showed that the highest sensitivity was observed for FDG PET, followed by the other nuclear imaging techniques, whereas the lowest sensitivity was observed by DE. Specificity was highest for DE, followed by FDG PET, <sup>201</sup>Tl RR, and MIBI, whereas the lowest specificity was observed for <sup>201</sup>Tl RI; however, the differences that were statistically significant (Tables 9 and 10, Figure 1).

The highest NPV was observed for FDG PET, followed by DE, fol-

lowed by the other nuclear imaging techniques. The highest PPV was observed for DE, followed by FDG PET,  $^{201}\text{Tl}$  RR, and MIBI, and the lowest PPV was observed for  $^{201}\text{Tl}$  RI (Tables 9 and 10, Figure 2).

In absolute figures, for all tests the NPVs and sensitivities were better than the PPVs and specificities.

### *Lower PPVs and Specificities*

The lower PPVs and specificities are caused by a substantial number of “test-viable” segments that do not improve in function after revascularization. There are several possible explanations for these findings:

1. *Vessel or graft patency.* Very few studies evaluated vessel or graft patency by coronary angiography. Hence, restenosis, reocclusion, or progression of disease cannot be ruled out. Viable segments located in these territories may not recover in function despite the presence of viable myocardium. Also, incomplete revascularization of viable segments may have prevented viable segments from revascularization recovery.
2. *Timing of assessment of recovery of function.* The majority of the studies had only a limited follow-up; the timing of assessment of function varied from 7 days to 14 months. Very early assessment of function postoperatively may be influenced by the presence of postsurgical stunning,<sup>88</sup> and thus prevented recovery of function. The exact duration of postsurgical stunning is not known but has been reported up to 7 days after coronary bypass surgery.<sup>89</sup> Therefore early assessment of function after revascularization may not be theoretically ideal. In most studies, functional outcome was evaluated within 6 months after revascularization. Two studies, however, have demonstrated that delayed recovery may occur up to 12 to 14 months after revascularization.<sup>21,43</sup> Cornel et al<sup>43</sup> have recently studied the time course of functional recovery after revascularization in patients with severely depressed LV function. The patients underwent a radionuclide ventriculography at 3 months and 14 months after revascularization. The LVEF improved from  $32\% \pm 8\%$  to  $37\% \pm 12\%$  at 3 months with a further improvement to  $42\% \pm 9\%$  at 14 months. Thus, although most of the patients exhibit functional recovery at 3 months after revascularization, a substantial additional improvement occurs late after revascularization. It is possible that different degrees of myocardial damage are responsible for this variation in recovery time. Severely damaged myocardium from long-standing hibernation may need longer time to recover in function after restoration of adequate perfusion.<sup>90,91</sup>

**TABLE 4a.** Studies that used stress-rest-redistribution to assess viability

Reference	No. of patients	% Male	Mean age (y)	Mean LVEF (%) (SD)
Vanoverschelde <sup>16</sup>	73	85	59	36 (±12)
Ohtani et al <sup>56</sup>	24	75	62	NA
Arnese et al <sup>14</sup>	38	68	59	31 (NA)
Bax et al <sup>18</sup>	17	82	57	36 (±11)
Tamaki et al <sup>57</sup>	11	NA	NA	NA
Dilsizian et al <sup>58</sup>	20	88	58	NA
Haque et al <sup>23</sup>	26	81	55	43 (±14)
Taki et al <sup>59</sup>	34	88	60	49 (±9)
Lipiecki et al <sup>60</sup>	15	93	53	41 (±10)
Gürsürer et al <sup>61</sup>	12	83	58	32 (±3)
Kostopoulos et al <sup>27</sup>	31	84	48	41 (±6)

See Table 1a for abbreviations.

**TABLE 4b.** Sensitivity, specificity, PPV, and NPV of <sup>201</sup>Tl reinjection imaging to detect improvement in regional contractile function after revascularization (301 patients, 11 studies)

Reference	Sensitivity (%) (segments)	Specificity (%) (segments)	PPV (%) (segments)	NPV (%) (segments)
Vanoverschelde et al <sup>16</sup>	80 (213/267)	47 (198/425)	48 (213/440)	79 (198/252)
Ohtani et al <sup>56</sup>	89 (33/37)	50 (12/24)	73 (33/45)	75 (12/16)
Arnese et al <sup>14</sup>	89 (34/38)	48 (63/132)	30 (34/113)	94 (63/67)
Bax et al <sup>18</sup>	93 (25/27)	43 (28/65)	40 (25/62)	93 (28/30)
Tamaki et al <sup>57</sup>	95 (38/40)	38 (6/16)	79 (38/48)	75 (6/8)
Dilsizian et al <sup>58</sup>	95 (35/37)	80 (8/10)	95 (35/37)	80 (8/10)
Haque et al <sup>23</sup>	100 (33/33)	40 (4/10)	85 (33/39)	100 (4/4)
Taki et al <sup>59</sup>	33 (2/6)	72 (13/18)	29 (2/7)	76 (13/17)
Lipiecki et al <sup>60</sup>	93 (37/40)	66 (46/70)	61 (37/61)	78 (46/59)
Gürsürer et al <sup>61</sup>	99 (80/81)	16 (3/19)	83 (80/96)	75 (3/4)
Kostopoulos et al <sup>27</sup>	91 (67/74)	69 (62/90)	71 (67/95)	90 (62/69)
Weighted mean	88 (597/680)	50 (443/879)	57 (597/1043)	83 (443/536)

3. *Myocardial ischemia/injury during the study.* Injury or ischemia during the study period may affect improvement of function after revascularization. All studies excluded patients with a recent myocardial infarction or an episode of unstable angina (mostly within 1 month) before inclusion in the study protocol. Furthermore, nearly all studies have excluded patients with myocardial infarction during the revascularization, and the patients with an event before functional follow-up were also excluded. Still, ischemia (or necrosis) before, during, or after revascularization may have occurred and may have resulted in failure of improvement in function of viable segments. Also, the duration of existence of

<b>% Patients with MVD</b>	<b>PTCA/CABG</b>	<b>% Patients with MI</b>	<b>% of segments with recovery</b>	<b>Technique to assess RWM after revascularization</b>
79	30/70	68	38	RNV/Echo, 5.5 ± 2.5 mo
100	0/100	58	61	RNV, 4-8 wk
92	0/100	100	22	Echo, 3 mo
100	0/100	100	29	Echo, 3 mo
NA	0/100	NA	71	RNV, NA
61	100/0	NA	57	RNV, 3-6 mo
56	96/4	88	77	Echo, 3 mo
44	68/32	41	75	Echo/RNV, 18 ± 10 d
0	100/0	100	42	RNV, 2 mo
100	0/100	100	81	RNV, 8 wk
NA	39/61	100	45	Echo, 97 ± 12 d

hibernation before the revascularization may influence outcome. It was originally postulated that that necrosis could occur if an unfavorable balance between myocardial oxygen supply/need occurred after onset of hibernation.<sup>92</sup> Thus those with longer duration of hibernation may have areas of necrosis that will not recover after revascularization. Schwarz et al<sup>93</sup> have demonstrated that postoperative recovery was more favorable in patients with a short history of hibernation compared with patients with chronic hibernation.

4. *Severity of remodeling before revascularization.* It is plausible that the presence of severe remodeling or ventricular dilatation before revascularization does not allow recovery of function after revascularization, even if viable tissue is present. Currently, no data are available to substantiate this hypothesis. Gerber et al,<sup>94</sup> however, have demonstrated that patients with recovery of function after revascularization had significantly lower end-systolic and end-diastolic volumes.
5. *Improvement of resting function versus stress function.* Nearly all currently available studies have used improvement of resting LV function as the endpoint after revascularization. Although resting dysfunction may not improve in all patients with viable tissue, Afridi et al<sup>89</sup> showed that some of these patients had alleviation of stress-inducible ischemia after revascularization, which is not surprising. However, for assessment of improvement of LV dysfunction that is present at rest, only improvement at rest should be used.
6. *Impact of subendocardial scar.* Most techniques have been shown to be less accurate in segments with hypokinesia.<sup>16,35</sup> Many hypokinetic segments may represent a mixture of normal, viable epicardial

**TABLE 5a.** <sup>99m</sup>Tc-sestamibi scintigraphy studies without the addition of nitrates to assess viability

Reference	No. of patients	% Male	Mean age (y)	Mean LVEF (%) (SD)
Marzullo et al <sup>51</sup>	22	86	57	44 (±13)
Marzullo et al <sup>17</sup>	14	79	54	39 (±7)
Gonzalez et al <sup>62</sup>	36	89	57	52 (±15)
Marzullo et al <sup>63</sup>	14	93	55	43 (±9)
Maes et al <sup>64</sup>	23	NA	NA	40 (±13)
Udelson et al <sup>45</sup>	18	72	67	34 (±10)
Maublant et al <sup>65</sup>	25	92	62	52 (±15)
Matsunari et al <sup>47*</sup>	25	NA	NA	42 (±8)
Dakik et al <sup>66</sup>	21	90	63	41 (±13)
Lipiecki et al <sup>60</sup>	15	93	53	41 (±10)
Levine et al <sup>73</sup>	50	76	61	39 (±12)
Gunning et al <sup>39*†</sup>	30	90	61	24 (±8)
Gunning et al <sup>55*</sup>	15	93	61	23 (±8)

CV, Contrast ventriculography; all other abbreviations as in Table 1a.

\*<sup>99m</sup>Tc-tetrofosmin instead of <sup>99m</sup>Tc-sestamibi

†Recovery was defined as improvement of wall motion and/or perfusion.

‡Twenty-three patients completed the study.

**TABLE 5b.** Sensitivity, specificity, PPV, and NPV for <sup>99m</sup>Tc-sestamibi scintigraphy without the addition of nitrates to detect functional recovery after revascularization (308 patient, 13 studies)

Reference	Sensitivity (%) (segments)	Specificity (%) (segments)	PPV (%) (segments)	NPV (%) (segments)
Marzullo et al <sup>51</sup>	73 (40/55)	54 (27/50)	63 (40/63)	64 (27/42)
Marzullo et al <sup>17</sup>	75 (37/49)	84 (22/26)	90 (37/41)	65 (22/34)
Gonzalez et al <sup>62</sup>	80 (30/39)	35 (18/51)	48 (30/63)	67 (18/27)
Marzullo et al <sup>63</sup>	83 (35/42)	68 (21/31)	78 (35/45)	75 (21/28)
Maes et al <sup>64</sup>	92 (12/13)	60 (6/10)	75 (12/16)	86 (6/7)
Udelson et al <sup>45</sup>	94 (16/17)	86 (25/29)	80 (16/20)	96 (25/26)
Maublant et al <sup>65</sup>	100 (21/21)	67 (4/6)	91 (21/23)	100 (4/4)
Matsunari et al <sup>47</sup>	96 (47/49)	30 (9/30)	69 (47/68)	82 (9/11)
Dakik et al <sup>66</sup>	82 (45/55)	50 (15/30)	75 (45/60)	60 (15/25)
Lipiecki et al <sup>60</sup>	65 (24/37)	59 (41/70)	45 (24/53)	76 (41/54)
Levine et al <sup>73</sup>	95 (91/96)	56 (5/9)	96 (91/95)	50 (5/10)
Gunning et al <sup>39</sup>	63 (52/82)	62 (78/125)	53 (52/99)	72 (78/108)
Gunning et al <sup>55</sup>	62 (34/55)	61 (47/77)	53 (34/64)	69 (47/68)
Weighted mean	79 (484/610)	58 (318/544)	68 (484/710)	72 (318/444)

tissue and subendocardial necrosis.<sup>3</sup> Most techniques identify these segments as viable myocardium. Although these segments are indeed viable, all of them will not recover in function after revascularization, because the dysfunction may be related to the presence of subendocardial necrosis.<sup>95</sup> This observation emphasizes (1) that the terms *viability* and *recovery of function* are not interchangeable,

<b>% Patients with MVD</b>	<b>PTCA/CABG</b>	<b>% Patients with MI</b>	<b>% Segments with recovery</b>	<b>Technique to assess RWM after revascularization</b>
91	41/59	100	56	Echo, 11 ± 2 wk
93	36/64	100	65	Echo, 11 ± 2 wk
72	50/50	86	43	Echo, 28 ± 167 d
93	36/64	100	57	Echo, 12 ± 2 wk
NA	0/100	NA	57	RNV, 3 mo
NA	33/67	100	37	Echo, 20 ± 16 d
60	44/56	NA	78	CV, 90 ± 3 d
NA	36/64	NA	62	RNV, 24-135 d
100	0/100	86	65	RNV, 6-8 wk
0	100/0	100	42	RNV, 2 mo
NA	NA	78	91 <sup>†</sup>	Gated SPECT, 1-6 wk
100	0/100	100	40	MRI, 3-6 mo
100	0/100	100	42	MRI, 3-6 mo

(2) that normal myocardium contracting normally is also viable, and  
(3) that the important issue in hibernating myocardium is LV myocardial areas dysfunctional at rest that are viable and will recover after revascularization.

### Features of Different Viability Tests

The current study aimed at comparing the predictive accuracies of the different viability tests. As stated previously, the NPV of all techniques is “good” and is mostly comparable. In contrast, the PPVs of the techniques are somewhat lower; several reasons concerning all techniques are discussed in the previous text. FDG PET, <sup>201</sup>Tl RR, <sup>99m</sup>Tc-sestamibi, and DE had a significantly higher PPV compared with <sup>201</sup>Tl. Although the current analysis aimed at comparing the different techniques by pooling the results per technique, the analysis revealed the many differences and nonuniformity of the studies, which makes comparisons difficult.<sup>3</sup> A few features of each technique are discussed in the following sections.

**Dobutamine echocardiography.** The presence of contractile reserve during stimulation with low-dose dobutamine is considered the hallmark of viable myocardium with DE. Many studies have demonstrated that this technique can predict functional recovery after revascularization. Afridi et al<sup>40</sup> have shown that the use of a low- and high-dose dobutamine protocol may more accurately predict functional outcome. However, Tables 1a and

**TABLE 6a.** <sup>99m</sup>Tc-sestamibi scintigraphy with the addition of nitrates to detect functional recovery after revascularization (180 patients, 7 studies)

Reference	No. of Patients	% Male	Mean age (y)	Mean LVEF (%) (SD)
Maurea et al <sup>67</sup>	8	NA	NA	NA
Bisi et al <sup>68</sup>	19	89	57	35 (±10)
Bisi et al <sup>69</sup>	28	86	57	36 (±10)
Greco et al <sup>70</sup>	23	100	57	39
Li et al <sup>71</sup>	27	96	53	35 (±14)
Schneider et al <sup>72*</sup>	40	93	58	54 (±12)
Sciagra et al <sup>50</sup>	35	94	58	36 (±8)

See Table 1a for abbreviations.

\*Thirty-one patients with adequate revascularization.

**TABLE 6b.** Sensitivity, specificity, PPV, and NPV for <sup>99m</sup>Tc-sestamibi scintigraphy with the addition of nitrates to detect functional recovery after revascularization (180 patients, 7 studies)

Reference	Sensitivity (%) (segments)	Specificity (%) (segments)	PPV (%) (segments)	NPV (%) (segments)
Maurea et al <sup>67</sup>	88 (22/25)	89 (24/27)	88 (22/25)	89 (24/27)
Bisi et al <sup>68</sup>	91 (10/11)	88 (30/34)	71 (10/14)	97 (30/31)
Bisi et al <sup>69</sup>	95 (18/19)	88 (22/25)	86 (18/21)	96 (22/23)
Greco et al <sup>70</sup>	86 (12/14)	56 (5/9)	75 (12/16)	71 (5/7)
Li et al <sup>71</sup>	83 (80/96)	81 (83/102)	81 (80/99)	84 (83/99)
Schneider et al <sup>72</sup>	95 (18/19)	83 (10/12)	90 (18/20)	91 (10/11)
Sciagra et al <sup>50</sup>	77 (23/30)	77 (20/26)	79 (23/29)	74 (20/27)
Weighted mean	86 (183/214)	83 (194/235)	82 (183/224)	86 (194/225)
Total MIBI	81 (667/824)	66 (512/779)	71 (667/934)	77 (512/669)

1b, which represent the low-dose studies and the low-high dose studies, show the NPV of the high-dose protocol is better than the low-dose protocol (90% vs 83%) but the opposite is true for the PPV (70% vs 77%). The main advantage of the high-dose protocol is the opportunity to evaluate viability and stress-induced ischemia during the same test. The safety of the high-dose protocol in patients with severely depressed LV function has been reported<sup>96</sup>; however, adverse effects have been reported in a few patients.<sup>95</sup> Important disadvantages of DE are the subjective analysis of the test and the number of patients with an inadequate acoustic window.

**<sup>201</sup>Tl imaging.** Thallium 201 is a potassium analogue and its retention is dependent on integrity of the cell membrane (and thus viability).<sup>97</sup> Among all different <sup>201</sup>Tl protocols that are currently available, 2 protocols have been used extensively: <sup>201</sup>Tl RI and <sup>201</sup>Tl RR imaging.<sup>7</sup> The main difference between these 2 approaches is that the RI protocol provides infor-

<b>% Patients with MVD</b>	<b>PTCA/CABG</b>	<b>% Patients with MI</b>	<b>Segments with recovery (%)</b>	<b>Technique to assess RWM after revascularization</b>
NA	25/75	100	48	Echo, 5 ± 3 mo
84	21/79	100	24	Echo, 1-3 mo
61	36/64	100	43	RNV, 1-3 mo
100	0/100	100	61	Echo, 4-6 mo
15	0/100	100	48	RNV, 15 d
60	50/50	100	61	RNV, 4 mo
71	54/46	100	54	Echo, 1-3 mo

mation on both stress-induced ischemia and viability, whereas the RR protocol provides information only on viability.<sup>7</sup>

Most of the studies used SPECT, although some studies were performed with planar imaging. The SPECT systems provide better image contrast and superior evaluation of the inferior wall. The viability criteria that were predominantly used included defect reversibility and a cutoff level of <sup>201</sup>Tl activity on the redistribution or RI images.<sup>7</sup> The relatively lower PPV of the <sup>201</sup>Tl protocols (particularly the <sup>201</sup>Tl RI protocol) may be caused by the use of these cutoff levels.<sup>54,98,99</sup> A segment with ≥ 50% <sup>201</sup>Tl activity on the redistribution or RI images may represent an area of hibernation, stress-induced ischemia, or subendocardial necrosis. In the situation of hibernation, recovery of resting LV dysfunction can be anticipated after revascularization, whereas in the other situations this will not occur. Recent data have demonstrated that reversibility on both RI<sup>99</sup> and RR<sup>54</sup> imaging improved the predictive accuracy of these techniques.

**<sup>99m</sup>Tc-labeled agents.** Retention of <sup>99m</sup>Tc-sestamibi is dependent on intactness of the mitochondria.<sup>100</sup> Most studies used SPECT and a rest protocol. To assess viability on these resting images, different cutoff levels are used, varying from 35% to 65%. Similar to <sup>201</sup>Tl imaging, the PPV is lower when these activity levels are used (Table 4a, PPV 68%). Again, these cutoff levels cannot differentiate between hibernating myocardium and areas of subendocardial necrosis. Another aspect is the influence of attenuation. Recent data have shown that either attenuation correction<sup>101</sup> or the use of different cutoff levels for different myocardial regions<sup>72</sup> improved the accuracy to predict functional outcome.

Another approach to improve the accuracy of <sup>99m</sup>Tc-sestamibi is the addition of nitrates (to enhance resting perfusion in the area of a severely stenosed

**TABLE 7a.** FDG PET studies for assessment of viability

Reference	No. of Patients	% Male	Mean age (y)	Mean LVEF (%) (SD)
Marwick et al	16	88	NA	NA
Gerber et al <sup>12</sup>	39	87	60	33 ( $\pm$ 10)
Tamaki et al <sup>74</sup>	22	91	57	NA
Gropler et al <sup>75</sup>	34	76	60	NA
Maes et al <sup>64</sup>	23	NA	NA	41 ( $\pm$ 13)
Tamaki et al <sup>76</sup>	43	95	58	41 (NA)
Knuuti et al <sup>77</sup>	48	96	54	53 ( $\pm$ 11)
Baer et al <sup>24</sup>	42	90	59	40 ( $\pm$ 13)
Lucignani et al <sup>78</sup>	14	86	61	38 ( $\pm$ 5)
Carrel et al <sup>79</sup>	23	91	56	34 ( $\pm$ 14)
Tillisch et al <sup>80</sup>	17	94	NA	32 ( $\pm$ 14)
Tamaki et al <sup>57</sup>	11	NA	NA	NA
Wolpers et al <sup>81*</sup>	30	NA	55	43 ( $\pm$ 12)
Paolini et al <sup>82</sup>	9	NA	58	27 ( $\pm$ 5)
Pagano et al <sup>30</sup>	30	87	57	25 ( $\pm$ 7)
Fath-Ordoubadi et al <sup>83</sup>	47	91	60	32 ( $\pm$ 13)
Pagano et al <sup>84</sup>	35	89	58	23 ( $\pm$ 7)
Vom Dahl et al <sup>85</sup>	37	90	59	34 ( $\pm$ 10)
Vom Dahl et al <sup>86</sup>	52	92	56	47 ( $\pm$ 10)
Kitsiou et al <sup>87</sup>	26	88	59	31 ( $\pm$ 8)

CV, Contrast ventriculography; other abbreviations as in Table 1a.

\*Seven patients studied <4 weeks after MI.

artery) and use the redistribution on the “nitrate-enhanced” image (compared with the rest image) as the marker of viable myocardium (Table 4b).

**FDG PET.** FDG imaging allows noninvasive assessment of glucose uptake in the myocardium. First, the metabolic circumstances varied between the studies. In the fasting situation, FDG is taken up mainly by ischemic myocardium.<sup>102</sup> The other areas (both normal and scar tissue) do not take up FDG. This type of FDG imaging is also referred to as “hot-spot” imaging.<sup>102</sup> Oral glucose loading stimulates FDG uptake in both normal myocardium and in viable, jeopardized myocardium.<sup>103</sup> Disadvantages of this approach are the fluctuations in metabolic milieu,<sup>104</sup> the heterogenous FDG uptake in the different regions of the myocardium,<sup>105</sup> and the poor image quality obtained in patients with diabetes mellitus.<sup>106</sup> The hyperinsulinemic euglycemic clamp has been introduced to overcome these problems.<sup>104</sup> This approach yields stable metabolic conditions, homogenous FDG uptake, and high-quality images in all subsets of patients.<sup>104</sup> Second, various protocols, analyses, and viability criteria were used. The majority of the studies compared regional FDG uptake with perfusion. Although most studies used <sup>13</sup>N-ammonia to assess regional perfu-

<b>% Patients with MVD</b>	<b>PTCA/CABG</b>	<b>% Patients with MI</b>	<b>% Segments with recovery</b>	<b>Technique to assess RWM after revascularization</b>
44	56/44	100	41	Echo, 5 ± 2 mo
85	0/100	59	62	Echo, 5 ± 1.9 mo
NA	0/100	77	50	RNV, 5-7 wk
76	29/71	62	40	Echo/RNV, 2 mo
NA	0/100	NA	52	RNV, 3 mo
NA	44/56	100	39	CV/RNV, 4-8 wk
85	23/77	100	30	Echo, 3 wk-6 mo
74	48/52	100	62	Echo, 4-6 mo
93	0/100	NA	74	RNV, NA
NA	0/100	100	74	Echo, 3 mo
NA	0/100	94	55	CV/RNV, 3-18 wk
NA	0/100	NA	71	RNV, NA
53	0/100	100	57	CV/echo, 6.9 mo
100	0/100	100	65	RNV, 4 mo
100	0/100	100	57	Echo, 6 mo
NA	0/100	100	60	RNV, 4-6 mo
100	0/100	100	57	RNV, 6 mo
100	0/100	73	NA	RNV, 13 ± 13 wk
69	54/46	76	38	CV, 5 ± 2 mo
77	38/62	NA	57	MRI/RNV, 5.5 ± 8.8 mo

sion, others have used rubidium 82 or SPECT tracers ( $^{201}\text{Tl}$  or  $^{99\text{m}}\text{Tc}$ -sestamibi). Other studies used FDG in isolation. Various viability criteria were used: the perfusion-FDG mismatch, normal perfusion, normalized FDG uptake, and quantitative assessment of glucose utilization. Most of the analyses used a semiquantitative approach, some used absolute quantification of glucose utilization and perfusion, and some used a visual analysis.

### *Nuclear Imaging Versus DE*

The highest specificity is obtained with DE, whereas higher sensitivities are obtained with nuclear imaging techniques (Figure 1, Table 9). The data from the pooled analysis show that DE has the highest PPV, whereas the highest NPV is obtained with FDG PET (Figure 2, Table 9). It may be more correct, however, to evaluate the studies that have compared some form of nuclear imaging with DE in the same patients. This analysis (Figures 3 and 4, Tables 8 and 8a) confirmed the higher PPV/specificity of DE and the higher NPV/sensitivity of the scintigraphic studies. These findings implicate that nuclear imaging tends to overestimate functional

**TABLE 7b.** Sensitivity, specificity, PPV, and NPV of FDG PET to detect improvement in regional contractile function after revascularization (598 patients, 20 studies)

Reference	Sensitivity (%) (segments)	Specificity (%) (segments)	PPV (%) (segments)	NPV (%) (segments)
Marwick et al <sup>73</sup>	71 (25/35)	76 (38/50)	68 (25/37)	79 (38/48)
Gerber et al <sup>12</sup>	75 (18/24)	67 (10/15)	78 (18/23)	63 (10/16)
Tamaki et al <sup>74</sup>	78 (18/23)	78 (18/23)	78 (18/23)	78 (18/23)
Gropler et al <sup>75</sup>	83 (38/46)	50 (35/70)	52 (38/73)	81 (35/43)
Maes et al <sup>64</sup>	83 (10/12)	91 (10/11)	91 (10/11)	83 (10/12)
Tamaki et al <sup>76</sup>	88 (45/51)	82 (65/79)	76 (45/59)	92 (65/71)
Knuuti et al <sup>77</sup>	92 (23/25)	85 (50/59)	72 (23/32)	96 (50/52)
Baer et al <sup>24</sup>	92 (24/26)	88 (14/16)	92 (24/26)	88 (14/16)
Lucignani et al <sup>78</sup>	93 (37/40)	86 (12/14)	95 (37/39)	80 (12/15)
Carrel <sup>79</sup>	94 (16/17)	50 (3/6)	84 (16/19)	75 (3/4)
Tillisch et al <sup>80</sup>	95 (35/37)	80 (24/30)	85 (35/41)	92 (24/26)
Tamaki et al <sup>57</sup>	100 (40/40)	38 (6/16)	80 (40/50)	38 (6/16)
Wolpers et al <sup>81</sup>	NA	NA	90 (NA)	85 (NA)
Paolini et al <sup>82</sup>	88 (23/26)	79 (11/14)	88 (23/26)	79 (11/14)
Pagano et al <sup>30</sup>	99 (190/192)	33 (48/144)	66 (190/286)	96 (48/50)
Fath-Ordoubadi <sup>83</sup>	81 (NA)	88 (NA)	82 (NA)	88 (NA)
Pagano et al <sup>84</sup>	99 (190/192)	33 (48/144)	56 (190/286)	96 (48/50)
Vom Dahl et al <sup>85</sup>	NA	NA	48-86 (NA)*	84-100 (NA)*
Vom Dahl et al <sup>86</sup>	90 (19/21)	74 (25/34)	68 (19/28)	93 (25/27)
Kitsiou et al <sup>87</sup>	NA	NA	78 (NA)	82 (NA)
Weighted mean	93 (751/807)	58 (417/725)	71 (751-1059)	86 (417/483)

\*PPV and NPV varied according to different viability criteria used.

recovery, whereas DE tends to underestimate functional recovery. It has been demonstrated that a substantial number of segments that are nonviable on DE (ie, lack of contractile reserve) are viable by nuclear imaging.<sup>107,108</sup> Possibly these segments were more damaged; recent data have indeed shown that segments with viability on FDG PET without contractile reserve have more severe ultrastructural damage when compared with “FDG PET–viable segments” with contractile reserve.<sup>109,110</sup>

### Unresolved Issues

Considering the available studies, several issues remain to be elucidated:

1. The majority of the studies have focused on patients with a LVEF > 35%, whereas viability assessment is also important in patients with more severely depressed LVEF (< 35% and < 20%).
2. Besides prediction of improvement of regional function, larger studies with the different techniques focusing on the prediction of improvement of global LV function are needed.
3. A few studies have emphasized that the extent of viability (the number of viable segments) determines the magnitude of improvement of LVEF after revascularization.<sup>46,80,84,111-113</sup> This needs to be

**TABLE 8a.** Sensitivity and specificity of the studies performing direct comparisons between nuclear imaging and dobutamine echocardiography (563 patients, 18 studies)

Reference	Sensitivity (%)	Sensitivity (%)	Specificity (%)	Specificity (%)
	(segments) Nuclear	(segments) DE	(segments) Nuclear	(segments) DE
Gerber et al <sup>12</sup>	75 (18/24)	71 (17/24)	67 (10/15)	89 (13/15)
Baer et al <sup>24</sup>	92 (24/26)	96 (25/26)	88 (14/16)	69 (11/16)
Pagano et al <sup>30</sup>	99 (190/192)	61 (117/192)	33 (48/144)	63 (90/144)
Vanoverschelde et al <sup>16</sup>	80 (213/267)	79 (211/267)	47 (198/425)	80 (340/425)
Arnese et al <sup>14</sup>	89 (34/38)	74 (28/38)	48 (63/132)	96 (127/132)
Bax et al <sup>18</sup>	93 (25/27)	85 (23/27)	43 (28/65)	63 (41/65)
Haque et al <sup>23</sup>	100 (33/33)	94 (31/33)	40 (4/10)	80 (8/10)
Kostopoulos et al <sup>27</sup>	91 (67/74)	86 (64/74)	69 (62/74)	94 (85/90)
Marzullo et al <sup>17</sup>	86 (42/49)	82 (40/49)	92 (24/26)	94 (24/26)
Qureshi et al <sup>41</sup>	90 (38/42)	76 (32/42)	56 (59/106)	82 (87/106)
Alfieri et al <sup>21</sup>	94 (92/98)	91 (85/93)	64 (14/22)	78 (25/32)
Perrone-Filardi <sup>15</sup>	100 (73/73)	79 (58/73)	22 (8/36)	83 (30/36)
Charney et al <sup>13</sup>	95 (19/20)	71 (22/31)	85 (11/13)	93 (25/26)
Nagueh et al <sup>42</sup>	91 (42/46)	68 (23/34)	43 (27/63)	83 (49/59)
Pace et al <sup>36</sup>	76 (35/46)	52 (24/46)	74 (34/46)	87 (40/46)
Senior et al <sup>19</sup>	92 (108/118)	87 (103/118)	78 (39/50)	82 (41/65)
Sicari et al <sup>38</sup>	87 (110/126)	82 (103/126)	61 (60/99)	93 (92/99)
Gunning et al <sup>39</sup>	72 (59/82)	50 (41/82)	58 (73/125)	81 (101/125)
Weighted mean	88 (1222/1381)	76 (1047/1375)	53 (776/1467)	81 (1229/1518)

further evaluated.

4. The discrepancy in viability assessment between nuclear imaging and DE needs to be resolved; and an important direction from a clinical viewpoint is to assess whether combination of these tests improves the accuracy.
5. Will the combination of tests improve the sensitivity, specificity, and predictive accuracies?
6. Several retrospective analyses have recently shown that patients with viable myocardium who were treated medically, had an unfavorable outcome.<sup>114-118</sup> Both studies with nuclear imaging and DE have consistently demonstrated that this group of patients had a very high event rate.<sup>114-118</sup> Therefore the endpoint to determine the clinical value of viability assessment should perhaps also evaluate long-term prognosis.<sup>119</sup> Thus far, there are no prospective studies concerning this issue.
7. Prospective randomized trials are needed to evaluate whether optimal medical therapy (by year 2000 standards) plus revascularization is superior to optimal medical therapy (by year 2000 standards).

### *Limitations of Pooled Analysis*

**TABLE 8b.** PPV and NPV of the studies performing direct comparisons between nuclear imaging and dobutamine echocardiography (563 patients, 18 studies)

Reference	No. of Patients	Techniques	PPV (%) (segments) Nuclear
Gerber et al <sup>12</sup>	39	FDG PET/LDDE	78 (18/23)
Baer et al <sup>24</sup>	42	FDG PET/LDDE	92 (24/26)
Pagano et al <sup>30</sup>	30	FDG PET/LDDE	66 (190/286)
Vanoverschelde et al <sup>16</sup>	73	<sup>201</sup> Tl RI/LDDE	48 (213/440)
Arnese et al <sup>14</sup>	38	<sup>201</sup> Tl RI/LDDE	30 (34/113)
Bax et al <sup>18</sup>	17	<sup>201</sup> Tl RI/LDDE	40 (25/62)
Haque et al <sup>23</sup>	26	<sup>201</sup> Tl RI/LDDE	85 (33/39)
Kostopoulos et al <sup>27</sup>	31	<sup>201</sup> Tl RI/LDDE	71 (67/95)
Marzullo et al <sup>17</sup>	14	<sup>201</sup> Tl RR/LDDE	95 (42/44)
Qureshi et al <sup>41</sup>	34	<sup>201</sup> Tl RR/HDDE	45 (38/85)
Alferi et al <sup>21</sup>	13	<sup>201</sup> Tl RR/LDDE	92 (92/100)
Perrone-Filardi <sup>15</sup>	18	<sup>201</sup> Tl RR/LDDE	72 (73/101)
Charney et al <sup>13</sup>	14	<sup>201</sup> Tl RR/LDDE	90 (19/21)
Nagueh et al <sup>42*</sup>	19	<sup>201</sup> Tl RR/HDDE	54 (42/78)
Pace et al <sup>36</sup>	46	<sup>201</sup> Tl RR/LDDE	74 (35/47)
Senior et al <sup>19</sup>	22	<sup>201</sup> Tl RR/LDDE	91 (108/119)
Sicari et al <sup>38†</sup>	57	<sup>201</sup> Tl RR/LDDE	74 (110/149)
Gunning et al <sup>39‡§</sup>	30	<sup>201</sup> Tl RR/LDDE	53 (59/111)
Weighted mean			63 (1222/1939)

LDDE, Low-dose dobutamine echocardiography.

\*Eighteen patients underwent revascularization.

†Thirty patients underwent revascularization.

‡Twenty-three patients completed the study.

§Magnetic resonance imaging instead of echocardiography.

**TABLE 9.** Sensitivity, specificity, PPV, and NPV for the different techniques from the available studies

	No. of Studies	No. of Patients
Dobutamine echo (LDDE + HDDE)	32	1090
<sup>201</sup> Tl rest-redistribution	22	557
<sup>201</sup> Tl reinjection	11	301
<sup>99m</sup> Tc-based tracers	20	488
FDG PET	20	598
Direct comparison of DE and nuclear		
DE	11	325
Nuclear	11	325

LDDE, Low-dose dobutamine echocardiography; HDDE, high-dose dobutamine echocardiography.

Pooling the data to arrive at the mean sensitivities, specificities, and predictive values for the various tests has its limitations. Although the data are pooled according to the various techniques, the major shortcoming of pooling the data is the enormous heterogeneity in patient selection, performance of studies, data acquisition, time of analyses after revascularization, and data analysis. Moreover, patients excluded from the study are

<b>PPV (%) (segments) DE</b>	<b>NPV (%) (segments) Nuclear</b>	<b>NPV (%) (segments) DE</b>
89 (17/19)	63 (10/16)	65 (13/20)
83 (25/30)	88 (14/16)	92 (11/12)
68 (117/171)	96 (48/50)	55 (90/165)
71 (211/296)	79 (198/252)	86 (340/396)
85 (28/33)	94 (63/67)	93 (127/137)
49 (23/47)	93 (28/30)	91 (41/45)
94 (31/33)	100 (4/4)	80 (8/10)
93 (64/69)	90 (62/69)	89 (85/95)
95 (40/42)	77 (24/31)	73 (24/33)
63 (32/51)	94 (59/63)	90 (87/97)
92 (85/92)	70 (14/20)	76 (25/33)
91 (58/64)	100 (8/8)	67 (30/45)
92 (22/24)	92 (11/12)	74 (25/34)
70 (23/33)	87 (27/31)	82 (49/60)
80 (24/30)	76 (34/45)	65 (40/62)
92 (103/112)	80 (39/49)	73 (41/56)
94 (103/110)	79 (60/76)	80 (92/115)
63 (41/65)	76 (73/96)	71 (101/142)
79 (1047/1321)	83 (776/935)	79 (1229/1557)

<b>Sensitivity Mean (95% CI)</b>	<b>Specificity Mean (95% CI)</b>	<b>PPV Mean (95% CI)</b>	<b>NPV Mean (95% CI)</b>
81 (80-82)	80 (79-81)	77 (76-78)	85 (84-86)
86 (84-88)	59 (56-62)	69 (67-71)	80 (77-83)
88 (86-90)	50 (47-53)	57 (54-60)	83 (80-86)
81 (78-84)	66 (63-69)	71 (68-74)	77 (74-80)
93 (91-95)	58 (54-62)	71 (68-74)	86 (83-89)
74 (71-77)	78 (75-81)	84 (81-87)	69 (65-73)
90 (88-92)	57 (53-60)	75 (72-78)	80 (76-84)

usually not given. Concerning the patient selection, it is interesting to observe from Tables 1 and 7 the differences in the study populations, in terms of LVEF, incidence of recovery of function, time to assess recovery of function after revascularization, and so on. Moreover, the Appendices 1 to 5 demonstrate the variations (per technique) concerning the data acquisition and data analysis.

**TABLE 10.** P values for the differences between the various tests shown in Table 9

Variable	P value
Sensitivity	
FDG vs others	<.05
<sup>201</sup> Tl RI vs DE, MIBI	<.05
<sup>201</sup> Tl RI vs DE	<.05
Specificity	
DE vs others	<.05
Others vs <sup>201</sup> Tl RI	<.05
MIBI vs <sup>201</sup> Tl RR	<.05
PPV	
DE vs others	<.05
Others vs <sup>201</sup> Tl RI	<.05
NPV	
DE vs <sup>201</sup> Tl RR	<.05
DE vs MIBI	<.05
FDG vs MIBI	<.05

## Conclusion

The current analysis demonstrated that all techniques have a higher NPV/sensitivity compared with their PPV/specificity. Both pooled analyses of all available data and direct comparisons demonstrated that higher sensitivities/NPVs are obtained with nuclear imaging, whereas higher specificities/PPVs are obtained with DE.

## Addendum

Recently Kim et al<sup>120</sup> have reported on the results of gadolinium-enhanced MRI for diagnosis of hibernating myocardium. The PPV and NPV were 71% and 79%, respectively, but only for kinetic and dyskkinetic segments; the PPV and NPV were 88% and 89%, respectively.<sup>120,121</sup>

---

**G. A. Beller:** The authors have provided a superb review of the literature regarding the sensitivity, specificity, and predictive accuracy of the various noninvasive techniques for assessing myocardial viability and have compiled the most comprehensive pooled analysis to date. They clearly show that the enhanced sensitivity but lower specificity of the nuclear techniques compared to DE for predicting improved regional function after revascularization. The bottom line is that both approaches yield a comparable overall accuracy and that physicians should select the test that is performed with the highest quality in their local institutions or regions. Another emerging technique for viability assessment not reviewed is contrast-enhanced cine magnetic resonance imaging (Kim et al. *N Engl J Med* 2000;343:1445-53), which permits the quantitation of the transmural extent of myocardial scar by using the extent of delayed "hyperenhancement" as the variable reflective of myocardial scar.

It is interesting to speculate, as the authors have done, why certain segments show preoperative viability by the nuclear technique but do not show improved systolic thickening after revascularization. This occurrence is most likely caused by a limited subendocardial scar (eg, 25% fibrosis from endocardium surface to edge of epicardium). Such segments would show >50% uptake of Tl-201 but would not show functional improvement after revascularization because of the dependence of transmural thickening on subendocardial viability (Edwards et al. *Am J Physiol* 1992;62[2 pt 2]:H568-76).

Finally, we need long-term outcomes studies in which preoperative viability assessments are related to subsequent mortality and morbidity (eg, heart failure) rather than simply to subsequent changes in regional or global LV function.

---

## REFERENCES

1. Rahimtoola SH. Coronary bypass surgery for chronic angina—1981; a perspective. *Circulation* 1982;65:225-41.
2. Rahimtoola SH. A perspective on the three large multicenter randomized clinical trials of coronary bypass surgery for chronic stable angina. *Circulation* 1985;72(Suppl V):V123-V135.
3. Rahimtoola SH. Importance of diagnosing hibernating myocardium: how and in whom? *J Am Coll Cardiol* 1997;30:1701-6.
4. Bonow RO, Dilsizian V. Thallium-201 for assessing myocardial viability. *Semin Nucl Med* 1991;21:230-41.
5. The Multicenter Postinfarction Research Group. Risk stratification and survival after myocardial infarction. *N Engl J Med* 1983;309:331-6.
6. Blitz A, Laks H. The role of coronary revascularization in the management of heart failure: identification of candidates and review of results. *Curr Opin Cardiol* 1996;11:276-90.
7. Dilsizian V, Bonow RO. Current diagnostic techniques of assessing myocardial viability in hibernating and stunned myocardium. *Circulation* 1993;87:1-20.
8. Camici PG, Wijns W, Borgers M, De Silva R, Ferrari R, Heusch G, et al. Pathophysiological mechanisms of chronic reversible left ventricular dysfunction due to coronary artery disease (hibernating myocardium). *Circulation* 1997;96:3205-14.
9. Vanoverschelde JLJ, Wijns W, Borgers M, Heyndrickx G, Depre C, Flameng W, et al. Chronic myocardial hibernation in humans. From bedside to bench. *Circulation* 1997;95:1961-71.
10. Wijns W, Vatner SF, Camici PG. Hibernating myocardium. *N Engl J Med* 1998;339:173-81.
11. Bax JJ, Wijns W, Cornel JH, Visser FC, Fioretti PM. 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. *J Am Coll Cardiol* 1997;30:1451-60.
12. Gerber BL, Vanoverschelde J-LJ, Bol A, Michel C, Labar D, Wijns W, et al. Myocardial blood flow, glucose uptake and recruitment of inotropic reserve in chronic left ventricular ischemic dysfunction. Implications for the pathophysiology of chronic hibernation. *Circulation* 1996;94:651-9.
13. Charney R, Schwinger ME, Chun J, Cohen MV, Nanna M, Menegus MA, et al.

- Dobutamine echocardiography and resting-redistribution thallium-201 scintigraphy predicts recovery of hibernating myocardium after coronary revascularization. *Am Heart J* 1994;128:864-9.
14. Arnese M, Cornel JH, Salustri A, Maat APWM, Elhendy A, Reijs AEM, 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;91:2748-52.
  15. Perrone-Filardi P, Pace L, Prastaro M, Squame F, Betocchi S, Soricelli A, et al. Assessment of myocardial viability in patients with chronic coronary artery disease. Rest-4-hour-24-hour <sup>201</sup>Tl tomography versus dobutamine echocardiography. *Circulation* 1996;94:2712-9.
  16. Vanoverschelde J-LJ, D'Hondt A-M, Marwick T, Gerber BL, De Kock M, Dion R, 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;28:432-42.
  17. Marzullo P, Parodi O, Reisenhofer B, Sambuceti G, Picano E, Distanti A, et al. Value of rest thallium-201/technetium-99m sestamibi and dobutamine echocardiography for detecting myocardial viability. *Am J Cardiol* 1993;71:166-72.
  18. Bax JJ, Cornel JH, Visser FC, Fioretti PM, van Lingen A, Reijs AEM, et al. Prediction of recovery of myocardial dysfunction following revascularization: comparison of F18-fluorodeoxyglucose/thallium-201 single photon emission computed tomography, thallium-201 stress-reinjection single photon emission computed tomography and dobutamine echocardiography. *J Am Coll Cardiol* 1996;28:558-64.
  19. Senior R, Glenville B, Basu S, Sridhara BS, Anagnostou E, Stanbridge R, et al. Dobutamine echocardiography and thallium-201 imaging predict functional improvement after revascularization in severe ischaemic left ventricular dysfunction. *Br Heart J* 1995;74:358-64.
  20. Perrone-Filardi P, Pace L, Prastaro M, Piscione F, Betocchi S, Squame F, et al. Dobutamine echocardiography predicts improvement of hypoperfused dysfunctional myocardium after revascularization in patients with coronary artery disease. *Circulation* 1995;91:2556-65.
  21. Alfieri O, La Canna G, Giubbini R, Pardini A, Zogno M, Fucci C. Recovery of myocardial function. *Eur J Cardiothorac Surg* 1993;7:325-30.
  22. La Canna G, Alfieri O, Giubbini R, Gargano M, Ferrari R, Visioli O. Echocardiography during infusion of dobutamine for identification of reversible dysfunction in patients with chronic coronary artery disease. *J Am Coll Cardiol* 1994;23:617-626.
  23. Haque T, Furukawa T, Takahashi M, Kinoshita M. Identification of hibernating myocardium by dobutamine stress echocardiography: comparison with thallium-201 reinjection imaging. *Am Heart J* 1995;130:553-63.
  24. Baer FM, Voth E, Deutsch HJ, Schneider CA, Horst M, de Vivie ER, et al. Predictive value of low dose dobutamine transesophageal echocardiography and fluorine-18 fluorodeoxyglucose positron emission tomography for recovery of regional left ventricular function after successful revascularization. *J Am Coll Cardiol* 1996;28:60-9.
  25. DeFilippi CR, Willett DWL, Irani WN, Eichhorn EJ, Velasco CE, Grayburn PA. Comparison of myocardial contrast echocardiography and low-dose dobutamine stress echocardiography in predicting recovery of left ventricular function after coronary revascularization in chronic ischemic heart disease. *Circulation* 1995;92:2863-8.

26. Elhendy A, Cornel JH, Roelandt JRTC, van Domburg RT, Fioretti PM. Akinesis becoming dyskinesis during dobutamine stress echocardiography. A predictor of poor functional recovery after revascularization. *Chest* 1996;110:155-8.
27. Kostopoulos KG, Kranidis AI, Bouki KP, Antonellis JP, Kappos KG, Rodogianni FE, et al. Detection of myocardial viability in the prediction of improvement in left ventricular function after successful coronary revascularization by using the dobutamine stress echocardiography and quantitative SPECT rest-redistribution-reinjection <sup>201</sup>Tl imaging after dipyridamole infusion. *Angiology* 1996;47:1039-46.
28. Cornel JH, Bax JJ, Fioretti PM, Visser FC, Maat APWM, Boersma E, et al. Prediction of improvement of left ventricular function after revascularization. <sup>18</sup>F-fluorodeoxyglucose SPECT vs low-dose dobutamine echocardiography. *Eur Heart J* 1997;18:941-8.
29. Scognamiglio R, Fasoli G, Casarotto D, Miorelli M, Nistri S, Palisi M, et al. Postextrasystolic potentiation and dobutamine echocardiography in predicting recovery of myocardial function after coronary bypass revascularization. *Circulation* 1997;96:816-20.
30. Pagano D, Bonser RS, Townend JN, Ordoubadi F, Lorenzoni R, Camici PG. Predictive value of dobutamine echocardiography and positron emission tomography in identifying hibernating myocardium in patients with postischemic heart failure. *Heart* 1998;79:281-8.
31. Baer FM, Theissen P, Schneider CA, Voth E, Sechtem U, Schicha H, et al. Dobutamine magnetic resonance imaging predicts contractile recovery of chronically dysfunctional myocardium after successful revascularization. *J Am Coll Cardiol* 1998;31:1040-8.
32. Voci P, Bilotta F, Caretta Q, Mercanti C, Marino B. Low-dose dobutamine echocardiography predicts the early response of dysfunctioning myocardial segments to coronary artery bypass grafting. *Am Heart J* 1995;129:521-6.
33. Picano E, Ostojic M, Varga A, Sicari R, Djordjevic-Dikic A, Nedeljkovic I, et al. Combined low dose dipyridamole-dobutamine stress echocardiography to identify myocardial viability. *J Am Coll Cardiol* 1996;27:1422-8.
34. Elhendy A, Cornel JH, Roelandt JRTC, Nierop PR, Van Domburg RT, Geleijnse ML, et al. Impact of severity of coronary artery stenosis and the collateral circulation on the functional outcome of dyssynergic myocardium after revascularization in patients with healed myocardial infarction and chronic left ventricular dysfunction. *Am J Cardiol* 1997;79:883-8.
35. Cornel JH, Bax JJ, Elhendy A, Poldermans D, Vanoverschelde JLJ, Fioretti PM. Predictive accuracy of echocardiographic response of mildly dyssynergic myocardial segments to low-dose dobutamine. *Am J Cardiol* 1997;80:1481-4.
36. Pace L, Perrone-Filardi P, Mainenti P, Prastaro M, Vezzuto P, Varrone A, 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;25:744-50.
37. Sayad DE, Willett DL, Hundley G, Grayburn PA, Peshock RM. Dobutamine magnetic resonance imaging with myocardial tagging quantitatively predicts improvement in regional function after revascularization. *Am J Cardiol* 1998;82:1149-51.
38. Sicari R, Varga A, Picano E, Borges AC, Gimelli A, Marzullo P. Comparison of combination of dipyridamole and dobutamine during echocardiography with thallium scintigraphy to improve viability detection. *Am J Cardiol* 1999;83:6-10.
39. Gunning MG, Anagnostopoulos C, Knight CJ, Pepper J, Burman ED, Davies G, et

- al. Comparison of  $^{201}\text{Tl}$ ,  $^{99\text{m}}\text{Tc}$ -tetrofosmin, and dobutamine magnetic resonance imaging for identifying hibernating myocardium. *Circulation* 1998;98:1869-74.
40. 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;91:663-70.
  41. Qureshi U, Nagueh SF, Afridi I, Vaduganathan P, Blaustein A, Verani MS, et al. Dobutamine echocardiography and quantitative rest-redistribution  $^{201}\text{Tl}$  tomography in myocardial hibernation. Relation of contractile reserve to  $^{201}\text{Tl}$  uptake and comparative prediction of recovery of function. *Circulation* 1997;95:626-35.
  42. Nagueh SF, Vaduganathan P, Ali N, Blaustein A, Verani MS, Winters WL, 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;29:985-93.
  43. Cornel JH, Bax JJ, Elhendy A, Maat APWM, Kimman GJP, Geleijnse ML, et al. Biphasic response to dobutamine predicts improvement of global left ventricular function after surgical revascularization in patients with stable coronary artery disease. Implications of time course of recovery on diagnostic accuracy. *J Am Coll Cardiol* 1998;31:1002-10.
  44. Mori T, Minamiji K, Kurogane H, Ogawa K, Yoshida Y. Rest-injected thallium-201 imaging for assessing viability of severe asynergic regions. *J Nucl Med* 1991;32:1718-1724.
  45. Udelson JE, Coleman PS, Metherall J, Pandian NG, Gomez AR, Griffith AR, et al. Predicting recovery of severe regional ventricular dysfunction; comparison of rest-ing scintigraphy with  $^{201}\text{Tl}$  and  $^{99\text{m}}\text{Tc}$ -sestamibi. *Circulation* 1994;89:2552-61.
  46. Ragosta M, Beller GA, Watson DD, Kaul S, Gimple LW. Quantitative planar rest-redistribution Tl-201 imaging in detection of myocardial viability and prediction of improvement in left ventricular function after coronary artery bypass surgery in patients with severely depressed left ventricular function. *Circulation* 1993;87:1630-41.
  47. Matsunari I, Fujino S, Taki J, Senma J, Aoyama T, Wakasugi T, et al. Quantitative rest technetium-99m tetrofosmin imaging in predicting functional recovery after revascularization: comparison with rest-redistribution thallium-201. *J Am Coll Cardiol* 1997;29:1226-33.
  48. Cuocolo A, Nicolai E, Petretta M, Marisco C, De Luca N, Salvatore M, et al. One-year effect of myocardial revascularization on resting left ventricular function and regional thallium uptake in chronic CAD. *J Nucl Med* 1997;38:1684-92.
  49. Bax JJ, Visser FC, Van Lingen A, Sloof GW, Cornel JH, Visser CA. Comparison between  $360^\circ$  and  $180^\circ$  data sampling in thallium-201 rest-redistribution single-photon emission tomography to predict functional recovery after revascularization. *Eur J Nucl Med* 1997;24:516-22.
  50. Sciagra R, Bisi G, Santoro GM, Zeraushek F, Sestini S, Pedenovi P, et al. Comparison of baseline-nitrate technetium-99m sestamibi with rest-redistribution thallium-201 tomography in detecting viable hibernating myocardium and predicting postrevascularization recovery. *J Am Coll Cardiol* 1997;30:384-91.
  51. Marzullo P, Sambucetti G, Parodi O, Gimelli A, Picano E, Giorgetti A, et al. Regional concordance and discordance between rest thallium 201 and sestamibi imaging for assessing tissue viability: comparison with postrevascularization functional recovery. *J Nucl Cardiol* 1995;2:309-16.
  52. Matsunari I, Fujino S, Taki J, Senma J, Aoyama T, Wakasugi T, et al. Significance of late redistribution thallium-201 imaging after rest injection for detection of viable myocardium. *J Nucl Med* 1997;38:1073-8.

53. Sciagra R, Santoro GM, Bisi G, Pedenovi P, Fazzini PF, Pupi A. Rest-redistribution thallium-201 SPECT to detect myocardial viability. *J Nucl Med* 1998;39:384-90.
54. Bax JJ, Cornel JH, Visser FC, Fioretti PM, Van Lingen A, Huitink JM, et al. Comparison of fluorine-18-FDG with rest-redistribution thallium-201 SPECT to delineate viable myocardium and predict functional recovery after revascularization. *J Nucl Med* 1998;39:1481-6.
55. Gunning MG, Anagnostopoulos C, Davies G, Knight CJ, Pennell DJ, Fox KM, et al. Simultaneous assessment of myocardial viability and function for the detection of hibernating myocardium using ECG-gated <sup>99m</sup>Tc-tetrofosmin emission tomography: a comparison with <sup>201</sup>Tl emission tomography combined with cine magnetic resonance imaging. *Nucl Med Commun* 1999;20:209-14.
56. Ohtani H, Tamaki N, Yonekura Y, Mohiuddin IH, Hirata K, Ban T, et al. Value of thallium-201 reinjection after delayed SPECT imaging for predicting reversible ischemia after coronary artery bypass grafting. *Am J Cardiol* 1990;66:394-9.
57. Tamaki N, Ohtani H, Yamashita K, Magata Y, Yonekura Y, Nohara R, et al. Metabolic activity in the areas of new fill-in after thallium-201 reinjection: comparison with positron emission tomography using fluorine-18-deoxyglucose. *J Nucl Med* 1991;32:673-8.
58. Dilsizian V, Rocco TP, Freedman NMT, Leon MB, Bonow RO. Enhanced detection of ischemic but viable myocardium by the reinjection of thallium after stress-redistribution imaging. *N Engl J Med* 1990;323:141-6.
59. Taki J, Nakajima K, Matsunari I, Bunko H, Takata S, Kawasuji M, et al. Assessment of improvement of myocardial fatty acid uptake and function after revascularization using iodine-123-BMIPP. *J Nucl Med* 1997;38:1503-10.
60. Lipiecki J, Maublant JC, Citron B, Mestas D, Jousse F, Albuissou E, et al. Comparable uptake of thallium-201 and technetium-99m MIBI in hibernating and "maimed" myocardium. *Am J Cardiol* 1997;79:940-3.
61. Gürsürer M, Pinarli AE, Aksoy M, Tosun R, Yesilcimen K, Ersek B. Assessment of viable myocardium and prediction of postoperative improvement of left ventricular function in patients with severe left ventricular dysfunction by quantitative planar stress-redistribution-reinjection 201-Tl imaging. *Int J Cardiol* 1997;58:179-84.
62. Gonzalez P, Massardo T, Munoz A, Jofre J, Rivera A, Yovanovich J, et al. Is the addition of ECG gating to technetium-99m sestamibi SPECT of value in the assessment of myocardial viability? *Eur J Nucl Med* 1996;23:1315-22.
63. Marzullo P, Sambuceti G, Parodi O. The role of sestamibi scintigraphy in the radioisotopic assessment of myocardial viability. *J Nucl Med* 1992;33:1925-30.
64. Maes AF, Borgers M, Flameng W, Nuyts JL, Van de Werf F, Ausma JJ, et al. Assessment of myocardial viability in chronic coronary artery disease using technetium-99m sestamibi SPECT. Correlation with histologic and positron emission tomographic studies and functional follow-up. *J Am Coll Cardiol* 1997;29:62-8.
65. Maublant JC, Citron B, Lipiecki J, Mestas D, Bailly P, Veyre A, et al. Rest technetium 99m-sestamibi in hibernating myocardium. *Am Heart J* 1995;129:306-14.
66. Dakik HA, Howell JF, Lawrie GM, Espada R, Weillbaecher DG, He Z, et al. Assessment of myocardial viability with <sup>99m</sup>Tc-sestamibi tomography before coronary bypass graft surgery. Correlation with histopathology and postoperative improvement in cardiac function. *Circulation* 1997;96:2892-8.
67. Maurea S, Cuocolo A, Soricelli A, Castelli L, Nappi A, Squame F, et al. Enhanced detection of viable myocardium by technetium-99m-MIBI imaging after nitrate administration in chronic coronary artery disease. *J Nucl Med* 1995;36:1945-2.
68. Bisi G, Sciagra R, Santoro GM, Fazzini PF. Rest technetium-99m sestamibi tomog-

- raphy in combination with short-term administration of nitrates: feasibility and reliability for prediction of postrevascularization outcome of asynergic territories. *J Am Coll Cardiol* 1994;24:1282-9.
69. Bisi G, Sciagrà R, Santoro GM, Rossi V, Fazzini PF. Technetium-99m-sestamibi imaging with nitrate infusion to detect viable hibernating myocardium and predict postrevascularization recovery. *J Nucl Med* 1995;36:1994-2000.
  70. Greco C, Tanzilli G, Ciavolella M, Sinatra R, Banic M, Schillaci O, et al. Nitroglycerin-induced changes in myocardial sestamibi uptake to detect tissue viability: radionuclide comparison before and after revascularization. *Coron Artery Dis* 1996;7:877-84.
  71. Li S, Liu X, Lu Z, Shi R, Zhu X, Chen W, et al. Quantitative analysis of technetium 99m 2-methoxyisobutyl isonitrile single-photon emission computed tomography and isosorbide dinitrate infusion in assessment of myocardial viability before and after revascularization. *J Nucl Cardiol* 1996;3:457-63.
  72. Schneider CA, Voth E, Gawlich S, Baer FM, Horst M, Schicha H, et al. Significance of rest technetium-99m sestamibi imaging for the prediction of improvement of left ventricular dysfunction after Q wave myocardial infarction: importance of infarct location adjusted thresholds. *J Am Coll Cardiol* 1998;32:648-54.
  73. Levine MG, McGill CC, Ahlberg AW, White MP, Giri S, Shareef B, et al. Functional assessment with electrocardiographic gated single-photon computed tomography improves the ability of technetium-99m sestamibi myocardial perfusion imaging to predict myocardial viability in patients undergoing revascularization. *Am J Cardiol* 1999;83:1-5.
  74. Tamaki N, Yonekura Y, Yamashita K, Saji H, Magata Y, Senda M, et al. PET using fluorine-18 deoxyglucose in evaluation of coronary artery bypass grafting. *Am J Cardiol* 1989;64:860-5.
  75. Gropler RJ, Geltman EM, Sampathkumaran K, Perez JE, Schechtman KB, Conversano A, et al. Comparison of carbon-11-acetate with fluorine-18-fluorodeoxyglucose for delineating viable myocardium by positron emission tomography. *J Am Coll Cardiol* 1993;22:1587-97.
  76. Tamaki N, Kawamoto M, Tadamura E, Magata Y, Yonekura Y, Nohara R, et al. Prediction of reversible ischemia after revascularization. Perfusion and metabolic studies with positron emission tomography. *Circulation* 1995;91:1697-705.
  77. Knuuti MJ, Saraste M, Nuutila P, Härkönen R, Wegelius U, Haapanen A, et al. Myocardial viability: fluorine-18-deoxyglucose positron emission tomography in prediction of wall motion recovery after revascularization. *Am Heart J* 1994;127:785-96.
  78. Lucignani G, Paolini G, Landoni C, Zuccari M, Paganelli G, Galli L, et al. Presurgical identification of hibernating myocardium by combined use of technetium-99m hexakis 2-methoxyisobutylisonitrile SPECT and fluorine-18 fluoro-2-deoxy-D-glucose positron emission tomography in patients with coronary artery disease. *Eur J Nucl Med* 1992;19:874-81.
  79. Carrel T, Jenni R, Haubold-Reuter S, Von Schulthess G, Pasic M, Turina M. Improvement of severely reduced left ventricular function after surgical revascularization in patients with preoperative myocardial infarction. *Eur J Cardiothorac Surg* 1992;6:479-84.
  80. Tillisch J, Brunken R, Marshall R, Schwaiger M, Manderkern M, Phelps ME, et al. Reversibility of cardiac wall-motion abnormalities predicted by positron tomography. *N Engl J Med*;1986;314:884-8.
  81. Wolpers HG, Burchert W, Van den Hoff J, Weinhardt R, Meyer GJ, Lichtlen PR. Assess-

- ment of myocardial viability by use of  $^{14}\text{C}$ -acetate and positron emission tomography. Threshold criteria of reversible dysfunction. *Circulation* 1997;95:1417-24.
82. Paolini G, Lucignani G, Zuccari M, Landoni C, Vanoli G, Di Credico G, et al. Identification and revascularization of hibernating myocardium in angina-free patients with left ventricular dysfunction. *Eur J Cardiothorac Surg* 1994;8:139-44.
  83. Fath-Ordoubadi F, Pagano D, Marinho NVS, Keogh BE, Bonser RS, Camici PG. Coronary revascularization in the treatment of moderate and severe postischemic left ventricular dysfunction. *Am J Cardiol* 1998;82:26-31.
  84. Pagano D, Townend JN, Littler WA, Horton R, Camici PG, Bonser RS. Coronary artery bypass surgery as treatment for ischemic heart failure: the predictive value of viability assessment with quantitative positron emission tomography for symptomatic and functional outcome. *J Thorac Cardiovasc Surg* 1998;115:791-9.
  85. Vom Dahl J, Eitzman DT, Al-Aouar ZR, Kanter L, Kicks RJ, Deeb GM, et al. Relation of regional function, perfusion and metabolism in patients with advanced coronary artery disease undergoing surgical revascularization. *Circulation* 1994;90:2356-66.
  86. Vom Dahl J, Althoefer C, Sheehan FH, Beuchin P, Uebis R, Messmer BJ, et al. Recovery of regional left ventricular dysfunction after coronary revascularization. Impact of myocardial viability assessed by nuclear imaging and vessel patency at follow-up angiography. *J Am Coll Cardiol* 1996;28:948-58.
  87. Kitsiou AN, Bacharach SL, Bartlett ML, Srinivasan G, Summers RM, Quyyumi AA, et al.  $^{13}\text{N}$ -ammonia myocardial blood flow and uptake. Relation to functional outcome of asynergic regions after revascularization. *J Am Coll Cardiol* 1999;33:678-86.
  88. Kloner RA, Przyklenk K, Patel B. Altered myocardial states. The stunned and hibernating myocardium. *Am J Med* 1989;86(Suppl 1A):14-22.
  89. Afridi I, Qureshi U, Kopelen HA, Winters WL, Zoghbi WA. Serial changes in response of hibernating myocardium to inotropic stimulation after revascularization: a dobutamine echocardiographic study. *J Am Coll Cardiol* 1997;30:1233-40.
  90. Vanoverschelde J-L, Melin JA, Depre C, Borgers M, Dion R, Wijns W. Time-course of functional recovery of hibernating myocardium after coronary revascularization [abstract]. *Circulation* 1994;90(Pt 2):I-378.
  91. Rahimtoola SH. Hibernating myocardium: a brief article. *Basic Res Cardiol* 1995;90:38-40.
  92. Rahimtoola SH. The hibernating myocardium. *Am Heart J* 1989; 117:211-21.
  93. Schwarz ER, Schoendube FA, Kostin S, Schmiedtke N, Schulz G, Buell U, et al. Prolonged myocardial hibernation exacerbates cardiomyocyte degeneration and impairs recovery of function after revascularization. *J Am Coll Cardiol* 1998;31:1018-26.
  94. Gerber BL, Melin JA, Bol A, Labar D, Cogneau M, Michel C, et al. Nitrogen-13-ammonia and oxygen-15-water estimates of absolute myocardial perfusion in left ventricular ischemic dysfunction. *J Nucl Med* 1998;39:1655-62.
  95. Rahimtoola SH. Hibernating myocardium has reduced blood flow at rest that increases with low-dose dobutamine. *Circulation* 1996; 94:3055-61.
  96. Poldermans D, Rambaldi R, Bax JJ, Coronel JH, Thomson IR, Valkema R, et al. Safety and utility of atropine addition during dobutamine stress echocardiography for the assessment of viable myocardium in patients with severe left ventricular dysfunction. *Eur Heart J* 1998;19:1712-8.
  97. Beller GA. Assessment of myocardial viability. *Curr Opin Cardiol* 1997;12:459-67.
  98. Maddahi J. Nuclear cardiology: which clinical questions can be answered now and in the future? In: Van der Wall EE, Reiber JHC, editors. What's new in cardiovascular imaging? Dordrecht: Kluwer Academic; 1998. p. 261-78.

99. Kitsiou AN, Srinivasan G, Quyyumi AA, Summers RM, Bacharach SL, Dilsizian V. Stress-induced reversible and mild-to-moderate irreversible thallium defects: are they equally accurate for predicting recovery of regional left ventricular function after revascularization? *Circulation* 1998;98:501-8.
100. Piwnica-Worms D, Kronauge J, Chiu M. Uptake and retention of hexakis (2-methoxyisobutyl isonitrile) technetium(I) in cultured chick myocardial cells. Mitochondrial and plasma membrane potential dependence. *Circulation* 1990;82:1826-38.
101. Matsunari I, Böning G, Ziegler SI, Nekolla SG, Stollfuss JC, Kosa I, et al. Attenuation-corrected <sup>99m</sup>Tc-tetrofosmin single-photon emission computed tomography in the detection of viable myocardium: comparison with positron emission tomography using <sup>18</sup>F-fluorodeoxyglucose. *J Am Coll Cardiol* 1998;32:927-35.
102. Tamaki N. Myocardial FDG PET studies with the fasting, oral glucose loading or insulin clamp methods. *J Nucl Med* 1992;33:1263-8.
103. Gropler RJ. Methodology governing the assessment of myocardial glucose metabolism by PET and fluorine 18-labeled FDG. *J Nucl Cardiol* 1994;1:S4-S14.
104. Knuuti J, Nuutila P, Ruotsalainen U, Saraste M, Harkonen R, Ahonen A, et al. Euglycemic hyperinsulinemic clamp and oral glucose load in stimulating myocardial glucose utilization during positron emission tomography. *J Nucl Med* 1992;33:1255-62.
105. Gropler RJ, Siegel BA, Lee KJ, Moerlein SM, Perry DJ, Bergmann SR, et al. Nonuniformity in myocardial accumulation of fluorine-18-fluorodeoxyglucose in normal fasted humans. *J Nucl Med* 1990;31:1749-56.
106. Vom Dahl J, Hermann WH, Hicks RJ, Ortiz-Alonso FJ, Lee KS, Allman KC, et al. Myocardial glucose uptake in patients with insulin-dependent diabetes mellitus assessed by positron emission tomography. *Circulation* 1993;88:395-404.
107. Cornel JH, Bax JJ, Elhendy A, Visser FC, Boersma E, Poldermans D, et al. Agreement and disagreement between "metabolic viability" and "contractile reserve" in akinetic myocardium. *J Nucl Cardiol* 1999;6:383-8.
108. Panza JA, Dilsizian V, Laurienzo JM, Curiel RV, Katsiyannis PT. Relation between thallium uptake and contractile response to dobutamine. Implications regarding myocardial viability in patients with chronic coronary artery disease and left ventricular dysfunction. *Circulation* 1995;91:990-8.
109. Pagano D, Bonser DS, Townend JN, Parums D, Camici PG. Histopathological correlates of dobutamine echocardiography in hibernating myocardium [abstract]. *Circulation* 1996;94:I-543.
110. Baumgartner H, Porenta G, Lau Y, Wutte M, Klaar U, Mehrabi M, et al. Assessment of myocardial viability by dobutamine echocardiography, positron emission tomography and thallium-201 SPECT. Correlation with explanted hearts. *J Am Coll Cardiol* 1998;32:1701-8.
111. Meluzin J, Cerny J, Frelich M, Stetka F, Spinarova L, Popelova J, et al. Dobutamine echocardiography in predicting improvement in global left ventricular systolic function after coronary bypass or angioplasty in patients with healed myocardial infarcts. *Am J Cardiol* 1995;76:877-80.
112. Bax JJ, Cornel JH, Visser FC, Van Lingen A. The amount of viable tissue but not scar tissue predicts improvement of LVEF after revascularization. *Circulation* 1998;97(Suppl I):I369-I370.
113. Auerbach MA, Schöder H, Gambhir SS, Yaghoubi S, Sayre JW, Silverman D, et al.

- Prevalence of myocardial viability as detected by positron emission tomography in patients with ischemic cardiomyopathy. *Circulation* 1999;99:2921-6.
114. Eitzman D, Al-Aouar ZR, Kanter HL, vom Dahl J, Kirsch M, Deeb GM, et al. Clinical outcome of patients with advanced coronary artery disease after viability studies with positron emission tomography. *J Am Coll Cardiol* 1992;20:559-65.
  115. Di Carli M, Davidson M, Little R, Khanna S, Mody FV, Brunken RC, et al. Value of metabolic imaging with positron emission tomography for evaluating prognosis in patients with coronary artery disease and left ventricular dysfunction. *Am J Cardiol* 1994;73:527-33.
  116. Pagley PR, Beller GA, Watson DD, Gimple LW, Ragosta M. Improved outcome after coronary bypass surgery in patients with ischemic cardiomyopathy and residual myocardial viability. *Circulation* 1997;96:793-800.
  117. Afridi I, Grayburn PA, Panza JA, Oh JK, Zoghbi WA, Marwick TH. Myocardial viability during dobutamine echocardiography predicts survival in patients with coronary artery disease and severe left ventricular systolic dysfunction. *J Am Coll Cardiol* 1998;32:921-6.
  118. Williams MJ, Odabashian J, Laurer MS, Thomas JD, Marwick TH. Prognostic value of dobutamine echocardiography in patients with left ventricular dysfunction. *J Am Coll Cardiol* 1996;27:132-9.
  119. Bonow RO. Identification of viable myocardium. *Circulation* 1996;94:2674-80.
  120. Kim RJ, Wu E, Rafael A, Chen E-L, Parker MA, Simonetti O, et al. The use of contrast-enhanced magnetic resonance imaging to identify reversible myocardial dysfunction. *N Engl J Med* 2000;34:1445-53.
  121. Beller GA. Non-invasive assessment of myocardial viability [editorial]. *N Engl J Med* 2000;343:1488-90.

*Appendixes 1-5 appear on pages 182-6*

**APPENDIX 1** Summary of protocols and viability criteria used in the dobutamine echo studies

Reference	Protocol-dose of dobutamine ( $\mu\text{g}/\text{kg}/\text{min}$ )	Stage duration (min)	Viability criteria	Analysis
Gerber et al <sup>12</sup>	5, 10	3	↑WM/T	Dig, cine
Charney et al <sup>13</sup>	5, 10	4	↑WM/T	Vid
Arnese et al <sup>14</sup>	5, 10, 20, 40, A	3	↑WM/T at low dose	Dig, cine
Perrone-Filardi et al <sup>15</sup>	5, 10	5	↑WM/T at low dose	Dig, cine
Vanoverschelde et al <sup>16</sup>	5-40	3	↑WM/T at low dose	Dig, cine
Marzullo et al <sup>17</sup>	5, 10	5	↑WM	Vid
Bax et al <sup>18</sup>	5, 10	5	↑WM	Dig, cine
Senior et al <sup>19</sup>	5, 10	5	↑WM	Dig, cine
Perrone-Filardi et al <sup>20</sup>	5, 10	5	↑WM/T	Vid
Alfieri et al <sup>21</sup>	5, 10	5	↑WM/T	Vid
La Canna et al <sup>22</sup>	5, 10	5	↑WM/T	Dig, cine
Haque et al <sup>23</sup>	A, 4, 8, 12, 20	4	↑WM/T at any dose	Dig, cine
Baer et al <sup>24</sup>	5, 10	5	↑WM/T	Dig, cine
DeFilippi et al <sup>25</sup>	5, 10, 15, 20	3	↑WM/T at any dose	Dig, cine
Elhendy et al <sup>26</sup>	5, 10, 20, 30, 40, A	3	↑WM/T at low dose	Dig, cine
Kostopoulos et al <sup>27</sup>	5, 10	5	↑WM/T	Vid
Cornel et al <sup>28</sup>	5, 10	5	↑WM/T	Dig, cine
Scognamiglio et al <sup>29</sup>	5, 10	5	↑WM/T	Dig, cine
Pagano et al <sup>30</sup>	5, 10	5	↑WM/T	Vid
Baer et al <sup>31*</sup>	10	5	↑Wall thickening, Q	Dig, cine
Voci et al <sup>32</sup>	5	5	↑Wall thickening, Q	Vid
Picano et al <sup>33†</sup>	5, 10	3	↑WM/T	Vid
Elhendy et al <sup>34</sup>	5, 10, 20, 30, 40, A	3	↑WM/T at low-dose	Dig, cine
Cornel et al <sup>35</sup>	5, 10	5	↑WM/T	Dig, cine
Pace et al <sup>36</sup>	5, 10	5	↑WM/T	Vid
Sayad et al <sup>37*</sup>	5, 10	6	↑Systolic wall thickness	Dig, cine
Sicari et al <sup>38</sup>	5, 10	3	↑WM	Vid
Gunning et al <sup>39*</sup>	5, 10	NA	↑Systolic wall thickness	Dig, cine
Afridi et al <sup>40</sup>	2.5, 5, 7.5, 10, 20, 30, 40	3	Biphasic response/worsening	Dig, cine
Qureshi et al <sup>41</sup>	2.5, 5, 7.5, 10, 20, 30, 40	3	Biphasic response/worsening	Dig, cine
Nagueh et al <sup>42</sup>	2.5, 5, 7.5, 10, 20, 30, 40	3	Biphasic response	Dig, cine
Cornel et al <sup>43</sup>	5, 10, 20, 30, 40, A	5	Biphasic response	Dig, cine

A, Atropine; NA, not available; WM, wall motion; T, thickening; Q, quantitative; dig, digitized; cine, cine loop; vid, videotape.

\*Magnetic resonance imaging instead of echocardiography

†With the addition of dipyridamole.

**APPENDIX 2** Summary of equipment, protocols, analyses, and viability criteria used in the <sup>201</sup>Tl rest-redistribution studies

Reference	Equipment	Protocol	Viability criteria	Analysis
Mori et al <sup>44</sup>	Planar	RR	Rev	SQ (NTM <sup>201</sup> Tl uptake)
Marzullo et al <sup>17</sup>	Planar	RR	Act late (≥55%)	SQ (NTM <sup>201</sup> Tl uptake)
Udelson <sup>45</sup>	SPECT	RR	Act late (≥60%)	SQ (CP, NTM <sup>201</sup> Tl uptake)
Qureshi et al <sup>41</sup>	SPECT	RR	Act late (≥60%)	SQ (NTM <sup>201</sup> Tl uptake)
Ragosta et al <sup>46</sup>	Planar	RR	Act late (≥50%), rev	SQ (NTM <sup>201</sup> Tl uptake)
Alferi et al <sup>21</sup>	NA	RR	Rev	NA
Charney et al <sup>13</sup>	SPECT	R (24 h)-R	Act late	Visual analysis
Perrone-Firaldi et al <sup>15</sup>	SPECT	R (3- to 4-h and 24-h)-R	Act late (≥ 50%), rev (≥12%)	SQ (NTM <sup>201</sup> Tl uptake)
Nagueh et al <sup>42</sup>	SPECT	RR	Act (≥60%)	SQ (NTM <sup>201</sup> Tl uptake)
Matsunari et al <sup>47</sup>	SPECT	RR	Act (≥55%), rev (≥10%)	SQ (CP, NTM <sup>201</sup> Tl uptake)
Cuocolo et al <sup>48</sup>	SPECT	RR	Act (≥50%), rev (≥10%)	SQ (CP, NTM <sup>201</sup> Tl uptake/normals)
Bax et al <sup>49</sup>	SPECT	RR	Act (≥75%), rev (≥5%)	SQ (CP, NTM <sup>201</sup> Tl uptake/normals)
Sciagra et al <sup>50</sup>	SPECT	RR	Act (>65%)	SQ (CP, NTM <sup>201</sup> Tl uptake)
Marzullo et al <sup>51</sup>	Planar	RR	Act (≥55%)	SQ (NTM <sup>201</sup> Tl uptake)
Matsunari et al <sup>52</sup>	SPECT	RR	Act (>60%), rev (≥10%)	SQ (CP, NTM <sup>201</sup> Tl uptake)
Sciagra et al <sup>53</sup>	SPECT	RR	Act (≥60%), rev (>10%)	SQ (CP, NTM <sup>201</sup> Tl uptake)
Bax et al <sup>54</sup>	SPECT	RR	Act (≥75%), rev (≥5%)	SQ (CP, NTM <sup>201</sup> Tl uptake/normals)
Pace et al <sup>36</sup>	SPECT	RR	Act (≥65%), rev (≥12%)	SQ (NTM <sup>201</sup> Tl uptake)
Senior et al <sup>19</sup>	Planar/SPECT	RR	Act late	Visual analysis
Gunning et al <sup>39</sup>	SPECT	RR	Act late (≥60%)	SQ (NTM <sup>201</sup> Tl uptake)
Gunning et al <sup>55</sup>	SPECT	RR	Act late (≥55%)	SQ (NTM <sup>201</sup> Tl uptake)
Sicari et al <sup>38</sup>	NA	RR	Act late (≥55%)	SQ (NTM <sup>201</sup> Tl uptake)

CP, Circumferential profiles; NA, not available; RR, rest-redistribution (3- to 4-hour redistribution unless otherwise stated); act, activity; act late, activity on late image; rev, reversibility; NTM, normalized to maximum; SQ, Semiquantitative.

**APPENDIX 3** Summary of the equipment, protocols, analyses, and viability criteria used in the  $^{201}\text{Tl}$  reinjection studies

Reference	Equipment	Protocol	Viability criteria	Analysis
Vanoverschelde et al <sup>16</sup>	SPECT	S-RD-RI	Act (>50%), rev (>10%)	SQ (CP, NTM $^{201}\text{Tl}$ uptake)
Ohtani et al <sup>56</sup>	SPECT	S-RD-RI	Rev	Visual analysis
Arnese et al <sup>14</sup>	SPECT	S-RI	Act ( $\geq$ 50%), rev	SQ (CP, NTM $^{201}\text{Tl}$ uptake)
Bax et al <sup>18</sup>	SPECT	S-RI	Act ( $\geq$ 50%), rev	SQ (CP, NTM $^{201}\text{Tl}$ uptake)
Tamaki et al <sup>57</sup>	SPECT	S-RD-RI	Rev	Visual analysis
Dilsizian et al <sup>58</sup>	SPECT	S-RD-RI	Rev	SQ (CP, NTM $^{201}\text{Tl}$ uptake/normals)
Haque et al <sup>23</sup>	SPECT	S-RD-RI	Act ( $\geq$ 50%), rev	SQ (NTM $^{201}\text{Tl}$ uptake)
Taki et al <sup>59</sup>	SPECT	S-RI	Act ( $\geq$ 50%), rev	SQ (NTM $^{201}\text{Tl}$ uptake)
Lipiecki et al <sup>60</sup>	SPECT	S-RD-RI	Act, rev	Visual analysis
Gürsürer et al <sup>61</sup>	Planar	S-RD-RI	Act ( $\geq$ 50%), rev	SQ (NTM $^{201}\text{Tl}$ uptake)
Kostopoulos et al <sup>27</sup>	SPECT	S-RD-RI*	Act ( $\geq$ 50%), redistribution	SQ (NTM $^{201}\text{Tl}$ uptake)

CP, Circumferential profiles; S-RD-RI, stress-redistribution-reinjection; S-RI, stress-reinjection; act, activity; rev, reversibility; NTM, normalized to maximum; SQ, Semiquantitative.

\*Pharmacologic stress by dipyridamole.

**APPENDIX 4** Summary of the equipment, protocols, analyses, and viability criteria used in the  $^{99m}\text{Tc}$ -sestamibi/tetrofosmin studies

Reference	Equipment	Protocol	Viability criteria	Analysis
Marzullo et al <sup>51</sup>	Planar	Rest MIBI	Act ( $\geq 54\%$ )	SQ (NTM MIBI uptake)
Marzullo et al <sup>17</sup>	Planar	Rest MIBI	Act ( $\geq 54\%$ )	SQ (NTM MIBI uptake)
Gonzalez et al <sup>62</sup>	SPECT	Rest-stress MIBI (1-day)	Rev	Visual analysis
Marzullo et al <sup>63</sup>	Planar	Rest MIBI	Act ( $\geq 55\%$ )	SQ (NTM MIBI uptake)
Maes et al <sup>64</sup>	SPECT	Rest MIBI	Act ( $> 50\%$ )	SQ (NTM MIBI uptake)
Udelson et al <sup>45</sup>	SPECT	Rest MIBI	Act ( $\geq 60\%$ )	SQ (CP, NTM MIBI uptake)
Maublant et al <sup>65</sup>	SPECT	Rest MIBI	Act	Visual analysis
Matsunari et al <sup>47</sup>	SPECT	Rest TF	Act ( $\geq 50\%$ )	SQ (CP, NTM TF uptake)
Dakik et al <sup>66</sup>	SPECT	Rest MIBI	Act ( $\geq 55\%$ )	SQ (CP, NTM MIBI uptake/normals)
Sciagra et al <sup>50</sup>	SPECT	Rest-oral nitrate MIBI	Act ( $> 65\%$ ), rev (after nitrate)	SQ (CP, NTM MIBI uptake)
Lipiecki et al <sup>60</sup>	SPECT	Stress-rest MIBI (2-day)	Act	Visual analysis
Maurea et al <sup>67</sup>	SPECT	Rest-oral nitrate MIBI	Act ( $\geq 50\%$ ), rev ( $\geq 10\%$ )	SQ (NTM MIBI uptake/normals)
Bisi et al <sup>68</sup>	SPECT	Rest-intravenous nitrate MIBI	$\downarrow$ in % defect on the nitrate MIBI (vs rest MIBI)	SQ (CP, NTM MIBI uptake/normals)
Bisi et al <sup>69</sup>	SPECT	Rest-intravenous nitrate MIBI	$> 10\%$ $\downarrow$ in defect on the nitrate MIBI (vs rest MIBI)	SQ (CP, NTM MIBI uptake/normals)
Greco et al <sup>70</sup>	SPECT	Rest-intravenous nitrate MIBI	Rev (after nitrate)	Visual analysis
Li et al <sup>71</sup>	SPECT	Rest-intravenous nitrate MIBI	Rev (after nitrate)	SQ (CP, NTM MIBI uptake)
Schneider et al <sup>72</sup>	SPECT	Rest-oral nitrate MIBI	Act ( $\geq 50\%$ anterior wall, $\geq 35\%$ inferior wall)	SQ (NTM MIBI uptake)
Levine et al <sup>73</sup>	Gated SPECT	Rest MIBI	Act (estimated $> 50\%$ ) and/or preserved wall motion	Visual analysis
Gunning et al <sup>39</sup>	SPECT	Rest TF	Act ( $\geq 64\%$ )	SQ (NTM TF uptake)
Gunning et al <sup>55</sup>	SPECT	Rest TF	Act ( $\geq 55\%$ )	SQ (NTM TF uptake)

CP, Circumferential profiles; MIBI,  $^{99m}\text{Tc}$ -sestamibi; TF,  $^{99m}\text{Tc}$ -tetrofosmin; act, activity; rev, reversibility; NTM, normalized to maximum; SQ, semiquantitative.

**APPENDIX 5** Summary of the metabolic conditions, tracers, viability criteria, and analyses used in the FDG PET studies

Reference	Metabolic conditions	Tracers	Viability criteria	Analysis
Marwick et al	OG load	FDG/rubidium 82	Mismatch, normal perfusion	SQ (normalized to segment with NP)
Gerber et al <sup>12</sup>	HEC	FDG/ <sup>13</sup> N-ammonia	Mismatch	SQ (CP, compared with normals)
Tamaki et al <sup>74</sup>	Fasting	FDG/ <sup>13</sup> N-ammonia	Mismatch	SQ (CP, compared with normals)
Gropler et al <sup>75</sup>	OG load	FDG/ <sup>11</sup> C-acetate	Mismatch, FDG >2 SD normal	SQ (CP, compared with normals)
Maes et al <sup>64</sup>	HEC	FDG/ <sup>13</sup> N-ammonia	Mismatch, NP	AQ (flow and rMGU)
Tamaki et al <sup>76</sup>	Fasting	FDG/ <sup>13</sup> N-ammonia	Mismatch	SQ (CP/FDG utilization index)
Knuuti <sup>77</sup>	OG load	FDG/ <sup>201</sup> Tl, MIBI SPECT	Normal FDG uptake, mismatch	SQ (normalized to segment with NP)
Baer et al <sup>24</sup>	OG load	FDG	Normal FDG uptake (≥50% of maximum)	SQ (CP, normalized to maximum FDG uptake)
Lucignani et al <sup>78</sup>	Fasting	FDG/MIBI SPECT	Mismatch	Visual analysis
Carrel et al <sup>79</sup>	NA	FDG/rubidium 82	Mismatch	NA
Tillisch et al <sup>80</sup>	OG load	FDG/ <sup>13</sup> N-ammonia	Mismatch, NP	SQ (CP, compared with normals)
Tamaki et al <sup>57</sup>	Fasting	FDG/ <sup>13</sup> N-ammonia	Mismatch	SQ (CP, compared with normals)
Wolpers et al <sup>81</sup>	OG load	FDG/ <sup>11</sup> C-acetate	Mismatch	AQ (flow and rMGU)
Paolini et al <sup>82</sup>	Fasting	FDG/MIBI SPECT	Mismatch	Visual analysis
Pagano et al <sup>30</sup>	HEC	FDG	rMGU ≥0.25 μmol/min/g	AQ (rMGU normalized to normally contracting segments)
Ordoubadi et al <sup>83</sup>	HEC	FDG	rMGU	AQ (rMGU)
Pagano et al <sup>84</sup>	HEC	FDG	rMGU ≥0.25 μmol/min/g	AQ (rMGU normalized to normally contracting segments)
Vom Dahl et al <sup>85</sup>	OG load	FDG/ <sup>13</sup> N-ammonia	Mismatch, NP, mild match*	Visual analysis
Vom Dahl et al <sup>86</sup>	OG load	FDG/MIBI SPECT	Mismatch, NP, mild match*	SQ (normalized to segment with maximum MIBI uptake)
Kitsiou et al <sup>87</sup>	OG load	FDG/ <sup>13</sup> N-ammonia	Normal <sup>13</sup> N-ammonia/FDG (≥65% of normal) uptake	SQ (normalized to segment with maximum <sup>201</sup> Tl uptake)

AQ, Absolute quantification; CP, circumferential profiles; FDG, fluorine 18 deoxyglucose; HEC, hyperinsulinemic euglycemic clamp; MIBI, <sup>99m</sup>Tc-sestamibi; NA, not available; NP, normal perfusion; OG, oral glucose; rMGU, regional myocardial glucose utilization; SQ, semiquantitative.

\*Mild match represents mild reduction in perfusion and FDG uptake without mismatch present.