

ACC/AHA Guideline

ACC/AHA/ASNC Guidelines for the Clinical Use of Cardiac Radionuclide Imaging—Executive Summary

A Report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (ACC/AHA/ASNC Committee to Revise the 1995 Guidelines for the Clinical Use of Cardiac Radionuclide Imaging)

Committee Members

Francis J. Klocke, MD, MACC, FAHA, Chair;
 Michael G. Baird, MD, FACC, FAHA; Beverly H. Lorell, MD, FACC, FAHA;
 Timothy M. Bateman, MD, FACC, FAHA; Joseph V. Messer, MD, MACC, FAHA;
 Daniel S. Berman, MD, FACC, FAHA; Patrick T. O’Gara, MD, FACC;
 Blase A. Carabello, MD, FACC, FAHA; Richard O. Russell, Jr, MD, FACC;
 Manuel D. Cerqueira, MD, FACC, FAHA; Martin G. St. John Sutton, MBBS, FACC;
 Anthony N. DeMaria, MD, MACC, FAHA; James E. Udelson, MD, FACC;
 J. Ward Kennedy, MD, MACC, FAHA; Mario S. Verani, MD, FACC*;
 Kim Allan Williams, MD, FACC, FAHA

Task Force Members

Elliott M. Antman, MD, FACC, FAHA, Chair; Sidney C. Smith, Jr, MD, FACC, FAHA, Vice-Chair;
 Joseph S. Alpert, MD, FACC; Gabriel Gregoratos, MD, FACC, FAHA;
 Jeffrey L. Anderson, MD, FACC; Loren F. Hiratzka, MD, FACC, FAHA;
 David P. Faxon, MD, FACC, FAHA; Sharon Ann Hunt, MD, FACC, FAHA;
 Valentin Fuster, MD, PhD, FACC, FAHA; Alice K. Jacobs, MD, FACC, FAHA;
 Raymond J. Gibbons, MD, FACC, FAHA†‡; Richard O. Russell, MD, FACC†

Table of Contents

I. Introduction.....	1319	B. Detection of AMI When Conventional Measures Are Nondiagnostic	1320
II. Acute Syndromes.....	1320	C. Radionuclide Testing in Risk Assessment: Prognosis and Assessment of Therapy After STEMI	1320
A. Myocardial Perfusion Imaging in the Assessment of Patients Presenting With Chest Pain to the Emergency Department	1320	D. Radionuclide Testing in Risk Assessment: Prognosis and Assessment of Therapy After NSTEMI or UA.	1320
		III. Chronic Syndromes	1321

The ACC/AHA Task Force on Practice Guidelines makes every effort to avoid any actual or potential conflicts of interest that might arise as a result of an outside relationship or personal interest of a member of the writing panel. Specifically, all members of the writing panel are asked to provide disclosure statements of all such relationships that might be perceived as real or potential conflicts of interest. These statements are reviewed by the parent task force, reported orally to all members of the writing panel at the first meeting, and updated as changes occur.

This document was approved by the American College of Cardiology Foundation Board of Trustees in July, 2003, the American Heart Association Science Advisory and Coordinating Committee in July, 2003, and the American Society of Nuclear Cardiology Board of Directors in July, 2003.

When citing this document, the American College of Cardiology Foundation, the American Heart Association, and the American Society of Nuclear Cardiology request that the following citation format be used: Klocke FJ, Baird MG, Bateman TM, Berman DS, Carabello BA, Cerqueira MD, DeMaria AN, Kennedy JW, Lorell BH, Messer JV, O’Gara PT, Russell RO Jr, St. John Sutton MG, Udelson JE, Verani MS, Williams KA. ACC/AHA/ASNC guidelines for the clinical use of cardiac radionuclide imaging—executive summary: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (ACC/AHA/ASNC Committee to Revise the 1995 Guidelines for the Clinical Use of Radionuclide Imaging). *J Am Coll Cardiol* 2003;42:1318–33.

*Deceased.

†Former Task Force Member.

‡Former Task Force Chair.

(*J Am Coll Cardiol* 2003;42:1318–33)

©2003 by the American College of Cardiology Foundation and the American Heart Association, Inc.

- A. Detection (Diagnosis) of CAD..... 1321
 - 1. Sensitivity and Specificity..... 1321
 - 2. Effect of Referral Bias 1321
 - 3. Quantitative Analysis 1322
 - 4. ECG-Gated SPECT 1322
 - 5. Attenuation Correction 1322
 - 6. Positron Emission Tomography 1322
- B. Management of Patients With Known or Suspected Chronic CAD: Assessment of Disease Severity, Risk Stratification, Prognosis 1322
 - 1. Nongated Myocardial Perfusion Imaging.. 1322
 - 2. Gated SPECT..... 1322
 - 3. Radionuclide Angiography..... 1322
 - 4. Cost Effectiveness 1322
 - 5. Frequency of Testing..... 1322
 - 6. Evaluation of the Effects of Medical Therapy.. 1322
- C. Specific Patient Populations..... 1322
 - 1. African Americans..... 1322
 - 2. Women..... 1322
 - 3. Normal Resting ECG, Able to Exercise.... 1323
 - 4. Intermediate-Risk Duke Treadmill Score.. 1323
 - 5. Normal Resting ECG, Unable to Exercise. 1323
 - 6. LBBB/Pacemakers..... 1323
 - 7. Left Ventricular Hypertrophy..... 1323
 - 8. Patients With Nonspecific ST-T-Wave Changes..... 1323
 - 9. Elderly 1323
 - 10. Asymptomatic Patients 1323
 - 11. Obese Patients..... 1323
 - 12. Diabetes..... 1323
 - 13. After Coronary Calcium Screening 1324
 - 14. Before and After Revascularization..... 1324
 - 15. Radionuclide Imaging Before Noncardiac Surgery..... 1324
- D. Recommendations..... 1324
- IV. Heart Failure 1326
 - A. Introduction..... 1326
 - B. Assessment of LV Function..... 1327
 - 1. Assessment of LV Systolic Dysfunction... 1327
 - 2. Assessment of LV Diastolic Dysfunction . 1327
 - C. Assessment of CAD 1327
 - 1. Importance of Detecting CAD in Heart Failure Patients 1327
 - 2. Myocardial Perfusion Imaging to Detect CAD in Heart Failure Patients..... 1327
 - D. Assessment of Myocardial Viability..... 1327
 - 1. Goals of Assessing Myocardial Viability.. 1327
 - 2. General Principles of Assessing Myocardial Viability by Radionuclide Techniques..... 1328
 - 3. Techniques and Protocols for Assessing Myocardial Viability..... 1328
 - 4. Image Interpretation for Myocardial Viability: Quantitative Versus Visual Analysis of Tracer Activities 1328
 - 5. Comparison of Techniques..... 1328
 - E. Etiologies of Heart Failure..... 1329
 - 1. Dilated Cardiomyopathy..... 1329
 - 2. Dilated Cardiomyopathy Due to Doxorubicin/Anthracycline Cardiotoxicity. 1329

- 3. Dilated Cardiomyopathy Due to Myocarditis 1329
- 4. Posttransplantation Rejection and Allograft Vasculopathy..... 1329
- 5. Chagas Myocarditis and/or Cardiomyopathy... 1330
- 6. Sarcoid Heart Disease 1330
- 7. Cardiac Amyloidosis 1330
- 8. RV Dysplasia..... 1330
- 9. Hypertrophic Cardiomyopathy 1330
- 10. Hypertensive Heart Disease 1330
- 11. Valvular Heart Disease..... 1330
- 12. Adults With Congenital Heart Disease..... 1331
- References..... 1331

I. Introduction

The American College of Cardiology (ACC)/American Heart Association (AHA) Task Force on Practice Guidelines regularly reviews existing guidelines to determine when an update or full revision is needed. Guidelines for the Clinical Use of Cardiac Radionuclide Imaging were originally published in 1986 and updated in 1995. Important new developments have continued to occur since 1995, particularly in the areas of acute and chronic ischemic syndromes and heart failure. The Task Force therefore believed the topic should be revisited de novo and invited the American Society for Nuclear Cardiology (ASNC) to cosponsor the undertaking, which represents a joint effort of the 3 organizations.

The full-text guideline is available on the Internet (www.acc.org, www.americanheart.org, and www.asnc.org). It discusses the usefulness of nuclear cardiological techniques in 3 broad areas: acute ischemic syndromes, chronic syndromes, and heart failure. Utility is considered for diagnosis, severity of disease/risk assessment/prognosis, and assessment of therapy. An appendix provides descriptions of individual techniques. This Executive Summary includes recommended indications for the use of specific techniques and summary evaluations of topics addressed in the full-text document. Additional supporting evidence and a complete reference list are presented in the full-text document.

The current guideline overlaps with several previously published ACC/AHA guidelines for patient treatment that potentially involve cardiac radionuclide imaging. These include published guidelines for chronic stable angina (SA; 2002), unstable angina and non-ST-elevation myocardial infarction (UA/NSTEMI; 2002), heart failure (2001), perioperative cardiovascular evaluation for noncardiac surgery (2002), exercise testing (2002), valvular heart disease (1998), and acute myocardial infarction (AMI; 1999). The present report is not intended to include information previously covered in these guidelines or to provide a comprehensive treatment of the topics addressed in these guidelines.

The ACC/AHA classifications I, II, and III are used to summarize indications as follows:

Class I: Conditions for which there is evidence and/or general agreement that a given procedure or treatment is useful and effective

Class II: Conditions for which there is conflicting evidence and/or a divergence of opinion about the usefulness/efficacy of a procedure or treatment

TABLE 1. Recommendations for Emergency Department Imaging for Suspected ACS

Indication	Test	Class	Level of Evidence
1. Assessment of myocardial risk in possible ACS patients with nondiagnostic ECG and initial serum markers and enzymes, if available.	Rest MPI	I	A
2. Diagnosis of CAD in possible ACS patients with chest pain with nondiagnostic ECG and negative serum markers and enzymes or normal resting scan.	Same day rest/stress perfusion imaging	I	B
3. Routine imaging of patients with myocardial ischemia/necrosis already documented clinically, by ECG and/or serum markers or enzymes	Rest MPI	III	C

See Figure 6 of ACC/AHA 2002 Guideline Update for the Management of Patients With Unstable Angina and Non–ST-Segment Elevation Myocardial Infarction at <http://www.acc.org/clinical/guidelines/unstable/incorporated/figure6.htm> and Figure 1 of ACC/AHA Guidelines for the Management of Patients with Acute Myocardial Infarction at www.acc.org/clinical/guidelines/nov96/1999/jac1716f01.htm.

ACS indicates acute coronary syndromes; CAD, coronary artery disease; ECG, electrocardiogram; MPI, myocardial perfusion imaging.

IIa: Weight of evidence/opinion is in favor of usefulness/efficacy

IIb: Usefulness/efficacy is less well established by evidence/opinion

Class III: Conditions for which there is evidence and/or general agreement that the procedure/treatment is not useful/effective and in some cases may be harmful

Levels of evidence for individual class assignments are designated as follows:

- A:** Data derived from multiple randomized clinical trials
- B:** Data derived from a single randomized trial or from nonrandomized studies
- C:** Consensus opinion of experts

These guidelines will be reviewed annually by the Task Force and will be considered current unless the Task Force revises or withdraws them from distribution.

II. Acute Syndromes

A. Myocardial Perfusion Imaging in the Assessment of Patients Presenting With Chest Pain to the Emergency Department

Optimal decision-making in patients seen in the emergency department with chest pain requires triage into risk categories on the basis of the probability of AMI, UA, or both and the subsequent risk and potential interventional options. Within such an algorithm, radionuclide imaging provides clinically useful information for diagnosis and management. The UA guidelines use 4 risk levels for chest pain: noncardiac, chronic SA, possible acute coronary syndrome (ACS), and definite ACS (<http://www.acc.org/clinical/guidelines/unstable/unstable.pdf>) (1). Radionuclide imaging is most appropriate in patients with possible ACS. After initial triage on the basis of symptoms, ECG, and history, rest single-photon emission CT (SPECT) imaging appears to be useful for identifying patients at high risk (those with perfusion defects), who should be admitted, and patients with low risk (those with normal scans), who in general may be discharged home with a low risk for subsequent ischemic events. Randomized

clinical trials (2,3) now support several observational studies (see Table 1 in the full-text guideline) indicating a high negative predictive value for excluding ACS. Table 1 lists recommendations for emergency department imaging for suspected ACS.

B. Detection of AMI When Conventional Measures Are Nondiagnostic

Rest myocardial perfusion imaging with ^{99m}Tc tracers has a high sensitivity for diagnosing AMI. Because there is minimal redistribution of the radiopharmaceutical over time, imaging can be delayed for a few hours after the injection and still provide accurate information about myocardial perfusion at the time of injection, which reflects the area of myocardium at risk. Perfusion defects, however, do not distinguish among acute ischemia, acute infarction, or previous infarction.

C. Radionuclide Testing in Risk Assessment: Prognosis and Assessment of Therapy After STEMI

As discussed in the ACC/AHA Guidelines for the Management of Patients with Acute Myocardial Infarction: 1999 Update (4) (<http://www.acc.org/clinical/guidelines/nov96/1999/index.htm>), the prognosis of STEMI is primarily a function of ejection fraction (EF), infarct size, and residual myocardium at risk. Thus, acute or late measurement of EF, infarct size, and myocardium at risk provides important prognostic management information. Radionuclide techniques are also useful for assessing the presence and extent of stress-induced myocardial ischemia—information that is useful for immediate and long-term patient management (5–9). Table 2 lists recommendations for radionuclide testing in diagnosis, risk assessment, prognosis, and assessment of therapy after acute STEMI.

D. Radionuclide Testing in Risk Assessment: Prognosis and Assessment of Therapy After NSTEMI or UA

The ACC/AHA 2002 Guideline Update for the Management of Patients with UA/NSTEMI (1) recommends an early invasive strategy in patients with any of several high-risk

TABLE 2. Recommendations for Use of Radionuclide Testing in Diagnosis, Risk Assessment, Prognosis, and Assessment of Therapy After Acute STEMI

Patient Subgroup(s)	Indication	Test	Class	Level of Evidence
All	1. Rest LV function	Rest RNA or ECG-gated SPECT	I	B
Thrombolytic therapy without catheterization	2. Detection of inducible ischemia and myocardium at risk	Stress MPI with ECG-gated SPECT whenever possible	I	B
Acute STEMI	3. Assessment of infarct size and residual viable myocardium	MPI at rest or with stress using gated SPECT	I	B
	4. Assessment of RV function with suspected RV infarction	Equilibrium or FPRNA	Ila	B

ECG indicates electrocardiography; FPRNA, first-pass radionuclide angiography; LV, left ventricular; MPI, myocardial perfusion imaging; RNA, radionuclide angiography; RV, right ventricular; SPECT, single-photon emission computed tomography; STEMI, ST-segment elevation myocardial infarction.

indicators and no serious comorbidities. High-risk findings on noninvasive stress testing (eg, myocardial perfusion imaging) are one such indication. In the absence of high-risk findings, the guidelines endorse either an early conservative or early invasive strategy in patients without contraindications for revascularization. Myocardial perfusion imaging is particularly useful in the predischARGE risk stratification of patients with UA. The presence and extent of reversible perfusion defects on stress testing after the patient is stabilized are highly predictive of future events (10–14). Table 3 lists recommendations for radionuclide testing for risk assessment/prognosis in patients with NSTEMI or UA.

III. Chronic Syndromes

A. Detection (Diagnosis) of Coronary Artery Disease

A thorough discussion of the concepts of likelihood of coronary artery disease (CAD) is provided in the ACC/AHA 2002 Guideline Update for the Management of Patients With Chronic Stable Angina (15) (http://www.acc.org/clinical/guidelines/stable/stable_clean.pdf), accompanied by a simplified table for estimating pretest probability ranges. Myocardial perfusion imaging is most useful in patients with an

intermediate likelihood of angiographically significant CAD on the basis of age, sex, symptoms, risk factors, and the results of stress testing (for patients who have undergone prior stress testing).

1. Sensitivity and Specificity

Tables 5 and 6 in the full-text guideline summarize studies reporting sensitivities and specificities of exercise and vasodilator stress perfusion SPECT for the detection of angiographically significant (more than 50% stenosis) CAD. Sensitivities (generally uncorrected for referral bias) average 87% and 89%, respectively; specificities (also uncorrected) average 73% and 75%.

2. Effect of Referral Bias

In estimating the true sensitivity and specificity of noninvasive testing, referral or work-up bias needs to be taken into account. Table 7 in the full-text guideline summarizes studies in which effects of referral bias have been estimated. Because of the profound impact of referral bias on specificity, the concept of the normalcy rate has been developed. The term normalcy rate is used to describe the frequency of normal test results in patients with a low likelihood of CAD, to differentiate it from specificity.

TABLE 3. Recommendations for Use of Radionuclide Testing for Risk Assessment/Prognosis in Patients With NSTEMI and UA

Indication	Test	Class	Level of Evidence
1. Identification of inducible ischemia in the distribution of the “culprit lesion” or in remote areas in patients at intermediate or low risk for major adverse cardiac events.	Stress MPI with ECG gating whenever possible	I	B
2. Identification of the severity/extent of inducible ischemia in patients whose angina is satisfactorily stabilized with medical therapy or in whom diagnosis is uncertain.	Stress MPI with ECG gating whenever possible	I	A
3. Identification of hemodynamic significance of coronary stenosis after coronary arteriography.	Stress MPI	I	B
4. Measurement of baseline LV function.	RNA or gated SPECT	I	B
5. Identification of the severity/extent of disease in patients with ongoing suspected ischemia symptoms when ECG changes are not diagnostic.	Rest MPI	Ila	B

ECG indicates electrocardiography; LV, left ventricular; MPI, myocardial perfusion imaging; RNA, radionuclide angiography; SPECT, single-photon emission computed tomography.

3. Quantitative Analysis

Quantitative analysis of myocardial perfusion SPECT has been developed using a variety of approaches and, in general, has similar sensitivities and specificities compared with those of expert visual analysis.

4. ECG-Gated SPECT

The current state of the art is ECG-gated myocardial perfusion SPECT (gated SPECT). The ability to observe myocardial contraction in segments with apparent fixed perfusion defects permits the nuclear test reader to discern attenuation artifacts from true perfusion abnormalities. The ability of gated SPECT to provide measurement of left ventricular (LV) EF (LVEF), segmental wall motion, and absolute LV volumes also adds to the prognostic information that can be derived from a SPECT study.

5. Attenuation Correction

The field of attenuation correction continues to evolve rapidly, with some available systems having undergone more detailed and successful clinical validation than others. On the basis of current information and the rate of technology improvement, the Society of Nuclear Medicine and the American Society of Nuclear Cardiology have concluded that attenuation correction has become a method for which the weight of evidence/opinion is in favor of its usefulness (16).

6. Positron Emission Tomography

Studies involving several hundred patients (see Table 10 in the full-text guideline) indicate that perfusion imaging with positron emission tomography (PET) using dipyridamole and either ^{82}Rb or ^{13}N ammonia is also a sensitive and specific clinical means to diagnose CAD.

B. Management of Patients With Known or Suspected Chronic CAD: Assessment of Disease Severity, Risk Stratification, Prognosis

Nuclear tests are best applied for risk stratification in patients with a clinically intermediate risk of a subsequent cardiac event, analogous to the optimal diagnostic application of nuclear testing to patients with an intermediate likelihood of having CAD. Many of the major determinants of prognosis in CAD can be assessed by measurements of stress-induced perfusion and function. Studies including large patient samples have now demonstrated that factors estimating the extent of LV dysfunction (LVEF, the extent of infarcted myocardium, transient ischemic dilation of the LV, and increased lung uptake) are excellent predictors of cardiac mortality. In contrast, markers of provocative ischemia (exertional symptoms, electrocardiographic changes, the extent of reversible perfusion defects, and stress-induced ventricular dyssynergy) are better predictors of the subsequent development of acute ischemic syndromes (17).

1. Nongated Myocardial Perfusion Imaging

Notwithstanding the now well-demonstrated advantages of gated imaging, nongated perfusion scintigraphy has played a major role in risk stratification of CAD patients. The full-text guideline summarizes studies of stress myocardial perfusion imaging in definite or suspected CAD (see Table 12 in the full-text guideline). Normal stress perfusion SPECT results

are consistently predictive of a less than 1% annual risk of cardiac death or myocardial infarction.

2. Gated SPECT

The information contained in the combined assessment of perfusion and function with gated myocardial perfusion SPECT is likely to enhance its prognostic and diagnostic content. The most common current approach combines post-stress and/or rest LV function by gated SPECT with rest/stress perfusion measurements.

3. Radionuclide Angiography

Rest LVEF is universally recognized as one of the most important determinants of long-term prognosis in patients with chronic stable CAD. Radionuclide angiography (RNA) can also be helpful in evaluating dyspnea by establishing the state of right ventricular (RV) and LV performance. LV function during exercise reflects disease severity and provides prognostic information.

4. Cost Effectiveness

As indicated in the ACC/AHA 2002 Guideline Update for the Management of Patients With Chronic Stable Angina (15), cardiac imaging can serve as a gatekeeper to cardiac catheterization to minimize the rate of normal catheterizations and to enrich the angiographic population with a greater proportion of patients with significant, yet treatable, disease.

5. Frequency of Testing

Considerations for follow-up testing are also summarized in the ACC/AHA 2002 Guideline Update for the Management of Patients With Chronic Stable Angina (15). If patients develop new signs or symptoms suggesting a worsened clinical state, repeat testing at the time of worsening would be appropriate. In the absence of a change in clinical state, the estimated patient risk after initial testing (high, intermediate, or low, as defined earlier) should play an important role in individual recommendations (18).

6. Evaluation of the Effects of Medical Therapy

Although the available evidence suggests that the efficacy of therapy can be assessed with repeat SPECT procedures while the patient is under the effects of the medical treatment, information about the effects of medical therapy on outcomes is limited.

C. Specific Patient Populations

1. African Americans

The role of noninvasive imaging has been studied infrequently in African Americans or other minorities. Normal rest and stress SPECT perfusion studies have been associated with higher rates of AMI and/or cardiac death in African Americans than in other populations (19,20), but included higher than usual cardiac risk patients and did not account for the incidence of LV hypertrophy (LVH) (21).

2. Women

As discussed in the ACC/AHA 2002 Guideline Update for Exercise Testing (22) (http://www.acc.org/clinical/guidelines/exercise/exercise_clean.pdf), the use of radionuclide testing in women is influenced importantly by the later

presentation of CAD in women than in men and by sex-related limitations in exercise stress testing. These issues have provoked interest in the potential additive benefit of stress perfusion imaging in women, particularly those with at least an intermediate likelihood of coronary disease (23–26).

3. Normal Resting ECG, Able to Exercise

Patients with a normal resting ECG constitute a large and important subgroup. Most patients who present with multiple risk factors with or without cardiac symptoms have a normal resting ECG. Such patients are likely to have normal LV function and an excellent prognosis. For these reasons, a stepwise strategy is generally recommended in which an exercise ECG, and not a stress imaging procedure, is performed as the initial test in patients with an intermediate pretest likelihood of CAD who are not taking digoxin, have a normal resting ECG, and are able to exercise. A stress imaging technique should be used for patients with widespread rest ST depression (more than 1 mm), complete left bundle-branch block (LBBB), ventricular-paced rhythm, pre-excitation, or LVH with repolarization changes (15).

4. Intermediate-Risk Duke Treadmill Score

The Duke treadmill score combines various forms of information from stress testing and provides a simple way to calculate risk (27). Annual mortality rates according to risk groups are presented in the ACC/AHA 2002 Chronic Stable Angina Guideline Update (15). The score has been reported to work well for both inpatients and outpatients and equally well for men and women. Only a small number of elderly patients, however, have been studied. Several studies have demonstrated value of myocardial perfusion scintigraphy in further risk assessment of patients with an intermediate score associated with an intermediate risk of cardiac death (28–30).

5. Normal Resting ECG, Unable to Exercise

In patients with an intermediate to high likelihood of CAD who have a normal resting ECG but are unable to exercise, pharmacologic myocardial perfusion SPECT with adenosine or dipyridamole has been shown to be highly effective in diagnosis and risk stratification.

6. LBBB/Pacemakers

Pharmacologic stress perfusion imaging is preferable to exercise perfusion imaging for purposes of both diagnosis and risk stratification (31,32). Several studies have observed an increased prevalence of myocardial perfusion defects during exercise imaging, in the absence of angiographic coronary disease, in patients with LBBB. Given that ECG testing is nondiagnostic in patients with ventricular pacing in a manner similar to that observed with LBBB, it is likely that the considerations with regard to the use of radionuclide techniques for diagnostic and risk stratification purposes in patients with ventricular pacemakers are the same as those applied to patients with LBBB.

7. Left Ventricular Hypertrophy

In patients with LVH, with or without resting ST-segment abnormality, ST depression during exercise is frequently present in the absence of significant CAD. In these patients, stress nuclear techniques have similar diagnostic sensitivity

and specificity to those observed in patients without LVH. The diagnostic value of myocardial perfusion SPECT is not generally degraded by the presence of hypertension without evidence of LVH (33), although an increased frequency of false-positive studies has been reported in athletes (34). Similarly, although the number of reports is small, the prognostic value of myocardial perfusion SPECT in patients with LVH appears to be equal to that observed in patients without LVH (35).

8. Patients With Nonspecific ST-T-Wave Changes

Patients with nonspecific ST-T-wave changes, such as might occur with digoxin, Wolff-Parkinson-White syndrome (WPW), or other conditions, are considered to have nondiagnostic stress ECG responses with regard to ST-segment depression. Although there are limited data on the diagnostic and prognostic information for myocardial perfusion SPECT in these patients, those with intermediate to high likelihood of coronary disease can perhaps be effectively assessed for detection and risk stratification with myocardial perfusion SPECT.

9. Elderly

Prognostic value of perfusion scintigraphy in elderly patients has been reported (36).

10. Asymptomatic Patients

The relatively low prevalence of CAD and risk of future events will affect the performance of any diagnostic test in a manner predictable by Bayesian principles (ie, positive predictive value will usually be low). It is not clear that detecting asymptomatic preclinical CAD will lead to therapeutic intervention that will reduce risk beyond that indicated by risk factor profiling and currently recommended strategies to reduce risk (37).

Persons whose occupations may affect public safety (eg, airline pilots, truckers, bus drivers) or who are professional or high-profile athletes commonly undergo periodic exercise testing for statutory reasons (22). In some asymptomatic patients, testing may be appropriate when there is a high-risk clinical situation (eg, diabetes or multiple risk factors) (22). Patients with a more than 20% 10-year risk of developing coronary heart disease are considered to be at high risk in current National Cholesterol Education Program guidelines (37).

11. Obese Patients

Very obese patients constitute a special problem because most imaging tables used for SPECT have weight-bearing limits (often 300 lb [135 kg]) that preclude imaging very heavy subjects. These subjects can still be imaged by planar scintigraphy.

12. Diabetes

The increasing recognition of diabetes mellitus as a major risk factor for cardiovascular disease (38) has heightened interest in myocardial perfusion imaging for CAD diagnosis and risk stratification. Available studies are based on retrospective analyses of patients referred to the nuclear cardiology laboratory (24,39,40). Prospective information in asymptomatic diabetic patients drawn from the general diabetic

population is awaited (41). Currently available studies indicate that (1) ^{99m}Tc -sestamibi myocardial perfusion SPECT has comparable sensitivity, specificity, and normalcy rates for the diagnosis of CAD in diabetic and nondiabetic patients; (2) risk-adjusted event-free survival in patients with mildly and moderately to severely abnormal scans is worse in patients with diabetes than in those without diabetes; (3) the presence and extent of myocardial perfusion SPECT abnormality is an independent predictor of cardiac death alone, or of cardiac death and MI, in patients with or without diabetes; and (4) diabetic women have the worst outcome for any given extent of reversible myocardial defect.

13. After Coronary Calcium Screening

Although some patients can benefit from nuclear stress testing after electron-beam CT, it would clearly not be cost-effective for all patients with atherosclerosis according to electron-beam CT to go on to the more expensive nuclear cardiology testing. In general, when the electron-beam CT score is higher than the 75th percentile for age and sex, stress nuclear testing may sometimes be appropriate for purposes of risk stratification.

14. Before and After Revascularization

a. Radionuclide Imaging Before Revascularization Interventions

When there is uncertainty with regard to the appropriate choice of therapy after coronary angiography, stress nuclear testing can risk stratify 25% to 75% lesions usefully (42).

b. Radionuclide Imaging After Percutaneous Coronary Intervention

The ACC/AHA 2002 Guideline Update for Exercise Testing (22) summarizes the available information on exercise testing after percutaneous coronary intervention (PCI). Symptom status is an unreliable index of development of restenosis, with 25% of asymptomatic patients documented as having ischemia on exercise testing. Myocardial perfusion imaging can be helpful in appropriately selected patients. The major indication for perfusion imaging in patients after successful PCI is to evaluate symptoms suggesting new disease.

c. Radionuclide Imaging After Coronary Artery Bypass Graft Surgery

Myocardial perfusion scintigraphy can be useful in determining the location, extent, and severity of ischemia. Prognostic value has been demonstrated both early (43) and late (44,45) after coronary artery bypass graft (CABG) surgery.

15. Radionuclide Imaging Before Noncardiac Surgery

The ACC/AHA Guideline Update for Perioperative Cardiac Evaluation for Noncardiac Surgery (46) (http://www.acc.org/clinical/guidelines/perio/update/pdf/perio_update.pdf) has emphasized the importance of clinical, demographic, and surgical indicators of risk. In general, noninvasive preoperative testing is best directed at patients considered to be at intermediate clinical risk (diabetes, stable CAD, compensated heart failure) who are scheduled to undergo intermediate- or high-risk surgery. A thorough evaluation of appropriately selected patients will also afford an assessment of cardiac prognosis over the long term. Exercise stress is preferred in

patients capable of achieving adequate workloads; radionuclide techniques should be reserved for patients whose baseline ECGs render exercise interpretation invalid or who require pharmacologic stress because of the inability to exercise.

a. Myocardial Perfusion Imaging

The full-text guideline summarizes studies of perfusion imaging in the preoperative assessment of cardiac risk for vascular and nonvascular surgery (see Table 14 in the full-text guideline). For patients with radionuclide evidence of ischemia, the positive predictive value of such testing is uniformly low, in the range of 4% to 20%. The negative predictive value of a normal scan, however, is very high (96% to 100%). Patients with reversible defects are at greater risk for perioperative ischemia than are those with fixed defects; the latter defects may, in turn, be a marker for longer-term risk. The positive predictive value of perfusion imaging can be improved when testing is applied selectively to patients with a higher pretest likelihood of CAD and when the results are integrated into a clinical risk assessment. If a noninvasive assessment of ischemic jeopardy before noncardiac surgery is necessary, the choice between radionuclide stress perfusion imaging and dobutamine stress echocardiography should be made on the basis of institutional expertise and patient-specific attributes.

b. Radionuclide Ventriculography

Exercise radionuclide ventriculography is rarely performed to assess ischemic jeopardy before noncardiac surgery. The evaluation of resting LV function, however, is an important component of the preoperative assessment of patients with symptoms and/or signs of heart failure. LV systolic function is now routinely assessed with gated SPECT techniques at the time of myocardial perfusion imaging. Not unexpectedly, the risk of perioperative complications is highest among patients with a resting LVEF more than 0.35. Reduced LV systolic function is a predictor of perioperative heart failure but bears no consistent correlation with the risk of perioperative ischemia.

D. Recommendations

I. Cardiac Stress Myocardial Perfusion SPECT in Patients Able to Exercise: Recommendations for Diagnosis of Patients With an Intermediate Likelihood of CAD and/or Risk Stratification of Patients With an Intermediate or High Likelihood of CAD Who Are Able to Exercise (to at least 85% of Maximal Predicted Heart Rate)

Class I

1. Exercise myocardial perfusion SPECT to identify the extent, severity, and location of ischemia in patients who do not have LBBB or an electronically-paced ventricular rhythm but do have a baseline ECG abnormality that interferes with the interpretation of exercise-induced ST-segment changes (ventricular pre-excitation, LVH, digoxin ther-

apy, or more than 1-mm ST depression).
(Level of Evidence: B)

2. Adenosine or dipyridamole myocardial perfusion SPECT in patients with LBBB or electronically-paced ventricular rhythm. (Level of Evidence: B)
3. Exercise myocardial perfusion SPECT to assess the functional significance of intermediate (25% to 75%) coronary lesions. (Level of Evidence: B)
4. Exercise myocardial perfusion SPECT in patients with intermediate Duke treadmill score. (Level of Evidence: B)
5. Repeat exercise myocardial perfusion imaging after initial perfusion imaging in patients whose symptoms have changed to redefine the risk for cardiac event. (Level of Evidence: C)

Class IIa

1. Exercise myocardial perfusion SPECT at 3 to 5 years after revascularization (either PCI or CABG) in selected high-risk asymptomatic patients. (Level of Evidence: B)
2. Exercise myocardial perfusion SPECT as the initial test in patients who are considered to be at high risk (patients with diabetes or patients otherwise defined as having a more than 20% 10-year risk of a coronary heart disease event). (Level of Evidence: B)

Class IIb

1. Repeat exercise myocardial perfusion SPECT 1 to 3 years after initial perfusion imaging in patients with known or a high likelihood of CAD and stable symptoms and a predicted annual mortality of more than 1% to redefine the risk of a cardiac event. (Level of Evidence: C)
2. Repeat exercise myocardial perfusion SPECT on cardiac active medications after initial abnormal perfusion imaging to assess the efficacy of medical therapy. (Level of Evidence: C)
3. Exercise myocardial perfusion SPECT in symptomatic or asymptomatic patients who have severe coronary calcification (CT coronary calcium score more than the 75th percentile for age and sex) in the presence on the resting ECG of pre-excitation [Wolff-Parkinson-White syndrome] or more than 1 mm ST-segment depression. (Level of Evidence: B)
4. Exercise myocardial perfusion SPECT in asymptomatic patients who have a high-risk occupation. (Level of Evidence: B)

II. Cardiac Stress Myocardial Perfusion SPECT in Patients Unable to Exercise: Recommendations for Diagnosis of Patients With an Intermediate Likelihood

of CAD and/or Risk Stratification of Patients With an Intermediate or High Likelihood of CAD Who Are Unable to Exercise.

Class I

1. Adenosine or dipyridamole myocardial perfusion SPECT to identify the extent, severity, and location of ischemia. (Level of Evidence: B)
2. Adenosine or dipyridamole myocardial perfusion SPECT to assess the functional significance of intermediate (25% to 75%) coronary lesions. (Level of Evidence: B)
3. Adenosine or dipyridamole myocardial perfusion SPECT after initial perfusion imaging in patients whose symptoms have changed to redefine the risk for cardiac event. (Level of Evidence: C)

Class IIa

1. Adenosine or dipyridamole myocardial perfusion SPECT at 3 to 5 years after revascularization (either PCI or CABG) in selected high-risk asymptomatic patients. (Level of Evidence: B)
2. Adenosine or dipyridamole myocardial perfusion SPECT as the initial test in patients who are considered to be at high risk (patients with diabetes or patients otherwise defined as having a more than 20% 10-year risk of a coronary heart disease event). (Level of Evidence: B)
3. Dobutamine myocardial perfusion SPECT in patients who have a contraindication to adenosine or dipyridamole. (Level of Evidence: C)

Class IIb

1. Repeat adenosine or dipyridamole myocardial perfusion imaging 1 to 3 years after initial perfusion imaging in patients with known or a high likelihood of CAD and stable symptoms, and a predicted annual mortality of more than 1%, to redefine the risk of a cardiac event. (Level of Evidence: C)
2. Repeat adenosine or dipyridamole myocardial perfusion SPECT on cardiac active medications after initial abnormal perfusion imaging to assess the efficacy of medical therapy. (Level of Evidence: C)
3. Adenosine or dipyridamole myocardial perfusion SPECT in symptomatic or asymptomatic patients who have severe coronary calcification (CT Coronary Calcium Score more than the 75th percentile for age and sex) in the presence on the resting ECG of LBBB or an electronically-paced ventricular rhythm. (Level of Evidence: B)

4. Adenosine or dipyridamole myocardial perfusion SPECT in asymptomatic patients who have a high-risk occupation. (Level of Evidence: C)

III. Cardiac Stress Myocardial Perfusion PET: Recommendations for Diagnosis of Patients With an Intermediate Likelihood of CAD and/or Risk Stratification of Patients With an Intermediate or High Likelihood of CAD

Class I

1. Adenosine or dipyridamole myocardial perfusion PET in patients in whom an appropriately indicated myocardial perfusion SPECT study has been found to be equivocal for diagnostic or risk stratification purposes. (Level of Evidence: B)

Class IIa

1. Adenosine or dipyridamole myocardial perfusion PET to identify the extent, severity, and location of ischemia as the initial diagnostic test in patients who are unable to exercise. (Level of Evidence: B)
2. Adenosine or dipyridamole myocardial perfusion PET to identify the extent, severity, and location of ischemia as the initial diagnostic test in patients who are able to exercise but have LBBB or an electronically-paced rhythm. (Level of Evidence: B)

IV. Cardiac Stress Perfusion Imaging Before Noncardiac Surgery: Recommendations

Class I

1. Initial diagnosis of CAD in patients with intermediate pretest probability of disease and abnormal baseline ECG¹ or inability to exercise. (Level of Evidence: B)
2. Prognostic assessment of patients undergoing initial evaluation for suspected or proven CAD with abnormal baseline ECG¹ or inability to exercise. (Level of Evidence: B)
3. Evaluation of patients following a change in clinical status (eg, ACS) with abnormal baseline ECG¹ or inability to exercise. (Level of Evidence: B)
4. Initial diagnosis of CAD in patients with LBBB and intermediate pretest probability of disease, when used in conjunction with vasodilator stress. (Level of Evidence: B)
5. Prognostic assessment of patients with LBBB undergoing initial evaluation for suspected or proven CAD, when used in

conjunction with vasodilator stress. (Level of Evidence: B)

6. Assessment of patients with intermediate or minor clinical risk predictors² and poor functional capacity (less than 4 METS) who require high-risk noncardiac surgery³, when used in conjunction with pharmacologic stress. (Level of Evidence: C)
7. Assessment of patients with intermediate clinical risk predictors², abnormal baseline ECGs¹, and moderate or excellent functional capacity (more than 4 METS) who require high-risk noncardiac surgery. (Level of Evidence: C)

Class IIb

1. Routine assessment of active, asymptomatic patients who have remained stable for up to 5 years after CABG surgery. (Level of Evidence: C)
2. Routine evaluation of active asymptomatic patients who have remained stable for up to 2 years after previous abnormal coronary angiography or noninvasive assessment of myocardial perfusion. (Level of Evidence: C)
3. Diagnosis of restenosis and regional ischemia in active asymptomatic patients within weeks to months after PCI. (Level of Evidence: C)
4. Initial diagnosis or prognostic assessment of CAD in patients with right bundle-branch block or less than 1-mm ST depression on resting ECG. (Level of Evidence: C)

Class III

1. Routine screening of asymptomatic men or women with low pretest likelihood of CAD. (Level of Evidence: C)
2. Evaluation of patients with severe comorbidities that limit life expectancy or candidacy for myocardial revascularization. (Level of Evidence: C)
3. Initial diagnosis or prognostic assessment of CAD in patients who require emergency noncardiac surgery. (Level of Evidence: C)

IV. Heart Failure

A. Introduction

The clinical syndrome of heart failure in adults is commonly associated with the etiologies of ischemic and nonischemic

¹Baseline ECG abnormalities that interfere with interpretation of exercise-induced ST-segment changes include LBBB, ventricular pre-excitation, ventricular pacing, LVH with repolarization changes, more than 1-mm ST depression, and digoxin therapy.

²As defined in the ACC/AHA Guideline Update for Perioperative Cardiovascular Evaluation for Noncardiac Surgery (46), intermediate clinical risk predictors include mild angina, prior MI, compensated or prior heart failure, diabetes, and renal insufficiency. Minor clinical risk predictors include advanced age, abnormal ECG, rhythm other than sinus, low functional capacity, history of cerebrovascular accident, and uncontrolled hypertension.

³High-risk surgery is defined by emergent operations (particularly in the elderly), aortic and other major vascular surgery, peripheral vascular surgery, and other prolonged operations in which major fluid shifts are anticipated (ie, reported cardiac risk often more than 5%).

TABLE 4. Recommendations for the Use of Radionuclide Imaging in Patients With Heart Failure: Fundamental Assessment

Indication	Test	Class	Level of Evidence
1. Initial assessment of LV and RV function at rest*	Rest RNA	I	A
2. Assessment of myocardial viability for consideration of revascularization in patients with CAD and LV systolic dysfunction who do not have angina	MPI (see Table 5), PET	I	B
3. Assessment of the copresence of CAD in patients without angina	MPI	IIa	B
4. Routine serial assessment of LV and RV function at rest	Rest RNA	IIb	B
5. Initial or serial assessment of ventricular function with exercise	Exercise RNA	IIb	B

*National consensus treatment guidelines are directed by quantitative assessment of LVEF and identification of LVEF less than or equal to 40%.

CAD indicates coronary artery disease; LV, left ventricular; MPI, myocardial perfusion imaging; PET, positron emission tomography; RNA, radionuclide angiography.

dilated cardiomyopathy, hypertrophic cardiomyopathy, hypertensive heart disease, and valvular heart disease. Common principles of assessment that influence prognosis and therapy include the assessment of (1) LV function and remodeling, (2) the contribution of myocardial ischemia due to CAD, and (3) myocardial viability.

B. Assessment of LV Function

1. Assessment of LV Systolic Dysfunction

The clinician's choice of noninvasive imaging modality to detect and quantify LV systolic dysfunction in the individual patient with heart failure depends on several variables, including cost, ease of access at point-of-care, need for precise computed quantitative measurement, and local expertise. RNA can be used to compute quantitative estimates of LV, as well as RV, EF, and absolute volumes. A strength of RNA is that the quantitative computation of EF and chamber volumes does not depend on mathematical assumptions of ventricular geometry. Thus, radionuclide quantitative computations of LV chamber volume and EF are obtainable in ≈100% of patients. The long biological half-life of ^{99m}Tc-labeled blood pool agents in gated equilibrium studies also permits serial acquisition of data at rest and during exercise.

2. Assessment of LV Diastolic Dysfunction

The objective determination of the presence and severity of diastolic dysfunction is increasingly important in patients with the clinical syndrome of heart failure. The rate of change of counts in diastole can be analyzed to calculate indices of diastolic filling, including the peak LV filling rate, time to peak filling, and atrial contribution to filling. In contemporary practice, Doppler blood flow velocity indices of transmitral flow are more commonly used to assess LV diastolic filling parameters. Large population-based criteria, adjusted for age and sex, for normal versus abnormal diastolic function using RNA have not yet been established.

C. Assessment of CAD

1. Importance of Detecting CAD in Heart Failure Patients

Determining whether LV dysfunction is caused predominantly by the consequences of CAD or by one of the many

other etiologies included in the term “nonischemic” cardiomyopathy is a critical early step in the management of heart failure patients. Decisions about the need for cardiac catheterization and coronary angiography will be informed by the initial clinical and noninvasive assessment of these patients. A significant subgroup of patients with heart failure and underlying CAD has a potentially reversible degree of LV dysfunction with revascularization.

2. Myocardial Perfusion Imaging to Detect CAD in Heart Failure Patients

The sensitivity and negative predictive value of myocardial perfusion imaging in detecting CAD in patients with heart failure and LV dysfunction have been excellent in published studies. However, it is not clear how these studies, some of which involved relatively small numbers of patients and older techniques, may generalize to current patients and contemporary imaging techniques. The specificity of perfusion imaging to rule out coronary disease is modest, on the average 40% to 50%. The frequent false-positive studies are due to perfusion abnormalities in a significant number of patients with “nonischemic” cardiomyopathy, ie, those patients without epicardial coronary disease. Table 4 lists recommendations for radionuclide imaging in patients with heart failure.

D. Assessment of Myocardial Viability

1. Goals of Assessing Myocardial Viability

In patients with chronic coronary disease and LV dysfunction, an important subpopulation exists in which revascularization may significantly improve regional or global LV function, as well as symptoms and potentially natural history. The underlying pathophysiology involves reversible myocardial dysfunction (hibernation or stunning). Meta-analysis of a substantial body of literature indicates that those with evidence of preserved myocardial viability who underwent revascularization had a substantial reduction in the risk of death during long-term follow-up (47). If nonviability was predominant, the risk of death was intermediate and not affected by revascularization. These conclusions, however, are limited by lack of randomization and the fact that observational cohorts analyses are subject to selection biases.

TABLE 5. Recommendations for the Use of Radionuclide Techniques to Assess Myocardial Viability

Indication	Test	Class	Level of Evidence
1. Predicting improvement in regional and global LV function after revascularization	Stress/redistribution/reinjection ²⁰¹ Tl	I	B
	Rest-redistribution imaging	I	B
	Perfusion plus PET FDG imaging	I	B
	Resting sestamibi imaging	I	B
	Gated SPECT sestamibi imaging	IIa	B
	Late ²⁰¹ Tl redistribution imaging (after stress)	IIb	B
	Dobutamine RNA	IIb	C
	Postexercise RNA	IIb	C
2. Predicting improvement in heart failure symptoms after revascularization.	Perfusion plus PET FDG imaging	IIa	B
3. Predicting improvement in natural history after revascularization	²⁰¹ Tl imaging (rest-redistribution and stress/redistribution/reinjection)	I	B
	Perfusion plus PET FDG imaging	I	B

FDG indicates flurodeoxyglucose; PET, positron emission tomography; RNA, radionuclide angiography; SPECT, single-photon emission computed tomography; ²⁰¹Tl, thallium-201.

2. General Principles of Assessing Myocardial Viability by Radionuclide Techniques

Preservation of myocardial viability exists as a spectrum in a territory with regional ventricular dysfunction, from the possibility of no preserved viability (ie, complete transmural infarction) to completely preserved viability (ie, transmural hibernation or stunning with the potential for full recovery of function). Most studies evaluating the radionuclide techniques for assessing viability have focused on analysis of resting tracer uptake (as with ²⁰¹Tl, sestamibi, or tetrofosmin) or evidence of preserved metabolic activity at rest (by ¹⁸F-2-fluorodeoxyglucose [FDG] or ¹¹C-acetate).

3. Techniques and Protocols for Assessing Myocardial Viability

a. ²⁰¹Tl Stress Redistribution

The uptake of ²⁰¹Tl is an energy-dependent process requiring intact cell membrane integrity, and the presence of ²⁰¹Tl implies preserved myocyte cellular viability. The redistribution properties of ²⁰¹Tl have been used as an important marker of myocardial viability in stress imaging followed by a 3- to 4-hour redistribution image. The presence of a reversible perfusion defect and/or preserved ²⁰¹Tl uptake on the 3- to 4-hour redistribution images is an important sign of regional viability.

b. ²⁰¹Tl Reinjection

The 2 most widely studied protocols for assessing viability in the presence of an inconclusive result on initial stress/redistribution imaging involve ²⁰¹Tl reinjection and late redistribution imaging. The presence of a severe ²⁰¹Tl defect after reinjection identifies areas with a very low probability of improvement in function.

c. Late Redistribution Imaging

Although improvement in uptake on late redistribution images (24 to 48 hours after the initial stress ²⁰¹Tl injection) has good positive predictive value for identifying regions with potential improvement in function, the negative predictive value is suboptimal in some patients.

d. ²⁰¹Tl Rest Redistribution

The identification of a “reversible resting defect” (in 3- to 4-hour versus 15- to 20-minute images) generally reflects preserved viability. The finding appears to be an insensitive though specific sign of potential improvement in regional function.

e. ^{99m}Tc-Sestamibi and Tetrofosmin

Although the ^{99m}Tc-based tracers sestamibi and tetrofosmin do not share the redistribution properties of ²⁰¹Tl, their performance characteristics for predicting improvement in regional function after revascularization appear to be similar to those seen with ²⁰¹Tl.

f. PET Imaging

Positron tracers of blood flow and metabolism have been extensively studied for evaluation of myocardial viability. The most commonly used PET protocol involves evaluation of myocardial glucose metabolism with ¹⁸F-FDG in conjunction with PET or SPECT examination of MBF with ¹³N-ammonia or ^{99m}Tc-sestamibi, respectively. This approach appears to have slightly better overall accuracy for predicting recovery of regional function after revascularization than do single-photon techniques (48). The magnitude of improvement in heart failure symptoms after revascularization in patients with LV dysfunction correlates with the preoperative extent of ¹⁸F-FDG “mismatch” pattern (49).

Table 5 lists recommendations for the use of radionuclide techniques to assess myocardial viability.

4. Image Interpretation for Myocardial Viability:

Quantitative Versus Visual Analysis of Tracer Activities

Whether quantitative analysis of tracer uptake in radionuclide techniques is required for assessing viability is not established. Visual analyses need to be at least semiquantitative, accounting for defect severity.

5. Comparison of Techniques

All radionuclide techniques (and dobutamine echocardiography) perform in a relatively similar manner with regard to positive and negative predictive values for predicting improvements in regional function (48). A meta-analysis of outcome studies

TABLE 6. Recommendations for the Use of Radionuclide Imaging to Diagnose Specific Causes of Dilated Cardiomyopathy

Indication	Test	Class	Level of Evidence
1. Baseline and serial monitoring of LV function during therapy with cardiotoxic drugs (eg, doxorubicin)	Rest RNA	I	A
2. RV dysplasia	Rest RNA	IIa	B
3. Assessment of posttransplant obstructive CAD	Exercise perfusion imaging	IIb	B
4. Diagnosis and serial monitoring of Chagas disease	Exercise perfusion imaging	IIb	B
5. Diagnosis of amyloid heart disease	^{99m} Tc-pyrophosphate imaging	IIb	B
6. Diagnosis and serial monitoring of sarcoid heart disease	Rest perfusion imaging	IIb	B
	Rest ⁶⁷ Ga imaging	IIb	B
7. Detection of myocarditis	Rest ⁶⁷ Ga imaging	IIb	B
	¹¹¹ In antimyosin antibody imaging	IIb	C

⁶⁷Ga indicates gallium-67; ^{99m}Tc-pyrophosphate, Tc-99m-pyrophosphate; ¹¹¹In, indium-111; CAD, coronary artery disease; LV, left ventricular; RNA, radionuclide angiography; RV, right ventricular.

related to myocardial viability has demonstrated no difference among techniques commonly used to assess viability (PET versus single-photon radionuclide versus dobutamine echocardiography) with regard to reduction of mortality or unfavorable cardiac events after revascularization (47).

E. Etiologies of Heart Failure

1. Dilated Cardiomyopathy

Table 6 lists recommendations for the use of radionuclide imaging to diagnose specific causes of dilated cardiomyopathy.

2. Dilated Cardiomyopathy Due to Doxorubicin/Anthracycline Cardiotoxicity

RNA is an ideal noninvasive tool to provide longitudinal quantitative assessment of LV function in patients receiving doxorubicin and other anthracyclines such as epirubicin. EF should be measured in all patients before receiving doxorubicin; those with pre-existing heart disease and/or LV dysfunction are at greater risk of congestive heart failure. Continued use of doxorubicin after LV dysfunction has developed causes progressive chamber dilatation and deterioration in systolic function. Therapy with trastuzumab, a monoclonal antibody directed against the HER2 receptor,

may increase the risk of developing heart failure during standard-dose doxorubicin therapy (50). Radionuclide evaluation of EF is also important in monitoring the cardioprotective effects of agents such as dexrazoxane when doxorubicin is used in high dosages for solid malignant tumors (51).

3. Dilated Cardiomyopathy Due to Myocarditis

Radioisotope imaging has been reported to identify myocarditis of diverse etiologies with gallium (which detects inflammation), antimyosin antibody (which detects myocardial necrosis and is myosin specific), and metaiodobenzylguanidine (MIBG; which assesses adrenergic neuronal function). The usefulness of radionuclide imaging to detect myocarditis in heart failure patients is not well established, however, and data describing use of this approach are based on nonrandomized studies.

4. Posttransplantation Rejection and Allograft Vasculopathy

¹¹¹In antimyosin antibody imaging has been described as a technique to detect rejection after cardiac transplantation in small observational studies. Because of many false-positive results, endomyocardial biopsy continues to be the technique of choice for serial monitoring and detection of acute rejection. Radionuclide evaluation of allograft vasculopathy, the

TABLE 7. Recommendations for the Use of Radionuclide Imaging to Evaluate Hypertrophic Heart Disease

Indication	Test	Class	Level of Evidence
1. Diagnosis of CAD in hypertrophic cardiomyopathy	Rest and exercise perfusion imaging	IIb	B
2. Diagnosis and serial monitoring of hypertensive hypertrophic heart disease	Rest RNA	IIb	B
3. Diagnosis and serial monitoring of hypertrophic cardiomyopathy, with and without outflow obstruction	Rest RNA	III	B

CAD indicates coronary artery disease; RNA, radionuclide angiography.

TABLE 8. Recommendations for the Use of Radionuclide Imaging in Valvular Heart Disease

Indication	Test	Class	Level of Evidence
1. Initial and serial assessment of LV and RV function	Rest RNA	I	B
2. Initial and serial assessment of LV function	Exercise RNA	Ib	B
3. Assessment of the copresence of coronary disease	MPI	Ib	B

LV indicates left ventricular; RNA, radionuclide imaging angiography; RV, right ventricular; MPI, myocardial perfusion imaging.

major limitation for long-term survival in transplant recipients, is limited by variable sensitivity and specificity. A SPECT study with no reversible perfusion defects may be useful in excluding coronary lesions appropriate for revascularization (52).

5. Chagas Myocarditis and/or Cardiomyopathy

Chagas myocarditis and/or cardiomyopathy has several distinctive features in comparison with dilated cardiomyopathy due to presumed viral myocarditis. Observational studies using RNA and perfusion imaging have reported that chronic Chagas cardiomyopathy is frequently associated with LV regional wall motion abnormalities and perfusion defects in the absence of epicardial CAD, and RV dyssynergy is common in asymptomatic patients with no other clinical signs of heart failure (53). In correlative investigations, there has been a topographic association between regional defects in sympathetic denervation detected by ¹²³I-MIBG imaging and perfusion defects detected by ²⁰¹Tl imaging (54).

6. Sarcoid Heart Disease

Myocardial SPECT with ^{99m}Tc-sestamibi has been used to detect myocardial involvement in patients with sarcoidosis. Perfusion defects are more common in the RV than the in LV and correlate with atrioventricular block, heart failure, and ventricular tachycardia of RV origin (55). These defects are frequently reversible, which makes it unlikely that they represent deposition of granulomata or fibrosis. ⁶⁷Ga was formerly used in sarcoidosis as a marker of the activity and extent of the disease and for predicting the efficacy of corticosteroids, but it has been largely superseded by serial chest CT and pulmonary function tests.

7. Cardiac Amyloidosis

Radionuclide angiography enables assessment of diastolic and systolic function, including peak filling rates and LV filling volumes during rapid filling and atrial contraction, respectively (56). ¹³¹I-MIBG imaging has indicated a high incidence of sympathetically denervated but viable myocardium (57). Although ^{99m}Tc-pyrophosphate imaging has been reported to have diagnostic utility, echocardiography appears to be more useful because it enables complete characterization of the altered LV and RV myocardium, as well as valvular and pericardial involvement.

8. RV Dysplasia

The RV in arrhythmogenic RV dysplasia is characterized by marked dilatation and depressed EF, which can be readily identified with RV RNA (58).

9. Hypertrophic Cardiomyopathy

Radionuclide angiographic studies are not usually indicated in the diagnosis of hypertrophic cardiomyopathy. Chest pain is a frequent symptom, raising the possibility of coexistent CAD. However, fixed and reversible exercise-induced myocardial perfusion defects suggesting scar or ischemia occur in the absence of significant epicardial coronary artery stenoses. Reversible perfusion defects may reflect ischemia related to diminished coronary flow reserve or decreased sympathoneural function in hypertrophied areas. Table 7 lists recommendations for the use of radionuclide imaging to evaluate hypertrophic heart disease.

10. Hypertensive Heart Disease

RNA allows recognition of abnormal diastolic and systolic function in hypertensive subjects, even when resting systolic global function and regional function are normal. A significant proportion of such patients have hypertensive hypertrophic heart disease.

Hypertension is common in patients presenting with chest pain for stress testing in whom CAD is suspected. The role of stress perfusion imaging in patients with and without LVH has been covered in the section on Chronic Syndromes.

11. Valvular Heart Disease

a. Diagnosis and Risk Stratification

In daily practice, 2D Doppler echocardiography studies have become the modality of choice for diagnosing valvular heart disease. The potential usefulness of RNA in assessing valvular heart disease stems from the ability of RNA to quantify LV and RV function. In addition, myocardial perfusion imaging has been used to examine for the presence of flow-limiting coronary disease, especially in aortic stenosis.

b. Aortic Stenosis

Because of the lack of specificity and sensitivity of angina for the concomitant presence of coronary disease in aortic

TABLE 9. Recommendations for the Use of Radionuclide Imaging in Adults With Congenital Heart Disease

Indication	Test	Class	Level of Evidence
1. Initial and serial assessment of LV and RV function	Rest RNA	I	B
2. Shunt detection and quantification	FPRNA	Ila	B

FPRNA indicates first-pass radionuclide angiography; LV, left ventricular; RV, right ventricular; RNA, radionuclide angiography.

stenosis, there has been much interest in the use of myocardial perfusion imaging in preoperative evaluation. The sensitivity and specificity of stress perfusion are relatively good but probably not adequate for patients about to undergo valve surgery. Thus, in practice, perfusion imaging has not supplanted coronary angiography in the preoperative work-up of patients with aortic stenosis.

c. Aortic Regurgitation

The most promising use of RNA in valvular heart disease initially appeared to be in the evaluation of patients with aortic regurgitation, in whom a failure of EF to rise during exercise seemed to mark the onset of LV dysfunction and predict a poorer prognosis or indicate that the asymptomatic patient would soon become symptomatic (59). Subsequent studies indicated that exercise angiography does not usually add additional prognostic information to the measurement of resting LVEF and end-systolic dimension in predicting the response to aortic valve replacement (60). Enhanced prognostic ability of exercise RNA has been reported when the calculation of systolic wall stress is added (61).

d. Mitral Regurgitation

Perhaps the most compelling current use of RNA in valvular heart disease is in the preoperative evaluation of patients with mitral regurgitation. The echocardiogram does not evaluate RV function well, whereas RV function assessment is a strength of RNA. As with aortic regurgitation, resting EF is a useful guide to valve repair or replacement. Again, however, Doppler echocardiography can make this assessment and add other anatomic and prognostic information. RNA is useful postoperatively in gauging changes in LV and RV performance. Table 8 lists recommendations for the use of radionuclide imaging in valvular heart disease.

12. Adults With Congenital Heart Disease

As in other forms of heart disease, RNA can be used effectively to assess RV and LV systolic performance. In addition, left-to-right shunting causes persistently high levels of activity in the lung or RV during FPRNA because of early recirculation. The resultant time-activity curve can be used to calculate pulmonary to systemic flow ratios. The early appearance of tracer in the left chambers of the heart can be used to detect right-to-left shunts. ^{99m}Tc RNA appears to be useful in evaluating abnormal lung flow after the Fontan and Glenn procedures (62).

In general, however, radionuclide studies are now utilized infrequently in assessing congenital heart disease and are unlikely to be accurate if performed only occasionally. Table 9 lists recommendations for the use of radionuclide imaging in adults with congenital heart disease.

References

1. Braunwald E, Antman E, Beasley J. ACC/AHA 2002 guideline update for the management of patients with unstable angina and non-ST-segment elevation myocardial infarction: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (Committee to Update Guidelines on the Management of Patients with Unstable Angina). 2002; American College of Cardiology Web site. Available at: http://www.acc.org/clinical/guidelines/unstable/incorporated/UA_incorporated.pdf. Accessed June 12, 2003.
2. Stowers SA, Eisenstein EL, Th Wackers FJ, et al. An economic analysis of an aggressive diagnostic strategy with single photon emission computed tomography myocardial perfusion imaging and early exercise stress testing in emergency department patients who present with chest pain but nondiagnostic electrocardiograms: results from a randomized trial. *Ann Emerg Med* 2000;35:17–25.
3. Udelson JE, Beshansky JR, Ballin DS, et al. Myocardial perfusion imaging for evaluation and triage of patients with suspected acute cardiac ischemia: a randomized controlled trial. *JAMA* 2002;288:2693–700.
4. Ryan TJ, Antman EL, Brooks NH, et al. ACC/AHA guidelines for the management of patients with acute myocardial infarction: 1999 update: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (Committee on Management of Acute Myocardial Infarction). 1999; American College of Cardiology Web site. Available at: <http://www.acc.org/clinical/guidelines/nov96/1999/amipdf99.pdf>. Accessed July 30, 2002.
5. Basu S, Senior R, Dore C, et al. Value of thallium-201 imaging in detecting adverse cardiac events after myocardial infarction and thrombolysis: a follow up of 100 consecutive patients. *BMJ* 1996;313:844–8.
6. Brown KA, Heller GV, Landin RS, et al. Early dipyridamole (99m)Tc-sestamibi single photon emission computed tomographic imaging 2 to 4 days after acute myocardial infarction predicts in-hospital and postdischarge cardiac events: comparison with submaximal exercise imaging. *Circulation* 1999;100:2060–6.
7. Dakik HA, Mahmarian JJ, Kimball KT, et al. Prognostic value of exercise 201Tl tomography in patients treated with thrombolytic therapy during acute myocardial infarction. *Circulation* 1996;94:2735–42.
8. Shaw LJ, Eagle KA, Gersh BJ, et al. Meta-analysis of intravenous dipyridamole-thallium-201 imaging (1985 to 1994) and dobutamine echocardiography (1991 to 1994) for risk stratification before vascular surgery. *J Am Coll Cardiol* 1996;27:787–98.
9. Verani MS. Risk stratifying patients who survive an acute myocardial infarction. *J Nucl Cardiol* 1998;5:96–108.
10. Bodenheimer MM, Wackers FJ, Schwartz RG, et al. Prognostic significance of a fixed thallium defect one to six months after onset of acute myocardial infarction or unstable angina. Multicenter Myocardial Ischemia Research Group. *Am J Cardiol* 1994;74:1196–200.
11. Kroll D, Farah W, McKendall GR, et al. Prognostic value of stress-gated Tc-99m sestamibi SPECT after acute myocardial infarction. *Am J Cardiol* 2001;87:381–6.
12. Miller DD, Stratmann HG, Shaw L, et al. Dipyridamole technetium 99m sestamibi myocardial tomography as an independent predictor of cardiac event-free survival after acute ischemic events. *J Nucl Cardiol* 1994;1:72–82.
13. Brown KA. Prognostic value of thallium-201 myocardial perfusion imaging in patients with unstable angina who respond to medical treatment. *J Am Coll Cardiol* 1991;17:1053–7.
14. Stratmann HG, Younis LT, Wittry MD, et al. Exercise technetium-99m myocardial tomography for the risk stratification of men with medically treated unstable angina pectoris. *Am J Cardiol* 1995;76:236–40.
15. Gibbons RJ, Chatterjee K, Daley J, et al. ACC/AHA 2002 guideline update for the management of patients with chronic stable angina: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (Committee to Update the 1999 Chronic Stable Angina Guidelines). 2002; American College of Cardiology Web site. Available at: http://www.acc.org/clinical/guidelines/stable/stable_clean.pdf. Accessed August 20, 2002.
16. Hendel RC, Corbett JR, Cullom SJ, et al. The value and practice of attenuation correction for myocardial perfusion SPECT imaging: a joint position statement from the American Society of Nuclear Cardiology and the Society of Nuclear Medicine. *J Nucl Cardiol* 2002;9:135–43.
17. Sharir T, Germano G, Kang X, et al. Prediction of myocardial infarction versus cardiac death by gated myocardial perfusion SPECT: risk stratification by the amount of stress-induced ischemia and the poststress ejection fraction. *J Nucl Med* 2001;42:831–7.
18. Hachamovitch R, Hayes S, Friedman JD, et al. Determinants of risk and its temporal variation in patients with normal stress myocardial perfusion scans: what is the warranty period of a normal scan? *J Am Coll Cardiol* 2003;41:1329–40.
19. Akinboboye OO, Idris O, Onwuanyi A, et al. Incidence of major cardiovascular events in black patients with normal myocardial stress perfusion studies. *J Nucl Cardiol* 2001;8:541–7.
20. Alkeylani A, Miller DD, Shaw LJ, et al. Influence of race on the prediction of cardiac events with stress technetium-99m sestamibi tomo-

- graphic imaging in patients with stable angina pectoris. *Am J Cardiol* 1998;81:293-7.
21. Liao Y, Cooper RS, McGee D, et al. The relative effects of left ventricular hypertrophy, coronary artery disease, and ventricular dysfunction on survival among black adults. *JAMA* 1995;273:1592-7.
 22. Gibbons RJ, Balady GJ, Bricker JT, et al. ACC/AHA 2002 guideline update for exercise testing: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (Committee on Exercise Testing). 2003; American College of Cardiology Web site. Available at: http://www.acc.org/clinical/guidelines/exercise/exercise_clean.pdf. Accessed February 26, 2003.
 23. Amanullah AM, Kiat H, Friedman JD, et al. Adenosine technetium-99m sestamibi myocardial perfusion SPECT in women: diagnostic efficacy in detection of coronary artery disease. *J Am Coll Cardiol* 1996;27:803-9.
 24. Berman DS, Kang X, Hayes SW, et al. Adenosine myocardial perfusion single-photon emission computed tomography in women compared with men: impact of diabetes mellitus on incremental prognostic value and effect on patient management. *J Am Coll Cardiol* 2003;41:1125-33.
 25. Iskandrian AE, Heo J, Nallamothu N. Detection of coronary artery disease in women with use of stress single-photon emission computed tomography myocardial perfusion imaging. *J Nucl Cardiol* 1997;4:329-35.
 26. Taillefer R, DePuey EG, Udelson JE, et al. Comparative diagnostic accuracy of Tl-201 and Tc-99m sestamibi SPECT imaging (perfusion and ECG-gated SPECT) in detecting coronary artery disease in women. *J Am Coll Cardiol* 1997;29:69-77.
 27. Mark DB, Shaw L, Harrell FE Jr., et al. Prognostic value of a treadmill exercise score in outpatients with suspected coronary artery disease. *N Engl J Med* 1991;325:849-53.
 28. Gibbons RJ, Hodge DO, Berman DS, et al. Long-term outcome of patients with intermediate-risk exercise electrocardiograms who do not have myocardial perfusion defects on radionuclide imaging. *Circulation* 1999;100:2140-5.
 29. Hachamovitch R, Berman DS, Kiat H, et al. Exercise myocardial perfusion SPECT in patients without known coronary artery disease: incremental prognostic value and use in risk stratification. *Circulation* 1996;93:905-14.
 30. Shaw LJ, Hachamovitch R, Peterson ED, et al. Using an outcomes-based approach to identify candidates for risk stratification after exercise treadmill testing. *J Gen Intern Med* 1999;14:1-9.
 31. Gil VM, Almeida M, Ventosa A, et al. Prognosis in patients with left bundle branch block and normal dipyridamole thallium-201 scintigraphy. *J Nucl Cardiol* 1998;5:414-7.
 32. Wagdy HM, Hodge D, Christian TF, et al. Prognostic value of vasodilator myocardial perfusion imaging in patients with left bundle-branch block. *Circulation* 1998;97:1563-70.
 33. Elhendy A, van Domburg RT, Sozzi FB, et al. Impact of hypertension on the accuracy of exercise stress myocardial perfusion imaging for the diagnosis of coronary artery disease. *Heart* 2001;85:655-61.
 34. Bartram P, Toft J, Hanel B, et al. False-positive defects in technetium-99m sestamibi myocardial single-photon emission tomography in healthy athletes with left ventricular hypertrophy. *Eur J Nucl Med* 1998;25:1308-12.
 35. Amanullah AM, Berman DS, Kang X, et al. Enhanced prognostic stratification of patients with left ventricular hypertrophy with the use of single-photon emission computed tomography. *Am Heart J* 2000;140:456-62.
 36. Hilton TC, Shaw LJ, Chaitman BR, et al. Prognostic significance of exercise thallium-201 testing in patients aged greater than or equal to 70 years with known or suspected coronary artery disease. *Am J Cardiol* 1992;69:45-50.
 37. Grundy SM, Pasternak R, Greenland P, et al. Assessment of cardiovascular risk by use of multiple-risk-factor assessment equations: a statement for healthcare professionals from the American Heart Association and the American College of Cardiology. *Circulation* 1999;100:1481-92.
 38. Diabetes mellitus: a major risk factor for cardiovascular disease. A joint editorial statement by the American Diabetes Association; The National Heart, Lung, and Blood Institute; The Juvenile Diabetes Foundation International; The National Institute of Diabetes and Digestive and Kidney Diseases; and The American Heart Association. *Circulation* 1999;100:1132-3.
 39. Giri S, Shaw LJ, Murthy DR, et al. Impact of diabetes on the risk stratification using stress single-photon emission computed tomography myocardial perfusion imaging in patients with symptoms suggestive of coronary artery disease. *Circulation* 2002;105:32-40.
 40. Kang X, Berman DS, Lewin HC, et al. Incremental prognostic value of myocardial perfusion single photon emission computed tomography in patients with diabetes mellitus. *Am Heart J* 1999;138:1025-32.
 41. Wackers FJ, Zaret BL. Detection of myocardial ischemia in patients with diabetes mellitus. *Circulation* 2002;105:5-7.
 42. Miller DD, Donohue TJ, Younis LT, et al. Correlation of pharmacological 99mTc-sestamibi myocardial perfusion imaging with poststenotic coronary flow reserve in patients with angiographically intermediate coronary artery stenoses. *Circulation* 1994;89:2150-60.
 43. Miller TD, Christian TF, Hodge DO, et al. Prognostic value of exercise thallium-201 imaging performed within 2 years of coronary artery bypass graft surgery. *J Am Coll Cardiol* 1998;31:848-54.
 44. Lauer MS, Lytle B, Pashkow F, et al. Prediction of death and myocardial infarction by screening with exercise-thallium testing after coronary-artery-bypass grafting. *Lancet* 1998;351:615-22.
 45. Zellweger MJ, Lewin HC, Lai S, et al. When to stress patients after coronary artery bypass surgery? Risk stratification in patients early and late post-CABG using stress myocardial perfusion SPECT: implications of appropriate clinical strategies. *J Am Coll Cardiol* 2001;37:144-52.
 46. Eagle KA, Berger PB, Calkins H, et al. ACC/AHA guideline update for perioperative cardiovascular evaluation for noncardiac surgery: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (Committee to Update the 1996 Guidelines on Perioperative Cardiovascular Evaluation for Noncardiac Surgery). 2002; American College of Cardiology Web site. Available at: http://www.acc.org/clinical/guidelines/perio/clean/pdf/perio_pdf.pdf. Accessed June 11, 2002.
 47. Allman KC, Shaw LJ, Hachamovitch R, et al. Myocardial viability testing and impact of revascularization on prognosis in patients with coronary artery disease and left ventricular dysfunction: a meta-analysis. *J Am Coll Cardiol* 2002;39:1151-8.
 48. Bax JJ, Wijns W, Cornel JH, et al. 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.
 49. Di Carli MF, Davidson M, Little R, 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.
 50. Feldman AM, Lorell BH, Reis SE. Trastuzumab in the treatment of metastatic breast cancer: anticancer therapy versus cardiotoxicity. *Circulation* 2000;102:272-4.
 51. Lopez M, Vici P, Di Lauro K, et al. Randomized prospective clinical trial of high-dose epirubicin and dexrazoxane in patients with advanced breast cancer and soft tissue sarcomas. *J Clin Oncol* 1998;16:86-92.
 52. Carlsen J, Toft JC, Mortensen SA, et al. Myocardial perfusion scintigraphy as a screening method for significant coronary artery stenosis in cardiac transplant recipients. *J Heart Lung Transplant* 2000;19:873-8.
 53. Marin-Neto JA, Bromberg-Marin G, Pazin-Filho A, et al. Cardiac autonomic impairment and early myocardial damage involving the right ventricle are independent phenomena in Chagas' disease. *Int J Cardiol* 1998;65:261-9.
 54. Simoes MV, Pintya AO, Bromberg-Marin G, et al. Relation of regional sympathetic denervation and myocardial perfusion disturbance to wall motion impairment in Chagas' cardiomyopathy. *Am J Cardiol* 2000;86:975-81.
 55. Eguchi M, Tsuchihashi K, Hotta D, et al. Technetium-99m sestamibi/tetrofosmin myocardial perfusion scanning in cardiac and noncardiac sarcoidosis. *Cardiology* 2000;94:193-9.
 56. Hongo M, Fujii T, Hirayama J, et al. Radionuclide angiographic assessment of left ventricular diastolic filling in amyloid heart disease: a study of patients with familial amyloid polyneuropathy. *J Am Coll Cardiol* 1989;13:48-53.
 57. Tanaka M, Hongo M, Kinoshita O, et al. Iodine-123 metaiodobenzylguanidine scintigraphic assessment of myocardial sympathetic innervation in patients with familial amyloid polyneuropathy. *J Am Coll Cardiol* 1997;29:168-74.
 58. Le Guludec D, Gauthier H, Porcher R, et al. Prognostic value of radionuclide angiography in patients with right ventricular arrhythmias. *Circulation* 2001;103:1972-6.

59. Borer JS, Bacharach SL, Green MV, et al. Exercise-induced left ventricular dysfunction in symptomatic and asymptomatic patients with aortic regurgitation: assessment by radionuclide cineangiography. *Am J Cardiol* 1978;42:351-7.
60. Bonow RO, Lakatos E, Maron BJ, et al. Serial long-term assessment of the natural history of asymptomatic patients with chronic aortic regurgitation and normal left ventricular systolic function. *Circulation* 1991;84:1625-35.
61. Borer JS, Hochreiter C, Herrold EM, et al. Prediction of indications for valve replacement among asymptomatic or minimally symptomatic

- patients with chronic aortic regurgitation and normal left ventricular performance. *Circulation* 1998;97:525-34.
62. Pruckmayer M, Zacherl S, Salzer-Muhar U, et al. Scintigraphic assessment of pulmonary and whole-body blood flow patterns after surgical intervention in congenital heart disease. *J Nucl Med* 1999;40:1477-83.

KEY WORDS: ACC/AHA Guidelines ■ imaging ■ radioisotopes ■ testing