

# Diagnosis of Stable Ischemic Heart Disease: Summary of a Clinical Practice Guideline From the American College of Physicians/American College of Cardiology Foundation/American Heart Association/American Association for Thoracic Surgery/Preventive Cardiovascular Nurses Association/Society of Thoracic Surgeons

Amir Qaseem, MD, PhD, MHA; Stephan D. Fihn, MD, MPH; Sankey Williams, MD; Paul Dallas, MD; Douglas K. Owens, MD, MS; and Paul Shekelle, MD, PhD, for the Clinical Guidelines Committee of the American College of Physicians\*

**Description:** The American College of Physicians (ACP) developed this guideline in collaboration with the American College of Cardiology Foundation (ACCF), American Heart Association (AHA), American Association for Thoracic Surgery, Preventive Cardiovascular Nurses Association, and Society of Thoracic Surgeons to help clinicians diagnose known or suspected stable ischemic heart disease.

**Methods:** Literature on this topic published before November 2011 was identified by using MEDLINE, Embase, Cochrane CENTRAL, PsychINFO, AMED, and SCOPUS. Searches were limited to human studies published in English. This guideline grades the evidence and

recommendations according to a translation of the ACCF/AHA grading system into ACP's clinical practice guidelines grading system.

**Recommendations:** This guideline includes 28 recommendations that address the following issues: the initial diagnosis of the patient who might have stable ischemic heart disease, cardiac stress testing to assess the risk for death or myocardial infarction in patients diagnosed with stable ischemic heart disease, and coronary angiography for risk assessment.

*Ann Intern Med.* 2012;157:729-734.

[www.annals.org](http://www.annals.org)

For author affiliations, see end of text.

## EXECUTIVE SUMMARY

This guideline presents the available evidence on the diagnosis of stable known or suspected ischemic heart disease (IHD). This is the first of 2 guidelines addressing stable IHD; the second guideline addresses the management of patients with stable IHD (1). Internists and other primary care physicians are the target audiences for this guideline. The target population is all adult patients with stable known or suspected IHD. These recommendations are based on the joint American College of Cardiology Foundation (ACCF), American Heart Association (AHA), American College of Physicians (ACP), American Association for Thoracic Surgery (AATS), Preventive Cardiovascular Nurses Association (PCNA), Society for Cardiovascular Angiography and Interventions (SCAI), and Society of Thoracic Surgeons (STS) guideline for the diagnosis and management of patients with stable IHD published in 2012, which ACP recognized as a scientifically valid, high-quality review of the evidence (2). Full details about methods and evidence are available in the **Appendix** at [www.annals.org](http://www.annals.org).

## Methods

The databases used for the literature search included MEDLINE, Embase, Cochrane CENTRAL, PsychINFO, AMED, and SCOPUS for studies published up until November 2011. The criteria for search included human participants and English-language articles. For more details on the methods, refer to the **Appendix** and the ACCF, AHA, ACP, AATS, PCNA, SCAI, and STS guideline for the diagnosis and management of patients with stable IHD (2).

### See also:

#### Print

Related article ..... 735

Editorial comment ..... 749

Summary for Patients ..... I-42

#### Web-Only

Appendix: Full Guideline Summary

CME quiz (preview on page I-34)

\* This paper, written by Amir Qaseem, MD, PhD, MHA; Stephan D. Fihn, MD, MPH; Sankey Williams, MD; Paul Dallas, MD; Douglas K. Owens, MD, MS; and Paul Shekelle, MD, PhD, was developed for the Clinical Guidelines Committee of the American College of Physicians: Paul Shekelle, MD, PhD (Chair); Roger Chou, MD; Molly Cooke, MD; Paul Dallas, MD; Thomas D. Denberg, MD, PhD; Nick Fitterman, MD; Mary Ann Forciea, MD; Robert H. Hopkins Jr., MD; Linda L. Humphrey, MD, MPH; Tanveer P. Mir, MD; Holger J. Schünemann, MD, PhD; Donna E. Sweet, MD; and Timothy Wilt, MD, MPH. Approved by the ACP Board of Regents on 16 April 2012.

**Table 1.** The American College of Physicians' Guideline Grading System\*

Quality of Evidence	Strength of Recommendation	
	Benefits Clearly Outweigh Risks and Burden or Risks and Burden Clearly Outweigh Benefits	Benefits Finely Balanced With Risks and Burden
High	Strong	Weak
Moderate	Strong	Weak
Low	Strong	Weak
Insufficient evidence to determine net benefits or risks		

\* Adopted from the classification developed by the GRADE (Grading of Recommendations Assessment, Development, and Evaluation) workgroup.

Because this document is based on the joint guideline, ACP translated the ACCF/AHA evidence and recommendation grades into ACP's guideline grading system (3) (Tables 1 and 2). We included only class I and class III statements from the joint guideline because the evidence for these statements very clearly demonstrates the tradeoff between benefits and harms (Table 2). For details on other recommendations, refer to the ACCF, AHA, ACP, AATS, PCNA, SCAI, and STS guideline for the diagnosis and management of patients with stable IHD (2).

The objective of this guideline is to synthesize the evidence for the following key questions:

1: How should a clinician evaluate a patient with chest pain that is consistent with IHD?

2: What is the role of noninvasive testing in the diagnosis of stable IHD?

## Recommendations

In interpreting these recommendations, it is important to distinguish between the probability of having IHD and the probability (risk) of death or myocardial infarction once the diagnosis of IHD is established.

### Initial Cardiac Testing to Establish Diagnosis of IHD

**Recommendation 1:** The organizations recommend that patients with chest pain should receive a thorough history and physical examination to assess the probability of IHD prior to additional testing (Grade: strong recommendation; low-quality evidence).

**Recommendation 2:** The organizations recommend that choices regarding diagnostic and therapeutic options should be made through a process of shared decision making involving the patient and provider, explaining information about risks, benefits, and costs to the patient (Grade: strong recommendation; low-quality evidence).

**Recommendation 3:** The organizations recommend that patients who present with acute angina must be categorized as stable or unstable; patients with unstable angina should be further categorized as high, moderate, or low risk (Grade: strong recommendation; low-quality evidence).

**Recommendation 4:** The organizations recommend a resting electrocardiography (ECG) in patients without an obvious noncardiac cause of chest pain for risk assessment (Grade: strong recommendation; moderate-quality evidence).

**Recommendation 5:** The organizations recommend standard exercise ECG for initial diagnosis in patients with an intermediate pretest probability of IHD who have an interpretable ECG and at least moderate physical functioning or no disabling comorbidity (Grade: strong recommendation; high-quality evidence).

**Recommendation 6:** The organizations recommend that exercise stress with radionuclide myocardial perfusion imaging or echocardiography should be used for patients with an intermediate to high pretest probability of IHD that have an uninterpretable ECG and at least moderate physical functioning or no disabling comorbidity (Grade: strong recommendation; moderate-quality evidence).

**Recommendation 7:** The organizations recommend that pharmacologic stress with radionuclide myocardial perfusion imaging, echocardiography, or cardiac magnetic resonance imaging should not be used for patients who have an interpretable ECG and at least moderate physical functioning or no

**Table 2.** Comparison of Grading Systems From the ACP and ACCF/AHA

ACF's Grading System			ACCF/AHA's Grading System (Size vs. Certainty)		
Description	Grade (For or Against Intervention)		Grade	Class	
	Recommendation	Evidence		For	Against
Benefits clearly outweigh risks and burden or vice versa	Strong	High-quality	A	I	III
Benefits clearly outweigh risks and burden or vice versa	Strong	Moderate-quality	B	I	III
Benefits clearly outweigh risks and burden or vice versa	Strong	Low-quality	C	I	III
Benefits closely balanced with risks and burden	Weak	High-quality	A	IIa, IIb	NER
Benefits closely balanced with risks and burden	Weak	Moderate-quality	B	IIa, IIb	NER
Uncertainty, benefits may be closely balanced with risks and burden	Weak	Low-quality	C	IIa, IIb	NER

ACF = American College of Cardiology Foundation; ACP = American College of Physicians; AHA = American Heart Association; NER = no equivalent rating.

*disabling comorbidity (Grade: strong recommendation; low-quality evidence).*

**Recommendation 8:** *The organizations recommend that exercise stress with nuclear myocardial perfusion imaging should not be used as an initial test in low-risk patients who have an interpretable ECG and at least moderate physical functioning or no disabling comorbidity (Grade: strong recommendation; low-quality evidence).*

**Recommendation 9:** *The organizations recommend pharmacologic stress with radionuclide myocardial perfusion imaging or echocardiography for patients with an intermediate to high pretest probability of IHD who are incapable of at least moderate physical functioning or with disabling comorbidity (Grade: strong recommendation; moderate-quality evidence).*

**Recommendation 10:** *The organizations recommend that standard exercise ECG testing should not be used for patients that have an uninterpretable ECG or are incapable of at least moderate physical functioning or with disabling comorbidity (Grade: strong recommendation; low-quality evidence).*

**Recommendation 11:** *The organizations recommend assessing resting left ventricular systolic and diastolic ventricular function and evaluating for abnormalities of myocardium, heart valves, or pericardium using Doppler echocardiography in patients with known or suspected IHD and a prior myocardial infarction, pathologic Q waves, symptoms or signs suggestive of heart failure, complex ventricular arrhythmias, or an undiagnosed heart murmur (Grade: strong recommendation; moderate-quality evidence).*

**Recommendation 12:** *The organizations recommend that echocardiography, radionuclide imaging, cardiac magnetic resonance imaging, or cardiac computed tomography should not be used for routine assessment of left ventricular function in patients with a normal ECG, no history of myocardial infarction, no symptoms or signs suggestive of heart failure, and no complex ventricular arrhythmias (Grade: strong recommendation; low-quality evidence).*

**Recommendation 13:** *The organizations recommend that routine reassessment (<1 year) of left ventricular function using technologies such as echocardiography radionuclide imaging, cardiac magnetic resonance imaging, or cardiac computed tomography should not be used in patients with no change in clinical status and for whom no change in therapy is contemplated (Grade: strong recommendation; low-quality evidence).*

#### **Cardiac Stress Testing to Assess Risk in Patients With Known Stable IHD Who Are Able to Exercise**

**Recommendation 14:** *The organizations recommend standard exercise ECG testing for risk assessment in patients who are able to exercise to an adequate workload and have an ECG that can be interpreted during exercise (Grade: strong recommendation; moderate-quality evidence).*

**Recommendation 15:** *The organizations recommend the addition of either radionuclide myocardial perfusion imaging or echocardiography to standard exercise ECG testing for risk*

*assessment, in patients with stable IHD who are able to exercise to an adequate workload but have an uninterpretable ECG not due to left bundle branch block or ventricular pacing (Grade: strong recommendation; moderate-quality evidence).*

**Recommendation 16:** *The organizations recommend that pharmacologic stress imaging (radionuclide myocardial perfusion imaging, echocardiography, cardiac magnetic resonance imaging) or cardiac computed tomography angiography should not be used for risk assessment in patients with stable IHD who are able to exercise to an adequate workload and have an interpretable ECG (Grade: strong recommendation; low-quality evidence).*

#### **Cardiac Stress Testing to Assess Risk in Patients With Known Stable IHD Who Are Unable to Exercise**

**Recommendation 17:** *The organizations recommend pharmacologic stress with either radionuclide myocardial perfusion imaging or echocardiography for risk assessment in patients who are unable to exercise to an adequate workload regardless of interpretability of ECG (Grade: strong recommendation; moderate-quality evidence).*

#### **Cardiac Stress Testing to Assess Risk in Patients With Stable IHD Regardless of Ability to Exercise**

**Recommendation 18:** *The organizations recommend pharmacologic stress with either radionuclide myocardial perfusion imaging or echocardiography for risk assessment in patients with stable IHD who have left bundle branch block on ECG, regardless of ability to exercise to an adequate workload (Grade: strong recommendation; moderate-quality evidence).*

**Recommendation 19:** *The organizations recommend either exercise or pharmacological stress with imaging (radionuclide myocardial perfusion imaging, echocardiography, or cardiac magnetic resonance) for risk assessment in patients being considered for revascularization of known coronary stenosis of unclear physiologic significance (Grade: strong recommendation; moderate-quality evidence).*

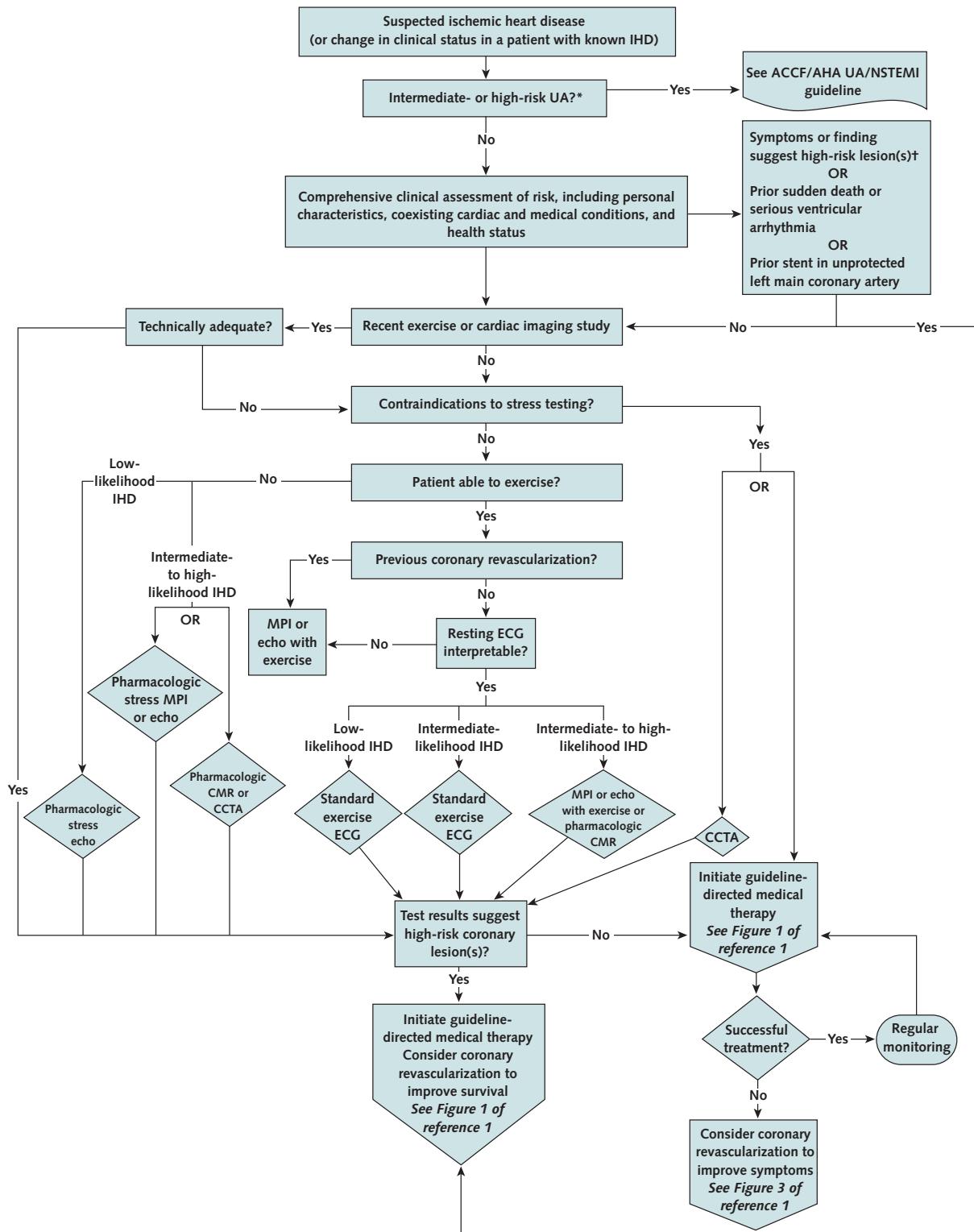
**Recommendation 20:** *The organizations recommend that a) more than 1 stress imaging study or b) a stress imaging study and cardiac computed tomography angiography at the same time should not be used for risk assessment in patients with stable IHD (Grade: strong recommendation; low-quality evidence).*

#### **Coronary Angiography as an Initial Testing Strategy to Assess Risk in Patients With Stable IHD**

**Recommendation 21:** *The organizations recommend that patients with stable IHD who have survived sudden cardiac death or potentially life-threatening ventricular arrhythmia undergo coronary angiography to assess cardiac risk (Grade: strong recommendation; moderate quality-evidence).*

**Recommendation 22:** *The organizations recommend that patients with stable IHD who develop symptoms and signs of heart failure should be evaluated to determine whether coro-*

Figure 1. Diagnosis of patients suspected of having ischemic heart disease.



CCTA = computed coronary tomography angiography; CMR = cardiac magnetic resonance; ECG = electrocardiogram; echo = echocardiography; IHD = ischemic heart disease; MPI = myocardial perfusion imaging; UA = unstable angina; UA/NSTEMI = unstable angina/non-ST-segment elevation myocardial infarction.

\* See Table 2 of reference 2 for short-term risk of death or nonfatal myocardial infarction in patients with UA/NSTEMI.

† CCTA is reasonable only for patients with intermediate probability of IHD.

nary angiography should be performed for risk assessment (Grade: strong recommendation; moderate quality-evidence).

**Recommendation 23:** The organizations recommend that patients with stable IHD and clinical characteristics that indicate a high likelihood of severe IHD should undergo coronary angiography to assess cardiac risk (Grade: strong recommendation; low-quality evidence).

#### Coronary Angiography to Assess Risk After Initial Workup With Noninvasive Testing

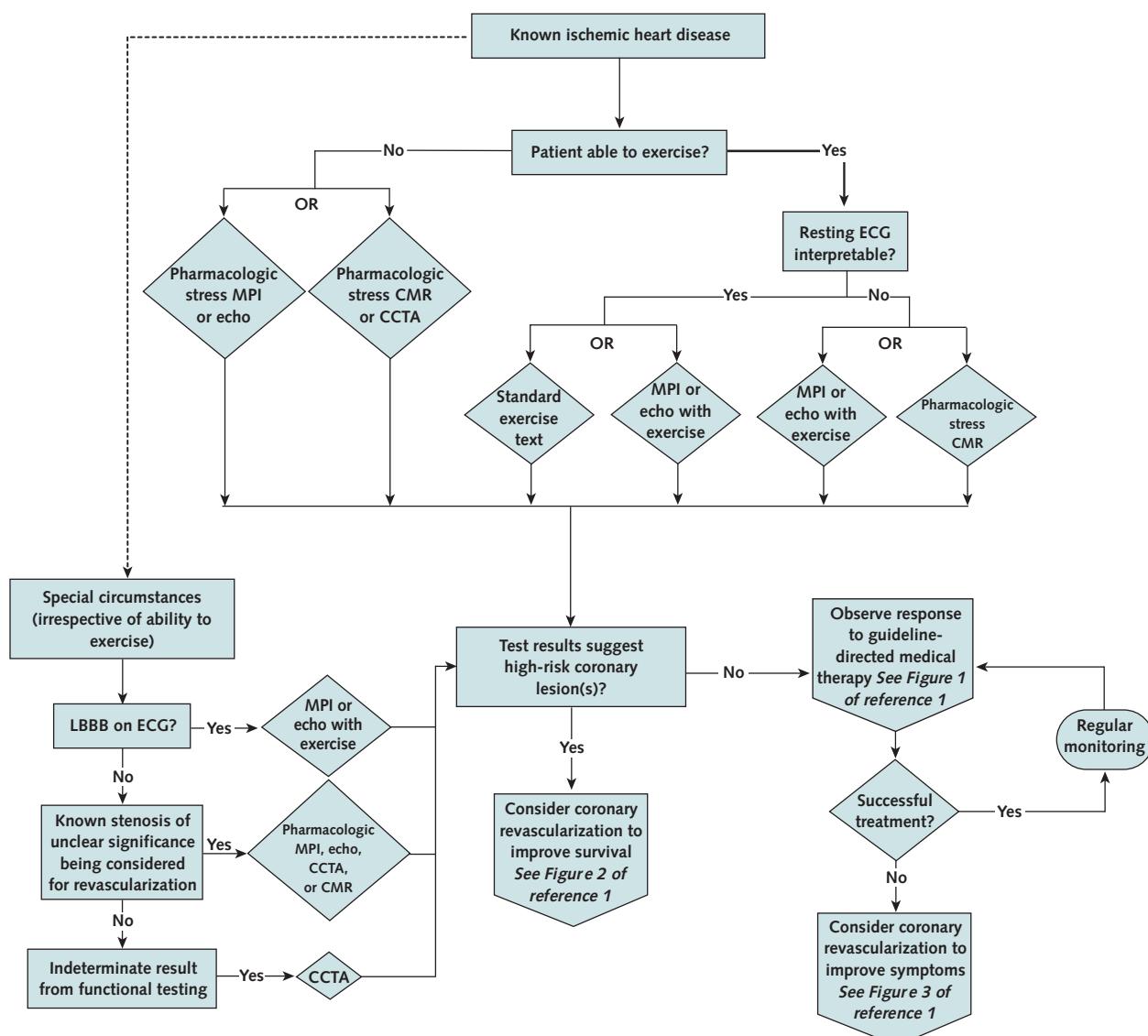
**Recommendation 24:** The organizations recommend that coronary arteriography should be used for risk assessment in patients with stable IHD whose clinical character-

istics and results of noninvasive testing indicate a high likelihood of severe IHD and when the benefits are deemed to exceed risk (Grade: strong recommendation; low-quality evidence).

**Recommendation 25:** The organizations recommend that coronary angiography for risk assessment should not be utilized for stable IHD patients who elect not to undergo revascularization or who are not candidates for revascularization based on comorbidities or individual preferences (Grade: strong recommendation; moderate-quality evidence).

**Recommendation 26:** The organizations recommend that coronary angiography should not be used to further assess risk in patients with stable IHD who have preserved left ventric-

Figure 2. Risk assessment of patients with stable ischemic heart disease.



CCTA = coronary computed tomography angiography; CMR = cardiac magnetic resonance; ECG = electrocardiogram; echo = echocardiography; LBBB = left bundle branch block; MPI = myocardial perfusion imaging.

*ular function (ejection fraction >50%) and low-risk criteria on noninvasive testing (Grade: strong recommendation; moderate-quality evidence).*

*Recommendation 27: The organizations recommend that coronary angiography should not be used to assess risk in patients who are at low risk based upon clinical criteria and who have not undergone noninvasive risk testing (Grade: strong recommendation; low-quality evidence).*

*Recommendation 28: The organizations recommend that coronary angiography should not be used to assess risk in asymptomatic patients with no evidence of ischemia on non-invasive testing (Grade: strong recommendation; low-quality evidence).*

## Summary

Physicians should integrate the information from their clinical evaluation with patient preferences when making decisions about further testing. Two patients with the same pretest probability of IHD may prefer different approaches because of variations in personal beliefs, economic considerations, or stage of life. A resting ECG helps in establishing a diagnosis and assessing the risk for stable IHD. Rest echocardiography and radionuclide imaging are helpful in assessing patients with clinically evident ventricular dysfunction. Cardiac stress testing is indicated in most symptomatic patients suspected of having IHD to establish the diagnosis, and it is indicated in most patients with both suspected and established IHD to identify patients at very high risk for death or myocardial infarction who might have lesions where anatomical intervention could be beneficial. See **Figure 1** for an algorithm on the diagnosis of patients suspected of having IHD and **Figure 2** for an algorithm on risk assessment in patients with established stable IHD.

From the American College of Physicians and University of Pennsylvania, Philadelphia, Pennsylvania; Department of Veterans Affairs, Seattle, Washington; Veterans Affairs Palo Alto Health Care System and Stanford University, Stanford, California; Virginia Tech Carilion School of Medicine, Roanoke, Virginia; and West Los Angeles Veterans Affairs Medical Center, Los Angeles, California.

**Note:** Clinical practice guidelines are “guides” only and may not apply to all patients and all clinical situations. Thus, they are not intended to

override clinicians’ judgment. All ACP clinical practice guidelines are considered automatically withdrawn or invalid 5 years after publication or once an update has been issued.

**Disclaimer:** The authors of this article are responsible for its contents, including any clinical or treatment recommendations.

**Financial Support:** Financial support for the development of this guideline comes exclusively from the ACP operating budget.

**Potential Conflicts of Interest:** Any financial and nonfinancial conflicts of interest of the group members were declared, discussed, and resolved according to ACP’s conflicts of interest policy. A record of conflicts of interest is kept for each Clinical Guidelines Committee meeting and conference call and can be viewed at [www.acponline.org/clinical\\_information/guidelines/conflicts\\_cgc.htm](http://www.acponline.org/clinical_information/guidelines/conflicts_cgc.htm). Author and peer reviewer disclosure information for the multisocietal stable IHD guideline, on which these guidelines are based, may be found in the published multisocietal document (2). Disclosures can also be viewed at [www.annals.org/authors/icmje/ConflictOfInterestForms.do?msNum=M12-1769](http://www.annals.org/authors/icmje/ConflictOfInterestForms.do?msNum=M12-1769).

**Requests for Single Reprints:** Amir Qaseem, MD, PhD, MHA, American College of Physicians, 190 N. Independence Mall West, Philadelphia, PA 19106; e-mail, [aqaseem@acponline.org](mailto:aqaseem@acponline.org).

Current author addresses and author contributions are available at [www.annals.org](http://www.annals.org).

## References

- Qaseem A, Fihn SD, Dallas P, Williams S, Owens DK, Shekelle P; for the Clinical Guidelines Committee of the American College of Physicians. Management of stable ischemic heart disease: summary of a clinical practice guideline from the American College of Physicians/American College of Cardiology Foundation/American Heart Association/American Association for Thoracic Surgery/Preventive Cardiovascular Nurses Association/Society of Thoracic Surgeons. Ann Intern Med. 2012;157:735-43.
- Fihn SD, Gardin JM, Abrams J, Berra K, Blankenship JC, Dallas P, et al. 2012 ACCF/AHA/AATS/PCNA/SCAI/STS guideline for the diagnosis and management of patients with stable ischemic heart disease: a report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines, and the American College of Physicians, American Association for Thoracic Surgery, Preventive Cardiovascular Nurses Association, Society for Cardiovascular Angiography and Interventions, and Society of Thoracic Surgeons. J Am Coll Cardiol. 2012. [Forthcoming].
- Qaseem A, Snow V, Owens DK, Shekelle P; Clinical Guidelines Committee of the American College of Physicians. The development of clinical practice guidelines and guidance statements of the American College of Physicians: summary of methods. Ann Intern Med. 2010;153:194-9. [PMID: 20679562]

**APPENDIX: DIAGNOSIS OF STABLE ISCHEMIC HEART DISEASE: A CLINICAL PRACTICE GUIDELINE SUMMARY FROM THE AMERICAN COLLEGE OF PHYSICIANS/AMERICAN COLLEGE OF CARDIOLOGY FOUNDATION/AMERICAN HEART ASSOCIATION/AMERICAN ASSOCIATION FOR THORACIC SURGERY/PREVENTIVE CARDIOVASCULAR NURSES ASSOCIATION/SOCIETY OF THORACIC SURGEONS**

Ischemic heart disease (IHD) is a major public health issue that affects an estimated 1 in 3 adults in the United States (4). Approximately 71 million Americans have some form of cardiovascular disease, including more than 13 million with coronary artery disease and more than 9 million with angina pectoris (4). The prevalence of IHD increases with age; approximately 23% of men and 15% of women aged 60 to 79 years in the United States have IHD. Although survival of patients with IHD has been steadily improving, it was still responsible for nearly 380 000 deaths in the United States in 2010, with an age-adjusted mortality rate of 113 per 100 000 population (5). The costs of caring for patients with IHD are enormous: \$156 billion in the U.S. for both direct and indirect costs in 2008 (6). These costs include hospitalizations, invasive procedures, emergency department visits, and long-term care.

The purpose of this guideline is to present the available evidence on the diagnosis of stable known or suspected IHD. This is the first of 2 guidelines addressing stable IHD; the second guideline addresses the management of patients with stable IHD (7). The target audience for this guideline is all internists and other primary care physicians. The target population is all adult patients with stable known or suspected IHD. These recommendations are based on the joint guideline on the diagnosis and management of patients with stable IHD from the American College of Cardiology Foundation (ACCF), American Heart Association (AHA), American College of Physicians (ACP), American Association for Thoracic Surgery (AATS), Preventive Cardiovascular Nurses Association (PCNA), Society for Cardiovascular Angiography and Interventions (SCAI), and Society of Thoracic Surgeons (STS), published in 2012, which ACP recognized as a scientifically valid, high-quality review of the evidence (8).

**Appendix Table 1. Clinical Classification of Chest Pain**

**Typical angina (definite)**

1. Substernal chest discomfort with a characteristic quality and duration that is
2. Provoked by exertion or emotional stress and
3. Relieved by rest or nitroglycerin

**Atypical angina (probable)**

Meets 2 of the above characteristics

**Noncardiac chest pain**

Meets 1 or none of the typical anginal characteristics

Adapted from Braunwald et al (9) with permission.

**Methods**

The databases used for the literature search included MEDLINE, Embase, Cochrane CENTRAL, PsychINFO, AMED, and SCOPUS for studies published up until November 2011. The criteria for search included human participants and English-language articles. For more details on the methods, please refer to the ACCF, AHA, ACP, AATS, PCNA, SCAI, and STS guideline for the diagnosis and management of patients with stable IHD (8).

ACP guideline recommendations are based on evidence from systematic reviews of high-quality evidence (several well-designed randomized, controlled trials) and meta-analyses where appropriate. Because this document is based on the joint ACCF, AHA, ACP, AATS, PCNA, SCAI, and STS guideline, ACP translated the ACCF/AHA evidence and recommendation grades into ACP's guideline grading system (Tables 1 and 2, in Executive Summary). We included only class I and class III statements from the joint guideline because the evidence very clearly demonstrated that benefits outweigh harms or vice versa (Table 2, in Executive Summary). For details on other recommendations, please refer to the ACCF, AHA, ACP, AATS, PCNA, SCAI, and STS guideline for the diagnosis and management of patients with stable IHD (8).

The objective of this guideline is to synthesize the evidence for the following key questions:

1. How should a clinician evaluate a patient with chest pain that is consistent with IHD?
2. What is the role of noninvasive testing in the diagnosis of stable IHDs?

**Clinical Evaluation of Patients With Chest Pain History**

A careful history is the initial step in evaluating a patient with chest pain. It should include a detailed description of such symptoms as quality, location, duration of pain, radiation, associated symptoms, provocative factors, and alleviating factors. Adjectives often used to describe anginal pain include "squeezing," "griplike," "suffocating," and "heavy"; it is rarely described as "sharp" or "stabbing," and it typically does not vary with position or respiration. The nature of the pain can help determine whether the pain is typical, atypical, or noncardiac pain (Appendix Table 1). Many patients do not, however, describe angina as frank pain but as tightness, pressure, or discomfort. Other patients, in particular women and the elderly, often describe sharp (atypical) chest pain or noncardiac symptoms, such as nausea, vomiting, or midepigastic discomfort. Patients presenting with acute angina should be categorized as stable or unstable. Those who have symptoms consistent with unstable angina should be further classified as to level of risk. Patients who are at high risk or moderate risk for short-term death should be promptly transferred to an emergency department or coronary care unit for evaluation and treatment (Appendix Table 2). Characterization of chest pain should be followed by the assessment of risk factors for IHD, including smoking, hyperlipidemia, diabetes, hypertension, family history of premature coronary artery disease, and history of cerebrovascular or peripheral vascular disease.

**Appendix Table 2. Short-Term Risk for Death or Nonfatal Myocardial Infarction in Patients With Unstable Angina\***

High Risk	Intermediate Risk	Low Risk
At least one of the following features must be present:		
Prolonged, ongoing (>20 min) pain at rest	No high-risk features but must have any of the following:	
Pulmonary edema, most likely related to ischemia	Prolonged (>20 min) rest angina, now resolved, with moderate or high likelihood of CAD	
Angina at rest with dynamic ST-segment changes $\geq 1$ mm	Rest angina (>20 min or relieved with sublingual nitroglycerin)	
Angina with new or worsening mitral regurgitation murmur	Nocturnal angina	
Angina with $S_3$ or new/worsening rales	Angina with dynamic T-wave changes	
Angina with hypotension	New-onset CCSC III or IV angina in the past 2 wk with moderate or high likelihood of CAD†	
	Pathologic Q waves or resting ST-segment depression $\leq 1$ mm in multiple lead groups (anterior, inferior, lateral)	
	Age $>65$ y	

CAD = coronary artery disease; CCSC = Canadian Cardiovascular Society Classification; ECG = electrocardiogram.

\* Estimation of the short-term risks for death and nonfatal myocardial infarction in unstable angina is a complex multivariable problem that cannot be fully specified in a table such as this. Therefore, it is meant to offer general guidance and illustration rather than rigid algorithms. Modified from Braunwald et al (9) with permission.

† CCSC III angina is defined by marked limitation of ordinary physical activity. CCSC IV angina is defined by the inability to carry out any physical activity without discomfort (10).

### Physical Examination

Physical examination is usually normal or nonspecific in patients with stable IHD but may reveal other related conditions, such as heart failure, valvular heart disease, hypertrophic cardiomyopathy, peripheral vascular disease, or other noncardiac reasons for chest pain (for example, pulmonary, gastrointestinal, musculoskeletal).

### Differential Diagnosis

Some patients with IHD have symptoms consistent with alternative diagnoses (Appendix Table 3). Coexisting conditions may precipitate angina symptoms by inducing or exacerbating myocardial ischemia through either increasing myocardial oxygen demand or decreasing myocardial oxygen supply. Causes for increased oxygen demand include hyperthermia (particularly if accompanied by volume contraction) (12), hyperthyroidism, cocaine abuse, sympathomimetic toxicity, severe uncontrolled hypertension, hypertrophic cardiomyopathy, and aortic stenosis. Causes for decreased myocardial oxygen supply include anemia, hypoxemia resulting from pulmonary disease, polycythemia, leukemia, thrombocytosis, and hypergammaglobulinemia.

### Developing a Probability Estimate of Stable IHD

The data gathered during the clinical evaluation should be used to determine the patient's probability of having IHD, which will then guide the patient's subsequent evaluation. The probability of coronary artery disease can be estimated on the basis of the characteristics of the pain and the patients' age, sex (Appendix Table 4) (15), and presence of risk factors (Appendix Table 5). When the probability of the disease is less than 5%, further testing (typically a standard exercise test) is usually not needed because the likelihood of a false-positive result is substantial. However, the probability of a false-negative result is high when the exercise test result is negative in a patient with high likelihood on the basis of the history. Intermediate pretest possibility is defined as between 10% and 90% (17–19).

### Noninvasive Testing for Diagnosis of IHD

Functional or stress testing using exercise or pharmacologic stress agents to increase myocardial work and oxygen demand has been the standard for noninvasive diagnosis of stable IHD. Depending on the duration and intensity of stress imposed, these techniques evoke graded ischemia that induces sequential changes

**Appendix Table 3. Alternative Diagnoses to Angina for Patients With Chest Pain**

Nonischemic Cardiovascular	Pulmonary Embolus	Gastrointestinal	Chest Wall	Psychiatric
Aortic dissection	Pulmonary embolus	Esophageal	Costochondritis	Anxiety disorders
Pericarditis	Pneumothorax	Esophagitis	Fibrosis	Hyperventilation
	Pneumonia	Spasm	Rib fracture	Panic disorder
	Pleuritis	Reflux	Sternoclavicular arthritis	Primary anxiety
		Biliary	Herpes zoster (before the rash)	Affective disorders (e.g., depression)
		Colic		Somatoform disorders
		Cholecystitis		Thought disorders (e.g., fixed delusions)
		Choledocholithiasis		
		Cholangitis		
		Peptic ulcer		
		Pancreatitis		

Reproduced from Gibbons et al (11) with permission.

**Appendix Table 4. Pretest Likelihood of Coronary Artery Disease in Symptomatic Patients According to Age and Sex\***

Age, y	Nonanginal Chest Pain, %		Atypical Angina, %		Typical Angina, %	
	Men	Women	Men	Women	Men	Women
30–39	4	2	34	12	76	26
40–49	13	3	51	22	87	55
50–59	20	7	65	31	93	73
60–69	27	14	72	51	94	86

\* Combined data from Diamond and Forrester's study (13) and Coronary Artery Surgery Study (14). Each value represents the percentage with significant coronary artery disease on catheterization. Adapted from Diamond and Forrester (13) with permission.

in perfusion, relaxation and contraction, wall motion, repolarization, and ultimately, symptoms. Abnormalities of regional or global ventricular function that occur later in the cascade are more likely to indicate severe stenoses and, thus, demonstrate a higher diagnostic specificity for stable IHD than perfusion defects, such as those seen on nuclear myocardial perfusion imaging. Isolated perfusion defects, on the other hand, may result from stenoses of borderline significance, raising the sensitivity of myocardial perfusion imaging for underlying coronary artery disease (CAD) but lowering the specificity for more severe stenosis. Coronary stenoses less than 70% are often undetected by functional testing.

Estimates of the sensitivity and specificity of noninvasive tests vary substantially, in part because of limitations in the design of some studies evaluating test performance. If a study preferentially refers patients for angiography who have a positive noninvasive test result (rather than referring all patients for angiography), the estimates of sensitivity and specificity will be subject to workup bias, also known as verification or post-test referral bias. This bias results in an overestimate of sensitivity and an underestimate of specificity.

For patients who are able to exercise, have an interpretable result on resting electrocardiography (ECG), and have an intermediate probability of IHD, standard exercise ECG should be the first-line test for diagnosis of suspected IHD. A meta-analysis of 147 studies of exercise testing found wide variation in reported sensitivity and specificity. When the analysis included only studies that avoided workup bias, sensitivity of exercise ECG was 50% and specificity was 90% (20). A rigorous study designed to minimize workup bias found a sensitivity for exercise ECG of 45% and a specificity of 85% (21). Although the reported sensitivities of stress imaging with nuclear myocardial perfusion imaging or with echocardiography are also biased, they are generally higher than those of exercise ECG. For this reason, stress imaging may be substituted for patients with normal results on resting ECG who are able to exercise and who have intermediate or high pretest probabilities of IHD (**Figure 1**, in Executive Summary).

Clinicians should be aware that the low sensitivity of exercise ECG and stress imaging modalities means that negative test results should be interpreted cautiously. When the pretest probability of IHD is high or intermediate, a negative result may not

diminish the probability of disease sufficiently enough to be diagnostically useful. For example, with a sensitivity of 45% and a specificity of 85% for exercise ECG (21), a patient who has a pretest probability of 50% for IHD will have a 39% post-test probability of disease after a negative exercise ECG result. Nonetheless, given its somewhat higher sensitivity compared with a standard exercise ECG, patients with a high pretest probability of IHD should undergo stress imaging with myocardial perfusion imaging or echocardiography to lessen the likelihood of a false-negative result in a potentially high-risk patient.

Although the sensitivity of exercise ECG is modest, the test also provides important prognostic information. Patients who have a low-risk Duke treadmill score, defined below, have a highly favorable prognosis. Most people who have a false-negative result with exercise ECG will also have a low-risk Duke treadmill score and therefore a favorable prognosis. Stress imaging with myocardial perfusion imaging or echocardiography, rather than standard exercise ECG, is preferred in patients who have an uninterpretable result on resting ECG because of complete left bundle branch block, electronically paced rhythm, pre-excitation (Wolff–Parkinson–White) syndrome, more than 1 mm of ST-segment depression at rest, or left ventricular (LV) hypertrophy.

Increasingly, patients suspected of having IHD are unable to exercise to a sufficient level because of obesity, coexisting conditions (such as arthritis), or general physical infirmity. In patients who cannot exercise and have a low probability of IHD, echocardiography with pharmacologic stress is preferred because of its greater specificity compared with myocardial perfusion imaging. For patients with intermediate or high probability of IHD, either test with pharmacologic stress is recommended.

The high prevalence of stable IHD in the elderly, which is often extensive, leads to higher sensitivity of exercise testing in older patients; however, data in the elderly are limited. Exercise testing in the elderly is often more difficult because of several factors, including limited exertional capacity due to muscle weakness and deconditioning, impaired gait and coordination, ten-

**Appendix Table 5. Comparing Pretest Likelihoods of Coronary Artery Disease in Low-Risk Symptomatic Patients and High-Risk Symptomatic Patients\***

Age, y	Nonanginal Chest Pain, %		Atypical Angina, %		Typical Angina, %	
	Men	Women	Men	Women	Men	Women
35	3–35	1–19	8–59	2–39	30–88	10–78
45	9–47	2–22	21–70	5–43	51–92	20–79
55	23–59	4–21	45–79	10–47	80–95	38–82
65	49–69	9–29	71–86	20–51	93–97	56–84

\* From the Duke Database. Each value represents the percentage with significant coronary artery disease. The first is the percentage for a low-risk, mid-decade patient without diabetes, smoking, or hyperlipidemia. The second is that of the same-age patient with diabetes, smoking, and hyperlipidemia. Both high- and low-risk patients have normal results on resting electrocardiography. If ST-T wave changes or Q waves had been present, the likelihood of coronary artery disease would be higher in each entry of the table. Reprinted from Pryor et al (16) with permission.

dency to grip or hold hand rails tightly, more frequent arrhythmias, and ST/T changes due to LV hypertrophy and conduction abnormalities. These factors are often indications for pharmacologic stress imaging in the elderly.

Several studies have reported an increased prevalence of myocardial perfusion defects during exercise imaging in the absence of angiographic coronary disease in patients with left bundle branch block (22–24). These defects often involve the interventricular septum, may be reversible or fixed, and are often absent during pharmacologic stress, meaning that perfusion imaging with pharmacologic vasodilation is more accurate for identifying IHD in patients with left bundle branch block (25–33). Right bundle branch block and left anterior hemiblock are not ordinarily associated with such perfusion defects.

Cardiac computed tomographic (CT) angiography is becoming more widely available as a result of improvements in equipment and technique. Five meta-analyses and 3 controlled clinical trials indicate that cardiac CT angiography using 64-slice technique provides a sensitivity of 93% to 97% and specificity of 80% to 90% in detecting IHD (34–42). The figures are, however, probably inflated because studies that were included in the meta-analyses were subject to workup bias given that enrolled patients had already been referred for invasive angiography. Other factors that reduce the accuracy of CT angiography include extensive coronary calcification and high body mass index (43). Unlike stress imaging techniques, CT angiography provides only anatomical data, and identifying a coronary stenosis does not necessarily mean it produces ischemia. On the other hand, a potential advantage of CT angiography over standard functional testing is its very high negative predictive value for obstructive coronary disease. In general, standard stress ECG or stress imaging with myocardial perfusion or echocardiography are preferred diagnostic studies. When used, cardiac CT angiography should be restricted to patients who have an intermediate pretest probability.

Computed tomography can also be used to quantify calcium deposition in coronary arteries, which is related to presence of obstructive lesions. A meta-analysis of 16 published reports yielded a weighted average sensitivity of 80% for coronary artery calcium scoring in detecting significant coronary stenosis among symptomatic patients, but because this technique has a specificity of only 40% (44–50), it is not recommended as a diagnostic test.

Recently, cardiac magnetic resonance imaging (CMR) has been applied in the diagnostic evaluation of patients suspected of having IHD. The imaging end point depends on the stress agent: for cine imaging with dobutamine stress, the end point is development of a new wall-motion abnormality; using vasodilator stress, the end point is a new perfusion abnormality. In a meta-analysis of 37 studies, the diagnostic sensitivity and specificity of dobutamine-induced (CMR) wall-motion imaging were 83% and 86%, respectively; whereas the diagnostic sensitivity and specificity of vasodilator stress-induced CMR myocardial perfusion imaging were both 91%. However, data are still emerging for this technology, which is costly and has limited availability (51, 52).

Positron emission tomography has promise for improving diagnosis and risk assessment in patients suspected of having IHD, but insufficient research has been conducted to date regarding the potential value of this technique.

## **Assessing the Risk for Death or Cardiac Events in Patients With Stable IHD**

### **Risk Stratification With Clinical Parameters**

Once IHD has been diagnosed, management should be guided, in part, by an accurate estimate of the likelihood of death or acute coronary events, such as myocardial infarction or unstable angina, and on patient symptoms. Risk assessment also provides a basis for educating patients so that they may make informed decisions about options for treatment. Numerous factors influence prognosis, including sociodemographic characteristics (age, sex, socioeconomic status), cardiovascular risk factors (smoking, hypertension, dyslipidemia, family history of premature IHD, obesity, sedentary lifestyle), coexisting medical conditions (diabetes; chronic kidney disease; chronic obstructive pulmonary disease; and inflammatory conditions, such as rheumatoid arthritis and systemic lupus erythematosus), coexisting cardiovascular conditions (heart failure, peripheral arterial or cerebrovascular disease), psychosocial characteristics (depression, poor social support), symptoms (especially anginal frequency), functional capacity, and severity of cardiac disease (degree and distribution of stenoses, findings on exercise testing and stress imaging, LV function). Nevertheless, there is no universally accepted approach for assessing patients with stable IHD, and the specific approach to assessing risk depends on the patient's clinical presentation.

Pryor and colleagues (53) identified 11 clinical characteristics that are important in estimating the likelihood of severe CAD: typical angina, previous myocardial infarction (MI), age, sex, duration of chest pain symptoms, risk factors (hypertension, diabetes, hyperlipidemia, smoking), carotid bruit, and chest pain frequency. Hubbard and colleagues identified 5 clinical parameters that were independently predictive of severe (3-vessel or left main) CAD: older age, typical angina, diabetes, male sex, and prior MI (per history or ECG findings). They subsequently developed a 5-point cardiac risk score that estimates the probability of severe CAD (54).

### **Risk Stratification With ECG and Chest Radiography**

Resting ECG (55–57) and chest radiography may be helpful in predicting prognosis for patients with stable IHD (58, 59). Patients with stable IHD who have the following abnormalities on a resting ECG have a worse prognosis than those with normal ECG results: evidence of prior MI, especially Q waves in multiple leads, with an R wave in V1 indicating a posterior infarction (60); persistent ST-T wave inversions, particularly in leads V1 to V3 (61–64); left bundle branch block, bifascicular block, second- or third-degree atrioventricular block, atrial fibrillation, or ventricular tachyarrhythmia (65); or LV hypertrophy (62, 66). Patients with stable IHD who have the following abnormalities on chest radiography have a worse prognosis: cardiomegaly, LV aneurysm, pulmonary venous congestion, or left atrial enlargement.

## **Risk Stratification With Imaging Studies to Assess LV Function (Echocardiography/Radionuclide Imaging)**

Rest echocardiography is of little value in assessing risk among patients with stable IHD who have a low likelihood of abnormal LV function, but it can be useful when symptoms or signs suggest heart failure (67). In addition, echocardiography can identify aortic valve disease, an LV aneurysm, and an LV thrombus (68) and can measure pulmonary artery pressure, LV mass, and ratio of wall thickness to chamber radius (69–77). Daly and colleagues (55) reported an index to estimate risk for death or nonfatal acute MI derived from data on an international sample of approximately 3000 patients presenting with angina and followed for 18 months. Components of this score include coexisting diabetes or other medical conditions, severity of angina, LV function, and ECG findings.

Although radionuclide imaging accurately measures ejection fraction, it does not provide information on diastolic or valvular function and requires exposure to ionizing radiation (78, 79). Although CMR is less widely applied, it also accurately measures LV performance and images myocardial and valvular structures (80). Cardiac CT also provides high-resolution detection of cardiac structures and ejection fraction, but all 3 tests are generally more expensive than resting ECG.

## **Risk Stratification Using Stress Testing**

Patients with known stable IHD should undergo noninvasive testing to assess their risk for future cardiac events unless there are contraindications to testing. The initial test can be a functional test, such as exercise ECG or a stress imaging test, or a structural test, such as CT angiography. The type of stress used with a functional test can be exercise or pharmacologic, and stress imaging can be performed with echocardiography, radionuclide myocardial perfusion study imaging, or magnetic resonance imaging. The choice of test is important because different tests have different diagnostic performance characteristics and provide different kinds of information (81–92). The main factors that should influence this choice are the patient's ability to exercise and interpretability of the resting ECG results. In general, when feasible, an exercise stress test should be performed rather than a test with pharmacologic stress because exercise capacity provides an objective assessment of functional capacity that correlates with activities of daily living. The price of the test is a less important factor because in many settings, reimbursement for these tests has become similar to remove potential financial incentives for performing a more expensive test.

Exercise ECG is recommended for patients who are able to exercise to an adequate workload and in whom ECG results can be interpreted during exercise (81–92). The occurrence of ST-segment depression at a reduced workload or persisting into recovery coupled with exertional symptoms is associated with a high risk for cardiovascular death (93). Other prognostic factors include low exercise capacity (generally defined as less than stage II of the Bruce protocol or  $\leq 20\%$  age- and sex-predicted values) (94), failure to increase systolic blood pressure to  $> 120$  mm Hg or a sustained  $> 10$  mm Hg drop during exercise, ST-segment elevation (excluding aortic valve replacement or leads showing a

resting Q wave), complex ventricular ectopy or arrhythmias during stress or recovery, and delayed heart rate recovery (for example, reduction of  $< 10$  or 12 beats/min in the first minute) (95) (95). It should be noted that the inability to perform an exercise test is itself a strong negative prognostic factor.

Whenever possible,  $\beta$ -blockers (and other anti-ischemic drugs) should be withheld for 4 to 5 half-lives (usually about 48 hours) before exercise stress testing for the diagnosis or initial risk stratification of patients suspected of having IHD. Ideally, these drugs should be tapered to avoid withdrawal that may precipitate events (96, 97). When stopping  $\beta$ -blockers poses a hazard to patients, stress testing on  $\beta$ -blockers may still detect myocardial ischemia, particularly in patients at highest risk. Although the test will be less reliable, the result will usually still be positive.

The Duke treadmill score remains the most widely used method to assess risk and prognosis (98, 99). This score is calculated as the exercise time in minutes minus ( $5 \times$  ST-segment deviation, during or after exercise, in millimeters) minus (0 if there is no angina, 4 if angina occurs, and 8 if angina is the reason for stopping the test). Among outpatients suspected of having IHD, the two thirds of patients with scores indicating low risk had an average annual mortality rate of 0.25%, and the 4% who had scores indicating high risk had an average annual mortality rate of 5%. The score works well for both inpatients and outpatients, and preliminary data suggest that it works equally well for men and women. However, the evidence is limited for elderly patients. Lauer and colleagues (100) developed a risk index incorporating variables from the history and exercise test using data from more than 32 000 individuals suspected of having IHD that was better able to identify those who had a low risk for death than was the Duke treadmill score.

Although for the reasons cited, exercise ECG remains the first-line test for risk assessment, stress nuclear myocardial perfusion imaging and stress echocardiography can provide prognostic information that is incremental to the clinical assessment (101–106). The addition of imaging is indicated for patients who have an uninterpretable result on baseline ECG (including left bundle branch block or ventricular pacing, LV hypertrophy, use of digitalis, resting ST-segment abnormality, or preexcitation syndromes) and may be of value in patients with an equivocal exercise or intermediate Duke treadmill score (107–109). The most commonly used tracers for myocardial perfusion imaging are 201-thallium and 99m-technetium, including the technetium-labeled agent sestamibi with multiple tomographic slices in 3 planes. Both men and women who have a normal or mildly abnormal result on exercise myocardial perfusion study or exercise stress echocardiography during which they achieve the age-predicted target heart rate have an annual risk for cardiac death and acute MI that is less than 1% (that is, approximating the risk in the general population) and a similarly low likelihood of worsening clinical status or referral for coronary revascularization. The length of time a patient remains at low risk depends on age, sex, and presence of other risk factors, such as diabetes. Moderate to severe abnormalities (such as abnormal wall motion in  $\geq 4$  segments or multivessel perfusion defects) predict an annual risk for cardiovascular death or MI rates of 5% or higher (that is, a 6- to

10-fold higher risk than for patients with a normal result) (101, 110–112).

In one third to one half of patients who undergo risk assessment, exercise stress is not recommended because of an inability to exercise or an abnormal result on ECG. For these patients, use of a pharmacologic stressor with imaging is helpful. Nuclear myocardial perfusion imaging with a vasodilator (dipyridamole, adenosine, or regadenoson) as the stressor accurately assesses the risk for subsequent events in patients with stable IHD; an annualized event rate of 1.6% was observed in patients with a normal study result compared with 10.6% in patients with a severely abnormal result (summed stress score  $\geq 13$ ) (113). Because of greater comorbidity in patients who cannot exercise, however, the annualized event rate of patients with a normal pharmacologic stress perfusion result is about double that of patients with a normal exercise stress result after adjustment for age and comorbidity (114). Similarly, stress echocardiography with dobutamine accurately classifies patients into high- and low-risk categories. A normal dobutamine echocardiogram is associated with a risk for an adverse cardiac event of 1% to 2% (106, 115). Classification as high risk is most reliable when ischemia is detected in the territory of the left anterior descending artery and is somewhat less reliable in patients with diabetes (116).

It is important to recognize that when relatively extensive ischemia is detected by stress imaging ( $\geq 10\%$ ), there is no evidence that early revascularization improves prognosis even in patients with diabetes or ventricular dysfunction (117). More studies are needed to evaluate the benefits of using stress imaging in patients at low risk for coronary events.

Stress CMR using a variety of techniques can provide accurate prognostic information. On the basis of a meta-analysis of 16 single-site studies involving 7200 patients, a normal result on stress CMR with vasodilator myocardial perfusion or inotropic stress cine imaging is associated with an annual rate of cardiac death or MI ranging from 0.01% to 0.6% (118, 119). Evidence of ischemia is associated with an elevated risk for cardiac death or MI (hazard ratio, 2.2 to 12) (52, 120). The emerging nature of data on diagnostic performance, limited availability, heterogeneity of imaging techniques and equipment, evolution of interpretative standards, and higher cost are all reasons that this test is not recommended for routine use.

Cardiac CT angiography identifies anatomical stenosis rather than ischemia but still appears to provide useful prognostic information. The finding of nonobstructive CAD supplements clinical information in predicting risk for death (121). For example, 20% to 25% of patients with an intermediate pretest likelihood of risk (1% to 3% annual mortality) based on clinical information were reassigned to a different risk category using information from cardiac CT angiography. At present, no conclusive data show that CT angiography results in better clinical outcomes than standard exercise testing or imaging methods.

### **Coronary Angiography**

Coronary angiography provides information about the extent of obstructive CAD in order to assess a patient's risk and potentially determine the feasibility and appropriateness of revascularization.

Information obtained includes location, length, diameter, and contour of the epicardial coronary arteries; presence and severity of coronary luminal obstruction(s); characterization of the nature of the obstruction; presence and extent of collateral flow; and assessment of coronary blood flow. Despite the availability of such modalities as CT angiography, magnetic resonance imaging, and positron emission tomography, coronary angiography remains the gold standard because there is scant evidence that information provided by these newer tests improves management or reduces the use of angiography.

In patients who have a high risk for coronary events or death on the basis of clinical data and noninvasive testing, coronary angiography can be considered to provide a more thorough risk assessment even though cardiac symptoms may not be severe. Patients with stable IHD who have survived sudden cardiac death, those with serious ventricular arrhythmias, and those who develop signs and symptoms of heart failure should undergo coronary angiography to assess cardiac risk (122–127). Among patients who are not at high risk for death due to IHD, those with an unsatisfactory quality of life due to anginal symptoms despite a regimen of guideline-directed medical therapy may also benefit from coronary angiography to determine whether they are candidates for revascularization for the purpose of relieving symptoms (117, 128).

Coronary angiography also has many limitations in addition to being invasive, risky, and expensive. These include variable reliability in interpretation issues due to technical quality (129) and interobserver reliability. As an anatomical test, angiography alone in isolation is not a reliable indicator of the functional significance of a given coronary stenosis because it provides only direct anatomical data. It cannot be used to accurately distinguish between plaques that are relatively stable and those that pose an imminent risk for rupture and precipitation of an acute coronary syndrome.

### **Summary**

Physicians should integrate the information from their clinical evaluation and model predictions and combine them with patient preferences when making decisions about further testing. Two patients with the same pretest probability of CAD may prefer different approaches because of variations in personal beliefs, economic considerations, or stage of life. A resting ECG helps in assessing the prognosis of stable IHD. Rest echocardiography and radionuclide imaging are helpful in patients with clinically evident ventricular dysfunction. Stress testing is indicated in most symptomatic patients suspected or known to have CAD to identify patients at very high risk for death or MI who might have lesions for which anatomical intervention might be beneficial. See **Figure 1** in the Executive Summary for an algorithm on the diagnosis of patients suspected of having IHD and **Figure 2** in the Executive Summary for an algorithm on risk assessment in patients with stable IHD.

### **Recommendations**

The recommendations were jointly developed by ACP, ACCF, AHA, AATS, PCNA, and STS; however, ACP translated the ACCF/AHA guideline and recommendation grading system

into ACP's guideline grading system (Tables 1 and 2, in the Executive Summary).

#### **Initial Cardiac Testing to Establish Diagnosis of IHD**

**Recommendation 1:** The organizations recommend that patients with chest pain should receive a thorough history and physical examination to assess the probability of IHD prior to additional testing (Grade: strong recommendation; low-quality evidence).

**Recommendation 2:** The organizations recommend that choices regarding diagnostic and therapeutic options should be made through a process of shared decision making involving the patient and provider, explaining information about risks, benefits, and costs to the patient (Grade: strong recommendation; low-quality evidence).

**Recommendation 3:** The organizations recommend that patients who present with acute angina must be categorized as stable or unstable; patients with unstable angina should be further categorized as high, moderate, or low risk (Grade: strong recommendation; low-quality evidence).

**Recommendation 4:** The organizations recommend a resting electrocardiography (ECG) in patients without an obvious noncardiac cause of chest pain for risk assessment (Grade: strong recommendation; moderate-quality evidence).

**Recommendation 5:** The organizations recommend standard exercise ECG for initial diagnosis in patients with an intermediate pretest probability of IHD who have an interpretable ECG and at least moderate physical functioning or no disabling comorbidity (Grade: strong recommendation; high-quality evidence).

**Recommendation 6:** The organizations recommend that exercise stress with radionuclide myocardial perfusion imaging or echocardiography should be used for patients with an intermediate to high pretest probability of IHD that have an uninterpretable ECG and at least moderate physical functioning or no disabling comorbidity (Grade: strong recommendation; moderate-quality evidence).

**Recommendation 7:** The organizations recommend that pharmacologic stress with radionuclide myocardial perfusion imaging, echocardiography, or cardiac magnetic resonance imaging should not be used for patients who have an interpretable ECG and at least moderate physical functioning or no disabling comorbidity (Grade: strong recommendation; low-quality evidence).

**Recommendation 8:** The organizations recommend that exercise stress with nuclear myocardial perfusion imaging should not be used as an initial test in low-risk patients who have an interpretable ECG and at least moderate physical functioning or no disabling comorbidity (Grade: strong recommendation; low-quality evidence).

**Recommendation 9:** The organizations recommend pharmacologic stress with radionuclide myocardial perfusion imaging or echocardiography for patients with an intermediate to high pretest probability of IHD who are incapable of at least moderate physical functioning or with disabling comorbidity (Grade: strong recommendation; moderate-quality evidence).

**Recommendation 10:** The organizations recommend that standard exercise ECG testing should not be used for patients that have an uninterpretable ECG or are incapable of at least moderate physical functioning or with disabling comorbidity (Grade: strong recommendation; low-quality evidence).

**Recommendation 11:** The organizations recommend assessing resting left ventricular systolic and diastolic ventricular function and evaluating for abnormalities of myocardium, heart valves, or pericardium using Doppler echocardiography in patients with known or suspected IHD and a prior myocardial infarction, pathologic Q waves, symptoms or signs suggestive of heart failure, complex ventricular arrhythmias, or an undiagnosed heart murmur (Grade: strong recommendation; moderate-quality evidence).

**Recommendation 12:** The organizations recommend that echocardiography, radionuclide imaging, cardiac magnetic resonance imaging, or cardiac computed tomography should not be used for routine assessment of left ventricular function in patients with a normal ECG, no history of myocardial infarction, no symptoms or signs suggestive of heart failure, and no complex ventricular arrhythmias (Grade: strong recommendation; low-quality evidence).

**Recommendation 13:** The organizations recommend that routine reassessment (<1 year) of left ventricular function using technologies such as echocardiography, radionuclide imaging, cardiac magnetic resonance imaging, or cardiac computed tomography should not be used in patients with no change in clinical status and for whom no change in therapy is contemplated (Grade: strong recommendation; low-quality evidence).

#### **Cardiac Stress Testing to Assess Risk in Patients With Known Stable IHD Who Are Able to Exercise**

**Recommendation 14:** The organizations recommend standard exercise ECG testing for risk assessment in patients who are able to exercise to an adequate workload and have an ECG that can be interpreted during exercise (Grade: strong recommendation; moderate-quality evidence).

**Recommendation 15:** The organizations recommend the addition of either radionuclide myocardial perfusion imaging or echocardiography to standard exercise ECG testing for risk assessment in patients with stable IHD who are able to exercise to an adequate workload but have an uninterpretable ECG not due to left bundle branch block or ventricular pacing (Grade: strong recommendation; moderate-quality evidence).

**Recommendation 16:** The organizations recommend that pharmacologic stress imaging (radionuclide myocardial perfusion imaging, echocardiography, cardiac magnetic resonance imaging) or cardiac computed tomography angiography should not be used for risk assessment in patients with stable IHD who are able to exercise to an adequate workload and have an interpretable ECG (Grade: strong recommendation; low-quality evidence).

#### **Cardiac Stress Testing to Assess Risk in Patients With Known Stable IHD Who Are Unable to Exercise**

**Recommendation 17:** The organizations recommend pharmacologic stress with either radionuclide myocardial perfusion imaging or echocardiography for risk assessment in patients who are unable to exercise to an adequate workload regardless of interpretability of ECG (Grade: strong recommendation; moderate-quality evidence).

## **Cardiac Stress Testing to Assess Risk in Patients With Stable IHD Regardless of Ability to Exercise**

**Recommendation 18:** The organizations recommend pharmacologic stress with either radionuclide myocardial perfusion imaging or echocardiography for risk assessment in patients with stable IHD who have left bundle branch block on ECG, regardless of ability to exercise to an adequate workload (Grade: strong recommendation; moderate-quality evidence).

**Recommendation 19:** The organizations recommend either exercise or pharmacological stress with imaging (radionuclide myocardial perfusion imaging, echocardiography, or cardiac magnetic resonance) for risk assessment in patients being considered for revascularization of known coronary stenosis of unclear physiologic significance (Grade: strong recommendation; moderate-quality evidence).

**Recommendation 20:** The organizations recommend that *a* more than 1 stress imaging study or *b* a stress imaging study and cardiac computed tomography angiography at the same time should not be used for risk assessment in patients with stable IHD (Grade: strong recommendation; low-quality evidence).

## **Coronary Angiography as an Initial Testing Strategy to Assess Risk in Patients With Stable IHD**

**Recommendation 21:** The organizations recommend that patients with stable IHD who have survived sudden cardiac death or potentially life-threatening ventricular arrhythmia undergo coronary angiography to assess cardiac risk (Grade: strong recommendation; moderate quality-evidence).

**Recommendation 22:** The organizations recommend that patients with stable IHD who develop symptoms and signs of heart failure should be evaluated to determine whether coronary angiography should be performed for risk assessment (Grade: strong recommendation; moderate quality-evidence).

**Recommendation 23:** The organizations recommend that patients with stable IHD and clinical characteristics that indicate a high likelihood of severe IHD should undergo coronary angiography to assess cardiac risk (Grade: strong recommendation; low-quality evidence).

## **Coronary Angiography to Assess Risk After Initial Workup With Noninvasive Testing**

**Recommendation 24:** The organizations recommend that coronary arteriography should be used for risk assessment in patients with stable IHD whose clinical characteristics and results of noninvasive testing indicate a high likelihood of severe IHD and when the benefits are deemed to exceed risk (Grade: strong recommendation; low-quality evidence).

**Recommendation 25:** The organizations recommend that coronary angiography for risk assessment should not be utilized for stable IHD patients who elect not to undergo revascularization or who are not candidates for revascularization based on comorbidities or individual preferences (Grade: strong recommendation; moderate-quality evidence).

**Recommendation 26:** The organizations recommend that coronary angiography should not be used to further assess risk in patients

with stable IHD who have preserved left ventricular function (ejection fraction >50%) and low-risk criteria on noninvasive testing (Grade: strong recommendation; moderate-quality evidence).

**Recommendation 27:** The organizations recommend that coronary angiography should not be used to assess risk in patients who are at low risk based upon clinical criteria and who have not undergone noninvasive risk testing (Grade: strong recommendation; low-quality evidence).

**Recommendation 28:** The organizations recommend that coronary angiography should not be used to assess risk in asymptomatic patients with no evidence of ischemia on noninvasive testing (Grade: strong recommendation; low-quality evidence).

## **APPENDIX REFERENCES**

4. Mensah GA, Brown DW. An overview of cardiovascular disease burden in the United States. *Health Aff.* 2007;26:38-48.
5. Murphy S, Xu J, Kochanek K. Deaths: preliminary data for 2010. *Natl Vital Stat Rep.* 2012;60:1-60.
6. Centers for Medicare & Medicaid Services. Medicare & Medicaid Statistical Supplement. 2008. Accessed at [www.cms.gov/Research-Statistics-Data-and-Systems/Statistics-Trends-and-Reports/MedicareMedicaidStatSupp/2008.html](http://www.cms.gov/Research-Statistics-Data-and-Systems/Statistics-Trends-and-Reports/MedicareMedicaidStatSupp/2008.html) on August 30, 2012
7. Qaseem A, Fihn SD, Dallas P, Williams S, Owens DK, Shekelle P; for the Clinical Guidelines Committee of the American College of Physicians. Management of stable ischemic heart disease: summary of a clinical practice guideline from the American College of Physicians/American College of Cardiology Foundation/American Heart Association/American Association for Thoracic Surgery/Preventive Cardiovascular Nurses Association/Society of Thoracic Surgeons. *Ann Intern Med.* 2012;157:735-43.
8. Fihn SD, Gardin JM, Abrams J, Berra K, Blankenship JC, Dallas P, et al. 2012 ACCF/AHA/AATS/PCNA/SCAI/STS guideline for the diagnosis and management of patients with stable ischemic heart disease: a report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines, and the American College of Physicians, American Association for Thoracic Surgery, Preventive Cardiovascular Nurses Association, Society for Cardiovascular Angiography and Interventions, and Society of Thoracic Surgeons. *J Am Coll Cardiol.* 2012. [Forthcoming].
9. Braunwald E, Mark D, Jones RH. Unstable angina: diagnosis and management. Clinical Practice Guideline Number 10. Rockville, MD: Agency for Health Care Policy and Research and the National Heart, Lung, and Blood Institute, Public Health Service, U.S. Department of Health and Human Services; 1994.
10. Campeau L. Letter: Grading of angina pectoris. *Circulation.* 1976;54:522-3. [PMID: 947585]
11. Gibbons RJ, Abrams J, Chatterjee K, Daley J, Deedwania PC, Douglas JS, et al; American College of Cardiology. ACC/AHA 2002 guideline update for the management of patients with chronic stable angina—summary article: a report of the American College of Cardiology/American Heart Association Task Force on practice guidelines (Committee on the Management of Patients With Chronic Stable Angina). *J Am Coll Cardiol.* 2003;41:159-68. [PMID: 12570960]
12. Knochel JP, Beisel WR, Herndon EG, Jr., Gerard ES, Barry KG. The renal, cardiovascular, hematologic and serum electrolyte abnormalities of heat stroke. *Am J Med.* 1961;30:299-309. [PMID: 13757159]
13. Diamond GA, Forrester JS. Analysis of probability as an aid in the clinical diagnosis of coronary-artery disease. *N Engl J Med.* 1979;300:1350-8. [PMID: 440357]
14. Chaitman BR, Bourassa MG, Davis K, Rogers WJ, Tyras DH, Berger R, et al. Angiographic prevalence of high-risk coronary artery disease in patient subsets (CASS). *Circulation.* 1981;64:360-7. [PMID: 7249303]
15. Diamond GA, Forrester JS. Analysis of probability as an aid in the clinical diagnosis of coronary-artery disease. *N Engl J Med.* 1979;300:1350-8. [PMID: 440357]
16. Pryor DB, Shaw L, McCants CB, Lee KL, Mark DB, Harrell FE Jr, et al. Value of the history and physical in identifying patients at increased risk for coronary artery disease. *Ann Intern Med.* 1993;118:81-90. [PMID: 8416322]

17. Diamond GA, Forrester JS, Hirsch M, Staniloff HM, Vas R, Berman DS, et al. Application of conditional probability analysis to the clinical diagnosis of coronary artery disease. *J Clin Invest.* 1980;65:1210-21. [PMID: 6767741]
18. Goldman L, Cook EF, Mitchell N, Flatley M, Sherman H, Rosati R, et al. Incremental value of the exercise test for diagnosing the presence or absence of coronary artery disease. *Circulation.* 1982;66:945-53. [PMID: 7127706]
19. Melin JA, Wijns W, Vanbutsele RJ, Robert A, De Coster P, Brasseur LA, et al. Alternative diagnostic strategies for coronary artery disease in women: demonstration of the usefulness and efficiency of probability analysis. *Circulation.* 1985;71:535-42. [PMID: 3971524]
20. Morise AP, Diamond GA. Comparison of the sensitivity and specificity of exercise electrocardiography in biased and unbiased populations of men and women. *Am Heart J.* 1995;130:741-7. [PMID: 7572581]
21. Froelicher VF, Lehmann KG, Thomas R, Goldman S, Morrison D, Edson R, et al. The electrocardiographic exercise test in a population with reduced workup bias: diagnostic performance, computerized interpretation, and multivariable prediction. Veterans Affairs Cooperative Study in Health Services #016 (QUEXTA) Study Group. Quantitative Exercise Testing and Angiography. *Ann Intern Med.* 1998;128:965-74. [PMID: 9625682]
22. Braat SH, Brugada P, Bär FW, Gorgels AP, Wellens HJ. Thallium-201 exercise scintigraphy and left bundle branch block. *Am J Cardiol.* 1985;55:224-6. [PMID: 3966386]
23. DePuey EG, Guertler-Krawczynska E, Robbins WL. Thallium-201 SPECT in coronary artery disease patients with left bundle branch block. *J Nucl Med.* 1988;29:1479-85. [PMID: 3261782]
24. Hirzel HO, Senn M, Nuesch K, Buettner C, Pfeiffer A, Hess OM, et al. Thallium-201 scintigraphy in complete left bundle branch block. *Am J Cardiol.* 1984;53:764-9. [PMID: 6702625]
25. Burns RJ, Galligan L, Wright LM, Lawand S, Burke RJ, Gladstone PJ. Improved specificity of myocardial thallium-201 single-photon emission computed tomography in patients with left bundle branch block by dipyridamole. *Am J Cardiol.* 1991;68:504-8. [PMID: 1872279]
26. Jukema JW, van der Wall EE, van der Vis-Melsen MJ, Kruyswijk HH, Bruschke AV. Dipyridamole thallium-201 scintigraphy for improved detection of left anterior descending coronary artery stenosis in patients with left bundle branch block. *Eur Heart J.* 1993;14:53-6. [PMID: 8432292]
27. Larcos G, Brown ML, Gibbons RJ. Role of dipyridamole thallium-201 imaging in left bundle branch block. *Am J Cardiol.* 1991;68:1097-8. [PMID: 1927927]
28. Lebthai NE, Stauffer JC, Delaloye AB. Left bundle branch block and coronary artery disease: accuracy of dipyridamole thallium-201 single-photon emission computed tomography in patients with exercise anteroseptal perfusion defects. *J Nucl Cardiol.* 1997;4:266-73. [PMID: 9278872]
29. Morais J, Soucy JP, Sestier F, Lamoureux F, Lamoureux J, Danais S. Dipyridamole testing compared to exercise stress for thallium-201 imaging in patients with left bundle branch block. *Can J Cardiol.* 1990;6:5-8. [PMID: 2310995]
30. O'Keefe JH Jr, Bateman TM, Barnhart CS. Adenosine thallium-201 is superior to exercise thallium-201 for detecting coronary artery disease in patients with left bundle branch block. *J Am Coll Cardiol.* 1993;21:1332-8. [PMID: 8473638]
31. Patel R, Bushnell DL, Wagner R, Stumbbris R. Frequency of false-positive septal defects on adenosine/201Tl images in patients with left bundle branch block. *Nucl Med Commun.* 1995;16:137-9. [PMID: 7770235]
32. Rockett JE, Wood WC, Moinuddin M, Loveless V, Parrish B. Intravenous dipyridamole thallium-201 SPECT imaging in patients with left bundle branch block. *Clin Nucl Med.* 1990;15:401-7. [PMID: 2354579]
33. Vaduganathan P, He ZX, Raghavan C, Mahmarian JJ, Verani MS. Detection of left anterior descending coronary artery stenosis in patients with left bundle branch block: exercise, adenosine or dobutamine imaging? *J Am Coll Cardiol.* 1996;28:543-50. [PMID: 8772737]
34. Schuijff JD, Bax JJ, Shaw LJ, de Roos A, Lamb HJ, van der Wall EE, et al. Meta-analysis of comparative diagnostic performance of magnetic resonance imaging and multislice computed tomography for noninvasive coronary angiography. *Am Heart J.* 2006;151:404-11. [PMID: 16442907]
35. Budoff MJ, Dowe D, Jollis JG, Gitter M, Sutherland J, Halamert E, et al. Diagnostic performance of 64-multidetector row coronary computed tomographic angiography for evaluation of coronary artery stenosis in individuals without known coronary artery disease: results from the prospective multicenter ACCURACY (Assessment by Coronary Computed Tomographic Angiography of Individuals Undergoing Invasive Coronary Angiography) trial. *J Am Coll Cardiol.* 2008;52:1724-32. [PMID: 19007693]
36. Hamon M, Biondi-Zocca GG, Malagutti P, Agostoni P, Morello R, Valgimigli M, et al. Diagnostic performance of multislice spiral computed tomography of coronary arteries as compared with conventional invasive coronary angiography: a meta-analysis. *J Am Coll Cardiol.* 2006;48:1896-910. [PMID: 17084268]
37. Janne d'Othée B, Siebert U, Cury R, Jadvar H, Dunn EJ, Hoffmann U. A systematic review on diagnostic accuracy of CT-based detection of significant coronary artery disease. *Eur J Radiol.* 2008;65:449-61. [PMID: 17590554]
38. Meijboom WB, Meijjs MF, Schuijff JD, Cramer MJ, Mollet NR, van Mieghem CA, et al. Diagnostic accuracy of 64-slice computed tomography coronary angiography: a prospective, multicenter, multivendor study. *J Am Coll Cardiol.* 2008;52:2135-44. [PMID: 19095130]
39. Miller JM, Rochitte CE, Dewey M, Arbab-Zadeh A, Niiuma H, Gottlieb I, et al. Diagnostic performance of coronary angiography by 64-row CT. *N Engl J Med.* 2008;359:2324-36. [PMID: 19038879]
40. Schuetz GM, Zacharopoulou NM, Schlattmann P, Dewey M. Meta-analysis: noninvasive coronary angiography using computed tomography versus magnetic resonance imaging. *Ann Intern Med.* 2010;152:167-77. [PMID: 20124233]
41. Stein PD, Beemath A, Kayali F, Skaf E, Sanchez J, Olson RE. Multidetector computed tomography for the diagnosis of coronary artery disease: a systematic review. *Am J Med.* 2006;119:203-16. [PMID: 16490463]
42. Sun Z, Jiang W. Diagnostic value of multislice computed tomography angiography in coronary artery disease: a meta-analysis. *Eur J Radiol.* 2006;60:279-86. [PMID: 16887313]
43. Min JK, Shaw LJ, Berman DS. The present state of coronary computed tomography angiography a process in evolution. *J Am Coll Cardiol.* 2010;55: 957-65. [PMID: 20202511]
44. O'Rourke RA, Brundage BH, Froelicher VF, Greenland P, Grundy SM, Hachamovitch R, et al. American College of Cardiology/American Heart Association Expert Consensus Document on electron-beam computed tomography for the diagnosis and prognosis of coronary artery disease. *J Am Coll Cardiol.* 2000;36:326-40. [PMID: 10898458]
45. Akram K, O'Donnell RE, King S, Superko HR, Agatston A, Voros S. Influence of symptomatic status on the prevalence of obstructive coronary artery disease in patients with zero calcium score. *Atherosclerosis.* 2009;203:533-7. [PMID: 18774135]
46. Cademartiri F, Maffei E, Palumbo A, Martini C, Seitun S, Tedeschi C, et al. Diagnostic accuracy of computed tomography coronary angiography in patients with a zero calcium score. *Eur Radiol.* 2010;20:81-7. [PMID: 19657651]
47. Keim RG, Gottlieb EL, Nelson AH, Vogels DS 3rd. 2002 JCO study of orthodontic diagnosis and treatment procedures. Part 2. Breakdowns of selected variables. *J Clin Orthod.* 2002;36:627-36; quiz 637-8. [PMID: 12514853]
48. Haberl R, Tittus J, Böhme E, Czernik A, Richartz BM, Buck J, et al. Multislice spiral computed tomographic angiography of coronary arteries in patients with suspected coronary artery disease: an effective filter before catheter angiography? *Am Heart J.* 2005;149:1112-9. [PMID: 15976796]
49. Henneman MM, Schuijff JD, Pundiuti G, van Werkhoven JM, van der Wall EE, Jukema JW, et al. Noninvasive evaluation with multislice computed tomography in suspected acute coronary syndrome: plaque morphology on multislice computed tomography versus coronary calcium score. *J Am Coll Cardiol.* 2008;52:216-22. [PMID: 18617071]
50. Rubinstein R, Gaspar T, Halon DA, Goldstein J, Peled N, Lewis BS. Prevalence and extent of obstructive coronary artery disease in patients with zero or low calcium score undergoing 64-slice cardiac multidetector computed tomography for evaluation of a chest pain syndrome. *Am J Cardiol.* 2007;99:472-5. [PMID: 17293187]
51. Bodí V, Sanchis J, Lopez-Lereu MP, Nunez J, Mainar L, Monmeneu JV, et al. Prognostic value of dipyridamole stress cardiovascular magnetic resonance imaging in patients with known or suspected coronary artery disease. *J Am Coll Cardiol.* 2007;50:1174-9. [PMID: 17868810]
52. Jahnke C, Nagel E, Gebker R, Kokociński T, Kelle S, Manka R, et al. Prognostic value of cardiac magnetic resonance stress tests: adenosine stress perfusion and dobutamine stress wall motion imaging. *Circulation.* 2007;115:1769-76. [PMID: 17353441]

53. Pryor DB, Shaw L, Harrell FE Jr, Lee KL, Hlatky MA, Mark DB, et al. Estimating the likelihood of severe coronary artery disease. *Am J Med.* 1991;90:553-62. [PMID: 2029012]
54. Hubbard BL, Gibbons RJ, Lapeyre AC 3rd, Zinsmeister AR, Clements IP. Identification of severe coronary artery disease using simple clinical parameters. *Arch Intern Med.* 1992;152:309-12. [PMID: 1739359]
55. Daly CA, De Stavola B, Sendon JL, Tavazzi L, Boersma E, Clemens F, et al; Euro Heart Survey Investigators. Predicting prognosis in stable angina—results from the Euro heart survey of stable angina: prospective observational study. *BMJ.* 2006;332:262-7. [PMID: 1641509]
56. Daly C, Norrie J, Murdoch DL, Ford I, Dargie HJ, Fox K; TIBET (Total Ischaemic Burden European Trial) study group. The value of routine non-invasive tests to predict clinical outcome in stable angina. *Eur Heart J.* 2003;24:532-40. [PMID: 12643886]
57. Hammermeister KE, DeRouen TA, Dodge HT. Variables predictive of survival in patients with coronary disease. Selection by univariate and multivariate analyses from the clinical, electrocardiographic, exercise, arteriographic, and quantitative angiographic evaluations. *Circulation.* 1979;59:421-30. [PMID: 761323]
58. Hemingway H, Shipley M, Christie D, Marmot M. Cardiothoracic ratio and relative heart volume as predictors of coronary heart disease mortality. The Whitehall study 25 year follow-up. *Eur Heart J.* 1998;19:859-69. [PMID: 9651709]
59. Schillinger M, Domanovits H, Paulis M, Niklfardjam M, Meron G, Kurkciyan I, et al. Clinical signs of pulmonary congestion predict outcome in patients with acute chest pain. *Wien Klin Wochenschr.* 2002;114:917-22. [PMID: 12528324]
60. Block WJ Jr, Crumpacker EL, Dry TJ, Gage RP. Prognosis of angina pectoris; observations in 6,882 cases. *J Am Med Assoc.* 1952;150:259-64. [PMID: 14955434]
61. Prospective randomised study of coronary artery bypass surgery in stable angina pectoris. Second interim report by the European Coronary Surgery Study Group. *Lancet.* 1980;2:491-5. [PMID: 6105556]
62. Frank CW, Weinblatt E, Shapiro S. Angina pectoris in men. Prognostic significance of selected medical factors. *Circulation.* 1973;47:509-17. [PMID: 4632503]
63. Murphy ML, Hultgren HN, Detre K, Thomsen J, Takaro T. Treatment of chronic stable angina. A preliminary report of survival data of the randomized Veterans Administration cooperative study. *N Engl J Med.* 1977;297:621-7. [PMID: 331107]
64. Proudfoot WJ, Bruschke AV, MacMillan JP, Williams GW, Sones FM Jr. Fifteen year survival study of patients with obstructive coronary artery disease. *Circulation.* 1983;68:986-97. [PMID: 6604590]
65. Ruberman W, Weinblatt E, Goldberg JD, Frank CW, Shapiro S, Chaudhary BS. Ventricular premature complexes in prognosis of angina. *Circulation.* 1980;61:1172-82. [PMID: 7371129]
66. Detre K, Peduzzi P, Murphy M, Hultgren H, Thomsen J, Oberman A, et al. Effect of bypass surgery on survival in patients in low- and high-risk subgroups delineated by the use of simple clinical variables. *Circulation.* 1981;63:1329-38. [PMID: 6971716]
67. Mock MB, Ringqvist I, Fisher LD, Davis KB, Chaitman BR, Kouchoukos NT, et al. Survival of medically treated patients in the coronary artery surgery study (CASS) registry. *Circulation.* 1982;66:562-8. [PMID: 6980062]
68. Levy D, Garrison RJ, Savage DD, Kannel WB, Castelli WP. Left ventricular mass and incidence of coronary heart disease in an elderly cohort. The Framingham Heart Study. *Ann Intern Med.* 1989;110:101-7. [PMID: 2521199]
69. Gibbons RJ, Balady GJ, Bricker JT, Chaitman BR, Fletcher GF, Froelicher VF, et al; American College of Cardiology/American Heart Association Task Force on Practice Guidelines. Committee to Update the 1997 Exercise Testing Guidelines. ACC/AHA 2002 guideline update for exercise testing: summary article. A report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (Committee to Update the 1997 Exercise Testing Guidelines). *J Am Coll Cardiol.* 2002;40:1531-40. [PMID: 12392846]
70. Badran HM, Elnoamany MF, Seteha M. Tissue velocity imaging with dobutamine stress echocardiography—a quantitative technique for identification of coronary artery disease in patients with left bundle branch block. *J Am Soc Echocardiogr.* 2007;20:820-31. [PMID: 17617308]
71. Hachamovitch R, Berman DS, Kiat H, Cohen I, Friedman JD, Shaw IJ. Value of stress myocardial perfusion single photon emission computed tomography in patients with normal resting electrocardiograms: an evaluation of incremental prognostic value and cost-effectiveness. *Circulation.* 2002;105:823-9. [PMID: 11854122]
72. Johansen A, Høilund-Carlsen PF, Vach W, Christensen HW, Møldrup M, Haghfelt T. Prognostic value of myocardial perfusion imaging in patients with known or suspected stable angina pectoris: evaluation in a setting in which myocardial perfusion imaging did not influence the choice of treatment. *Clin Physiol Funct Imaging.* 2006;26:288-95. [PMID: 16939506]
73. Koren MJ, Devereux RB, Casale PN, Savage DD, Laragh JH. Relation of left ventricular mass and geometry to morbidity and mortality in uncomplicated essential hypertension. *Ann Intern Med.* 1991;114:345-52. [PMID: 1825164]
74. Leischik R, Dworak B, Littwitz H, Güller H. Prognostic significance of exercise stress echocardiography in 3329 outpatients (5-year longitudinal study). *Int J Cardiol.* 2007;119:297-305. [PMID: 17113169]
75. Levy D, Garrison RJ, Savage DD, Kannel WB, Castelli WP. Prognostic implications of echocardiographically determined left ventricular mass in the Framingham Heart Study. *N Engl J Med.* 1990;322:1561-6. [PMID: 2139921]
76. Nagao T, Chikamori T, Hida S, Igarashi Y, Kuwabara Y, Nishimura S, et al; Q-PROVE Study Group. Quantitative gated single-photon emission computed tomography with <sup>99m</sup>Tc sestamibi predicts major cardiac events in elderly patients with known or suspected coronary artery disease: the QGS-Prognostic Value in the Elderly (Q-PROVE) Study. *Circ J.* 2007;71:1029-34. [PMID: 17587706]
77. Smith SC Jr, Feldman TE, Hirshfeld JW Jr, Jacobs AK, Kern MJ, King SB 3rd, et al; American College of Cardiology/American Heart Association Task Force on Practice Guidelines. ACC/AHA/SCAI 2005 guideline update for percutaneous coronary intervention: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (ACC/AHA/SCAI Writing Committee to Update the 2001 Guidelines for Percutaneous Coronary Intervention). *J Am Coll Cardiol.* 2006;47:e1-121. [PMID: 16386656]
78. Hunt SA, Abraham WT, Chin MH, Feldman AM, Francis GS, Ganiats TG, et al. 2009 focused update incorporated into the ACC/AHA 2005 Guidelines for the Diagnosis and Management of Heart Failure in Adults: a report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines: developed in collaboration with the International Society for Heart and Lung Transplantation. *Circulation.* 2009;119:e391-479. [PMID: 19324966]
79. Bello D, Shah DJ, Farah GM, Di Luzio S, Parker M, Johnson MR, et al. Gadolinium cardiovascular magnetic resonance predicts reversible myocardial dysfunction and remodeling in patients with heart failure undergoing beta-blocker therapy. *Circulation.* 2003;108:1945-53. [PMID: 14557364]
80. Epstein FH. MRI of left ventricular function. *J Nucl Cardiol.* 2007;14:729-44. [PMID: 17826327]
81. Christian TF, Miller TD, Bailey KR, Gibbons RJ. Exercise tomographic thallium-201 imaging in patients with severe coronary artery disease and normal electrocardiograms. *Ann Intern Med.* 1994;121:825-32. [PMID: 7794314]
82. Gibbons RJ, Zinsmeister AR, Miller TD, Clements IP. Supine exercise electrocardiography compared with exercise radionuclide angiography in noninvasive identification of severe coronary artery disease. *Ann Intern Med.* 1990;112:743-9. [PMID: 2331118]
83. Hachamovitch R, Hayes SW, Friedman JD, Cohen I, Berman DS. Stress myocardial perfusion single-photon emission computed tomography is clinically effective and cost effective in risk stratification of patients with a high likelihood of coronary artery disease (CAD) but no known CAD. *J Am Coll Cardiol.* 2004;43:200-8. [PMID: 14736438]
84. Ladenheim ML, Kotler TS, Pollock BH, Berman DS, Diamond GA. Incremental prognostic power of clinical history, exercise electrocardiography and myocardial perfusion scintigraphy in suspected coronary artery disease. *Am J Cardiol.* 1987;59:270-7. [PMID: 3812276]
85. Mattera JA, Arain SA, Sinusas AJ, Finta L, Wackers FJ. Exercise testing with myocardial perfusion imaging in patients with normal baseline electrocardiograms: cost savings with a stepwise diagnostic strategy. *J Nucl Cardiol.* 1998;5:498-506. [PMID: 9796897]
86. Mowatt G, Vale L, Brazzelli M, Hernandez R, Murray A, Scott N, et al. Systematic review of the effectiveness and cost-effectiveness, and economic evaluation, of myocardial perfusion scintigraphy for the diagnosis and management of angina and myocardial infarction. *Health Technol Assess.* 2004;8:iii-iv, 1-207. [PMID: 15248938]
87. Nallamothu N, Ghods M, Heo J, Iskandrian AS. Comparison of thallium-201 single-photon emission computed tomography and electrocardiographic re-

- sponse during exercise in patients with normal rest electrocardiographic results. *J Am Coll Cardiol.* 1995;25:830-6. [PMID: 7884084]
88. Sabharwal NK, Stoykova B, Taneja AK, Lahiri A. A randomized trial of exercise treadmill ECG versus stress SPECT myocardial perfusion imaging as an initial diagnostic strategy in stable patients with chest pain and suspected CAD: cost analysis. *J Nucl Cardiol.* 2007;14:174-86. [PMID: 17386379]
  89. Simari RD, Miller TD, Zinsmeister AR, Gibbons RJ. Capabilities of supine exercise electrocardiography versus exercise radionuclide angiography in predicting coronary events. *Am J Cardiol.* 1991;67:573-7. [PMID: 2000789]
  90. Garber AM, Solomon NA. Cost-effectiveness of alternative test strategies for the diagnosis of coronary artery disease. *Ann Intern Med.* 1999;130:719-28. [PMID: 10357690]
  91. Kuntz KM, Fleischmann KE, Hunink MG, Douglas PS. Cost-effectiveness of diagnostic strategies for patients with chest pain. *Ann Intern Med.* 1999;130:709-18. [PMID: 10357689]
  92. Lorenzoni R, Cortigiani L, Magnani M, Desideri A, Bigi R, Manes C, et al. Cost-effectiveness analysis of noninvasive strategies to evaluate patients with chest pain. *J Am Soc Echocardiogr.* 2003;16:1287-91. [PMID: 14652608]
  93. Weiner DA, Ryan TJ, McCabe CH, Chaitman BR, Sheffield LT, Ferguson JC, et al. Prognostic importance of a clinical profile and exercise test in medically treated patients with coronary artery disease. *J Am Coll Cardiol.* 1984;3:772-9. [PMID: 6229569]
  94. Gulati M, Black HR, Shaw LJ, Arnsdorf MF, Merz CN, Lauer MS, et al. The prognostic value of a nomogram for exercise capacity in women. *N Engl J Med.* 2005;353:468-75. [PMID: 16079370]
  95. Cole CR, Blackstone EH, Pashkow FJ, Snader CE, Lauer MS. Heart-rate recovery immediately after exercise as a predictor of mortality. *N Engl J Med.* 1999;341:1351-7. [PMID: 10536127]
  96. Egstrup K. Transient myocardial ischemia after abrupt withdrawal of anti-anginal therapy in chronic stable angina. *Am J Cardiol.* 1988;61:1219-22. [PMID: 2897781]
  97. Psaty BM, Koepsell TD, Wagner EH, LoGerfo JP, Inui TS. The relative risk of incident coronary heart disease associated with recently stopping the use of beta-blockers. *JAMA.* 1990;263:1653-7. [PMID: 1968518]
  98. Mark DB, Hlatky MA, Harrell FE Jr, Lee KL, Califf RM, Pryor DB. Exercise treadmill score for predicting prognosis in coronary artery disease. *Ann Intern Med.* 1987;106:793-800. [PMID: 3579066]
  99. Mark DB, Shaw L, Harrell FE Jr, Hlatky MA, Lee KL, Bengtson 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. [PMID: 1875969]
  100. Lauer MS, Pothier CE, Magid DJ, Smith SS, Kattan MW. An externally validated model for predicting long-term survival after exercise treadmill testing in patients with suspected coronary artery disease and a normal electrocardiogram. *Ann Intern Med.* 2007;147:821-8. [PMID: 18087052]
  101. Shaw LJ, Iskandrian AE. Prognostic value of gated myocardial perfusion SPECT. *J Nucl Cardiol.* 2004;11:171-85. [PMID: 15052249]
  102. McCully RB, Roger VL, Mahoney DW, Burger KN, Click RL, Seward JB, et al. Outcome after abnormal exercise echocardiography for patients with good exercise capacity: prognostic importance of the extent and severity of exercise-related left ventricular dysfunction. *J Am Coll Cardiol.* 2002;39:1345-52. [PMID: 11955853]
  103. Navare SM, Mather JF, Shaw LJ, Fowler MS, Heller GV. Comparison of risk stratification with pharmacologic and exercise stress myocardial perfusion imaging: a meta-analysis. *J Nucl Cardiol.* 2004;11:551-61. [PMID: 15472640]
  104. Hachamovitch R, Hayes S, Friedman JD, Cohen I, Shaw LJ, Germano G, 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. [PMID: 12706929]
  105. Elhendy A, Mahoney DW, Khandheria BK, Paterick TE, Burger KN, Pellikka PA. Prognostic significance of the location of wall motion abnormalities during exercise echocardiography. *J Am Coll Cardiol.* 2002;40:1623-9. [PMID: 12427415]
  106. Marwick TH, Case C, Sawada S, Rimmerman C, Brenneman P, Kovacs R, et al. Prediction of mortality using dobutamine echocardiography. *J Am Coll Cardiol.* 2001;37:754-60. [PMID: 11693748]
  107. Hachamovitch R, Berman DS, Kiat H, Cohen I, Cabico JA, Friedman J, 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. [PMID: 8598081]
  108. Gibbons RJ, Hodge DO, Berman DS, Akinboboye OO, Heo J, Hachamovitch R, et al. Long-term outcome of patients with intermediate-risk exercise electrocardiograms who do not have myocardial perfusion defects on radioisotope imaging. *Circulation.* 1999;100:2140-5. [PMID: 10571972]
  109. Hachamovitch R, Nutter B, Hlatky MA, Shaw LJ, Ridner ML, Dorbala S, et al; SPARC Investigators. Patient management after noninvasive cardiac imaging results from SPARC (Study of myocardial perfusion and coronary anatomy imaging roles in coronary artery disease). *J Am Coll Cardiol.* 2012;59:462-74. [PMID: 22281249]
  110. Hachamovitch R, Berman DS, Shaw LJ, Kiat H, Cohen I, Cabico JA, et al. Incremental prognostic value of myocardial perfusion single photon emission computed tomography for the prediction of cardiac death: differential stratification for risk of cardiac death and myocardial infarction. *Circulation.* 1998;97:535-43. [PMID: 9494023]
  111. Gehi AK, Ali S, Na B, Schiller NB, Whooley MA. Inducible ischemia and the risk of recurrent cardiovascular events in outpatients with stable coronary heart disease: the heart and soul study. *Arch Intern Med.* 2008;168:1423-8. [PMID: 18625923]
  112. Bouzas-Mosquera A, Peteiro J, Alvarez-García N, Broullón FJ, Mosquera VX, García-Bueno L, et al. Prediction of mortality and major cardiac events by exercise echocardiography in patients with normal exercise electrocardiographic testing. *J Am Coll Cardiol.* 2009;53:1981-90. [PMID: 19460612]
  113. Hachamovitch R, Berman DS, Kiat H, Cohen I, Lewin H, Amanullah A, et al. Incremental prognostic value of adenosine stress myocardial perfusion single-photon emission computed tomography and impact on subsequent management in patients with or suspected of having myocardial ischemia. *Am J Cardiol.* 1997;80:426-33. [PMID: 9285653]
  114. Rozanski A, Gransar H, Hayes SW, Friedman JD, Hachamovitch R, Berman DS. Comparison of long-term mortality risk following normal exercise vs adenosine myocardial perfusion SPECT. *J Nucl Cardiol.* 2010;17:999-1008. [PMID: 21076898]
  115. Poldermans D, Fioretti PM, Boersma E, Bax JJ, Thomson IR, Roelandt JR, et al. Long-term prognostic value of dobutamine-atropine stress echocardiography in 1737 patients with known or suspected coronary artery disease: A single-center experience. *Circulation.* 1999;99:757-62. [PMID: 9989960]
  116. Kamlesh M, Matorin R, Sawada S. Prognostic value of a negative stress echocardiographic study in diabetic patients. *Am Heart J.* 2002;143:163-8. [PMID: 11773928]
  117. Shaw LJ, Berman DS, Maron DJ, Mancini GB, Hayes SW, Hartigan PM, et al; COURAGE Investigators. Optimal medical therapy with or without percutaneous coronary intervention to reduce ischemic burden: results from the Clinical Outcomes Utilizing Revascularization and Aggressive Drug Evaluation (COURAGE) trial nuclear substudy. *Circulation.* 2008;117:1283-91. [PMID: 18268144]
  118. Bingham SE, Hachamovitch R. Incremental prognostic significance of combined cardiac magnetic resonance imaging, adenosine stress perfusion, delayed enhancement, and left ventricular function over preimaging information for the prediction of adverse events. *Circulation.* 2011;123:1509-18. [PMID: 21444886]
  119. Korosoglou G, Elhundi Y, Steen H, Schellberg D, Riedle N, Ahrens J, et al. Prognostic value of high-dose dobutamine stress magnetic resonance imaging in 1,493 consecutive patients: assessment of myocardial wall motion and perfusion. *J Am Coll Cardiol.* 2010;56:1225-34. [PMID: 20883929]
  120. Kelle S, Chiribiri A, Vierecke J, Egnell C, Hamdan A, Jahnke C, et al. Long-term prognostic value of dobutamine stress CMR. *JACC Cardiovasc Imaging.* 2011;4:161-72. [PMID: 21329901]
  121. Min JK, Dunning A, Lin FY, Achenbach S, Al-Mallah M, Budoff MJ, et al; CONFIRM Investigators. Age- and sex-related differences in all-cause mortality risk based on coronary computed tomography angiography findings results from the International Multicenter CONFIRM (Coronary CT Angiography Evaluation for Clinical Outcomes: An International Multicenter Registry) of 23,854 patients without known coronary artery disease. *J Am Coll Cardiol.* 2011;58:849-60. [PMID: 21835321]
  122. Survivors of out-of-hospital cardiac arrest with apparently normal heart. Need for definition and standardized clinical evaluation. Consensus Statement of the Joint Steering Committees of the Unexplained Cardiac Arrest Registry of Europe and of the Idiopathic Ventricular Fibrillation Registry of the United States. *Circulation.* 1997;95:265-72. [PMID: 8994445]
  123. Every NR, Fahrenbruch CE, Hallstrom AP, Weaver WD, Cobb LA. Influence of coronary bypass surgery on subsequent outcome of patients resuscitated from out-of-hospital cardiac arrest. *Circulation.* 2000;102:101-6. [PMID: 10702111]

- tated from out of hospital cardiac arrest. *J Am Coll Cardiol.* 1992;19:1435-9. [PMID: 1593036]
124. Spaulding CM, Joly LM, Rosenberg A, Monchi M, Weber SN, Dhainaut JF, et al. Immediate coronary angiography in survivors of out-of-hospital cardiac arrest. *N Engl J Med.* 1997;336:1629-33. [PMID: 9171064]
125. Califf RM, Harrell FE Jr, Lee KL, Rankin JS, Hlatky MA, Mark DB, et al. The evolution of medical and surgical therapy for coronary artery disease. A 15-year perspective. *JAMA.* 1989;261:2077-86. [PMID: 2784512]
126. Myers WO, Schaff HV, Gersh BJ, Fisher LD, Kosinski AS, Mock MB, et al. Improved survival of surgically treated patients with triple vessel coronary artery disease and severe angina pectoris. A report from the Coronary Artery Surgery Study (CASS) registry. *J Thorac Cardiovasc Surg.* 1989;97:487-95. [PMID: 2648078]
127. Myers WO, Gersh BJ, Fisher LD, Mock MB, Holmes DR, Schaff HV, et al. Medical versus early surgical therapy in patients with triple-vessel disease and mild angina pectoris: a CASS registry study of survival. *Ann Thorac Surg.* 1987;44:471-86. [PMID: 3499880]
128. Boden WE, O'Rourke RA, Teo KK, Hartigan PM, Maron DJ, Kostuk WJ, et al; COURAGE Trial Research Group. Optimal medical therapy with or without PCI for stable coronary disease. *N Engl J Med.* 2007;356:1503-16. [PMID: 17387127]
129. Leape LL, Park RE, Bashore TM, Harrison JK, Davidson CJ, Brook RH. Effect of variability in the interpretation of coronary angiograms on the appropriateness of use of coronary revascularization procedures. *Am Heart J.* 2000;139:106-13. [PMID: 10618570]

**Current Author Addresses:** Dr. Qaseem: American College of Physicians, 190 N. Independence Mall West, Philadelphia, PA 19106.  
Dr. Fihn: 1100 Olive Way, Seattle, WA 98101  
Dr. Williams: 423 Guardian Drive, Philadelphia, PA 19104.  
Dr. Dallas: 1906 Bellview Avenue, Roanoke, VA 24014.  
Dr. Owens: 117 Encina Commons, Stanford, CA 94305.  
Dr. Shekelle: 11301 Wilshire Boulevard, Los Angeles, CA 90073.

**Author Contributions:** Conception and design: A. Qaseem, S.D. Fihn, D.K. Owens, P. Shekelle.  
Analysis and interpretation of the data: A. Qaseem, S.D. Fihn, S. Williams, P. Dallas, D.K. Owens.  
Drafting of the article: A. Qaseem, S.D. Fihn, S. Williams, P. Dallas, D.K. Owens.  
Critical revision of the article for important intellectual content: A. Qaseem, S.D. Fihn, S. Williams, P. Dallas, D.K. Owens, P. Shekelle.  
Final approval of the article: A. Qaseem, S.D. Fihn, S. Williams, D.K. Owens, P. Shekelle.  
Statistical expertise: A. Qaseem.  
Administrative, technical, or logistic support: A. Qaseem.  
Collection and assembly of data: A. Qaseem, S.D. Fihn.