Evaluation of Primary Care Patients with Chronic Stable Angina: Guidelines from the American College of Physicians

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In 1999, the American College of Physicians (ACP), then the American College of Physicians–American Society of Internal Medicine, and the American College of Cardiology/American Heart Association (ACC/AHA) developed joint guidelines on the management of patients with chronic stable angina. The ACC/AHA then published an updated guideline in 2002, which the ACP recognized as a scientifically valid review of the evidence and background paper. This ACP guideline summarizes the recommendations of the 2002 ACC/AHA updated guideline and underscores the recommendations most likely to be important to physicians seeing patients in the primary care setting. This guideline is the first of 2 that will provide guidance on the management of patients with chronic stable angina. This document will cover diagnosis and risk stratification for symptomatic patients who have not had an acute myocardial infarction or revascularization procedure in the previous 6 months. Sections addressing asymptomatic patients are also included. *Asymptomatic* refers to patients with known or suspected coronary disease based on history or on electrocardiographic evidence of previous myocardial infarction, coronary angiography, or abnormal results on noninvasive tests. A future guideline will cover pharmacologic therapy and follow-up.

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This guideline is an update of the 1999 guidelines on chronic stable angina, which were published by the American College of Physicians (ACP) (then the American College of Physicians–American Society of Internal Medicine) and the American College of Cardiology/American Heart Association (ACC/AHA) (1). It covers diagnosis and risk stratification for patients with symptomatic chronic stable angina who have not had an acute myocardial infarction (MI) or revascularization procedure in the previous 6 months. Sections addressing asymptomatic patients are also included. *Asymptomatic* refers to patients with known or suspected coronary disease based on history or evidence on electrocardiography (ECG) of previous MI, coronary angiography, or abnormal results on noninvasive tests. This in no way constitutes an endorsement of noninvasive testing in asymptomatic patients for the purposes of "screening" but rather acknowledges the clinical reality that patients often present after having such an evaluation.

The target audience for this guideline is all clinicians who manage patients with chronic stable angina. The target patient population is all persons without known coronary disease whose symptoms suggest chronic stable angina, patients who present with known chronic stable angina, and asymptomatic patients with evidence suggesting coronary disease on previous testing. Chest pain is classified as typical angina, atypical angina, and noncardiac chest pain (**Table 1**). *Angina* is defined as a clinical syndrome characterized by discomfort in the chest, jaw, shoulder, back, or arm. It is typically aggravated by exertion or emotional stress and relieved by nitroglycerin. Angina is further classified as stable or unstable. *Unstable angina* is defined as angina that presents in 1 of 3 principal ways: rest angina, severe new-onset angina, or increasing angina. This guideline does not apply to patients with unstable angina because they have a high to moderate short-term risk for an acute coronary event.

In 2002, the ACC/AHA published an updated guideline, which the ACP recognized as a scientifically valid review of the evidence and background paper (2). This ACP guideline summarizes the recommendations of the 2002 ACC/AHA updated guideline and underscores the recommendations most likely to be important to physicians seeing patients in the primary care setting. For more in-depth analysis, readers should refer to the full-text guideline at www.acc.org/clinical/guidelines/stable/stable.pdf. This guideline is the first of 2 that will provide guidance on the management of patients with chronic stable angina. A future guideline will cover pharmacologic therapy and follow-up.

METHODS

The ACP has traditionally developed evidence-based guidelines. The College bases guideline recommendations on the results of systematic reviews of high-quality evidence (multiple, well-designed randomized, controlled trials) and meta-analyses where appropriate. In the absence of good evidence from randomized trials, the ACP will not

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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 criteria
Noncardiac chest pain Meets 1 or none of the above criteria

* Modified with permission from reference 2.

make recommendations but will underscore practices that are not supported by evidence. Since this document is based on the ACC/AHA guidelines, we have maintained the levels of evidence designated by the ACC/AHA in the recommendation statements: a level A recommendation is based on evidence from multiple randomized clinical trials with large numbers of patients; a level B recommendation is based on evidence from a limited number of randomized trials with small numbers of patients, careful analyses of nonrandomized studies, or observational registries; and a level C recommendation is based on expert consensus.

Diagnosis Using Clinical Variables

For persons with symptoms, the initial clinical evaluation will help to determine whether chest pain is due to coronary artery disease (CAD) or to other causes (**Figure 1**). Descriptive information about the chest pain itself is informative, especially when combined with other historical and diagnostic findings. The following characteristics of chest pain should be determined: quality, location, duration, and the presence of factors that trigger and relieve the pain. In this way, chest pain can be classified as typical or atypical angina (**Table 1**) or noncardiac chest pain. The stability of pain should also be established (stable vs. unstable angina).

In addition, the initial evaluation should include assessment of cardiovascular risk factors, including smoking, hyperlipidemia, diabetes mellitus, hypertension, family history of premature CAD, and postmenopausal status in women. Diabetes is a particularly important risk factor, since patients with diabetes are at high risk not only for macrovascular disease but also for concurrent hypertension and hyperlipidemia.

In addition, in all patients, particularly those with chest pain suggesting typical angina, comorbid conditions that may precipitate "functional" angina should be considered. These consist of conditions that create increased myocardial oxygen demand or decreased myocardial oxygen supply. The former include hyperthyroidism, hyperthermia, cocaine use, valvular disease such as aortic stenosis, and severe uncontrolled hypertension; the latter include anemia, hypoxemia secondary to pulmonary disease, and increased blood viscosity. Other causes of chest pain, such as pericarditis, aortic dissection, pulmonary embolism, and pleuritis, among others, should also be considered in the differential diagnosis.

The Role of Noninvasive Testing in the Diagnosis of CAD

Resting ECG should be performed in all patients with symptoms that suggest angina. However, more than 50% of patients with chronic stable angina have normal results on resting ECG (2). Findings on resting ECG that favor the diagnosis of CAD are evidence of left ventricular hypertrophy or ST-T wave changes consistent with ischemia and evidence of previous Q-wave MI. Abnormalities such as atrial fibrillation, ventricular tachyarrhythmias, left bundle-branch block, bifascicular block (often left anterior fascicular block plus right bundle-branch block), or second- or third-degree atrioventricular block are suggestive but nonspecific indicators of CAD. Chest radiography is not useful for the diagnosis of CAD unless the patient also has signs and symptoms of congestive heart failure, valvular heart disease, or pericardial disease. While severe coronary calcification on chest radiography increases the likelihood of clinically significant CAD, the sensitivity of this finding is only 40% (2).

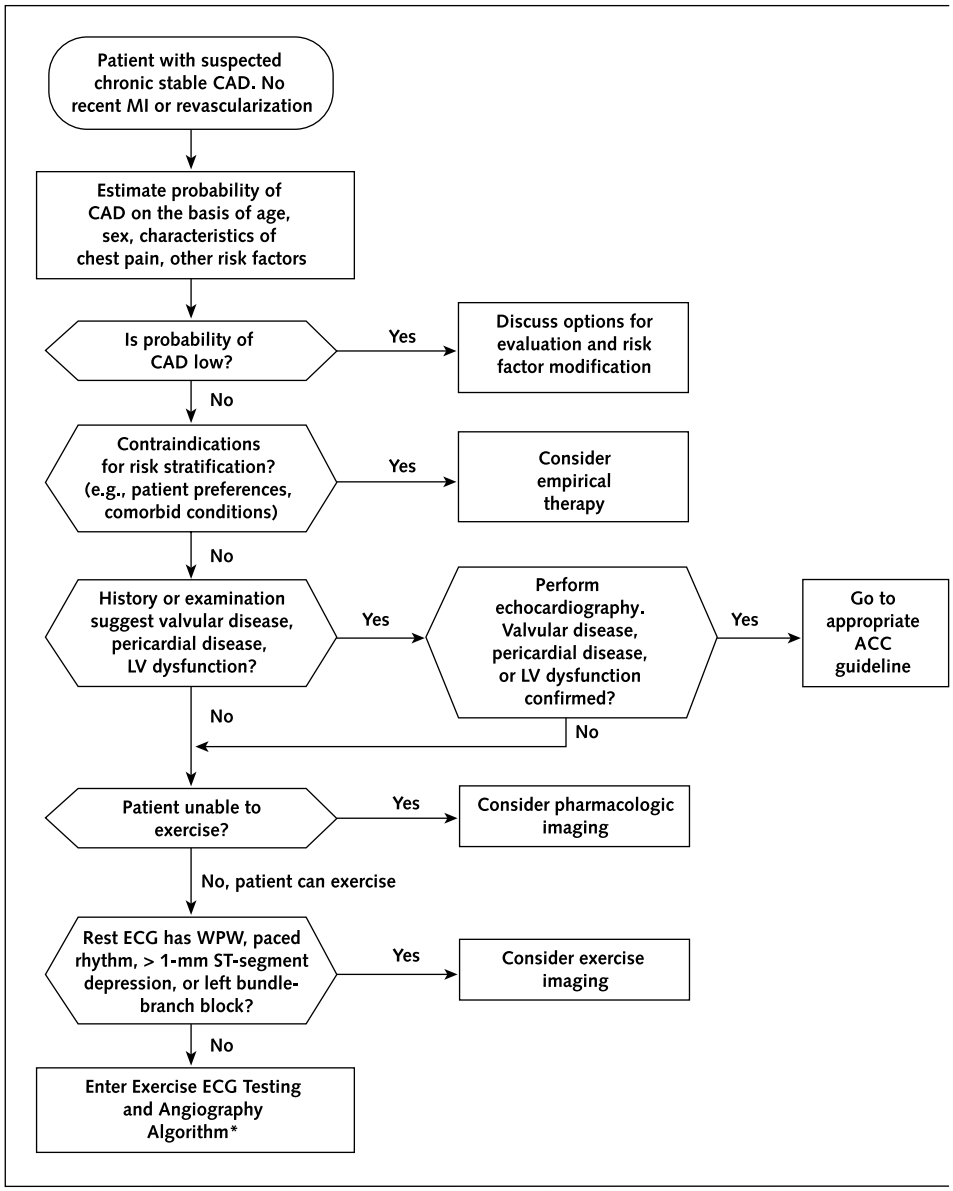
The ACC/AHA does not recommend electron-beam computed tomography, also known as ultra-fast computed tomography, as a screening test for CAD (3). In the ACC/AHA guideline, an analysis of 16 published studies found the pooled sensitivity and specificity of this test to be 90.5% and 49.2%, respectively, in highly selected patients. The weighted average (by sample size) for sensitivity and specificity was 80.4% and 39.9%, respectively, and the positive predictive value ranged from 55% to 84%. Marked variability in repeated measures of coronary calcium by electron-beam computed tomography has also been reported.

Estimating the Probability of Significant CAD

Recommendation 1: In patients presenting with chest pain, the probability of CAD should be estimated on the basis of patient age, sex, cardiovascular risk factors, and pain characteristics (level of evidence: B). Patients with intermediate or high probability should undergo risk stratification through further testing. For patients with a low probability of CAD, the decision to pursue further testing should be based on a shared discussion between the patient and clinician.

Estimating the probability of significant CAD in patients with stable angina is essential because this information guides all further decisions about additional testing and management. However, there is no commonly accepted range for high and low risk. On the basis of expert opinion, cutoff points of less than 10% to 20% and more than 80% to 90% have been recommended for low and high probability, respectively (2). All patients in between these cutoff points can be characterized as having interme-

Figure 1. **Evaluation of suspected coronary artery disease (*CAD*).**



*In unusual circumstances (patients who are survivors of sudden cardiac death, have congestive heart failure, have special occupational requirements, or have stable but severe symptoms and cardiac risk factors), direct referral for cardiac angiography may be appropriate. ACC = American College of Cardiology; ECG = electrocardiogram; LV = left ventricular; MI = myocardial infarction; WPW = Wolff–Parkinson–White syndrome.

diate probability of CAD. Since these cutoff points are not absolute, there is no definite threshold of risk below which no further work-up is warranted. Therefore, the decision to pursue further testing must often incorporate other issues, such as patients' understanding of risk estimates, patients' cultural and personal values, local system-of-care issues, presence of coexisting conditions, and patients' willingness to undergo further diagnostic and treatment strategies.

The probability of CAD can be readily estimated on the basis of the characteristics of the pain and the patients' age and sex (**Table 2**). The presence of risk factors, especially diabetes but also hyperlipidemia and smoking, increases the probability of CAD (**Table 3**). The probabilities

Table 2. **Pretest Likelihood of Coronary Artery Disease in Symptomatic Patients, according to Age and Sex***

Age	Nonanginal Chest Pain		Atypical Angina		Typical Angina	
	Men	Women	Men	Women	Men	Women
y	← % →					
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

* Each value represents the percentage of patients with significant coronary artery disease on catheterization. Modified with permission from reference 2.

Table 3. **Patients with Coronary Artery Disease in University Centers***

Age	Nonanginal Chest Pain				Atypical Angina			
	Men with CAD, without Diabetes, Smoking, or Hyperlipidemia	Men with CAD, with Diabetes, Smoking, or Hyperlipidemia	Women with CAD, without Diabetes, Smoking, or Hyperlipidemia	Women with CAD, with Diabetes, Smoking, or Hyperlipidemia	Men with CAD, without Diabetes, Smoking, or Hyperlipidemia	Men with CAD, with Diabetes, Smoking, or Hyperlipidemia	Women with CAD, without Diabetes, Smoking, or Hyperlipidemia	Women with CAD, with Diabetes, Smoking, or Hyperlipidemia
y	← % →							
35	3	35	1	19	8	59	2	39
45	9	47	2	22	21	70	5	43
55	23	59	4	25	45	79	10	47
65	49	69	9	29	71	86	20	51

* All values refer to patients with normal resting electrocardiogram. Data in table are the percentage of patients presenting to university centers with various types of chest pain syndromes who are found on testing to have coronary artery disease. CAD = coronary artery disease. Modified with permission from reference 4.

for nonanginal chest pain and atypical angina are larger in primary care practice.

Estimating Prognosis on the Basis of Resting Left Ventricular Function

Recommendation 2: The following patients who have chronic stable angina or are asymptomatic should have left ventricular function measured by resting echocardiography or resting radionuclide angiography: patients with a history of MI, patients with pathologic Q waves, patients with symptoms or signs suggestive of heart failure, and patients with complex ventricular arrhythmias (level of evidence for all patients: B).

Most patients undergoing a diagnostic evaluation for angina do not routinely need echocardiography. For risk stratification in a patient with chronic stable angina who has a history of documented MI or Q waves on ECG, measurement of global left ventricular systolic function (that is, ejection fraction) can be important in choosing appropriate medical or surgical therapy and making recommendations about activity level, rehabilitation, and work status (5, 6). In asymptomatic patients with a history of documented MI or Q waves on ECG, measurement of global left ventricular systolic function is also important because it is the strongest predictor of long-term survival. The recommendations listed in this section for symptomatic patients are applicable to asymptomatic patients. A decreased ejection fraction is prognostically important even in the absence of symptoms.

Exercise Testing for Diagnosis and Risk Stratification in Symptomatic Patients with Intermediate to High Probability of CAD

Recommendation 3: Exercise ECG, using the Bruce protocol and Duke treadmill score, should be the initial test for risk stratification in patients with symptomatic chronic stable angina who are able to exercise and are not taking digoxin (level of evidence: B). Exercise ECG testing is also recommended after a significant change in anginal pattern (level of evidence: C). Exercise ECG testing is not recommended when the following confounding factors are found on resting ECG: preexcitation (Wolff–Parkinson–White) syndrome, electronically paced ventricular rhythm, more than 1 mm of ST depression at rest, and complete left bundle-branch block (level of evidence for all factors: B).

Once it has been established that a patient has an intermediate to high probability of CAD, it is essential to determine the risk for subsequent coronary events and death (that is, risk stratification) to select the appropriate additional diagnostic and therapeutic interventions (**Figure 2**). The ACP agrees with the ACC/AHA recommendation that all patients with intermediate to high probability of CAD undergo exercise stress testing to assess risk for future cardiac events, unless they have confounding features on the resting ECG, are taking digoxin, or are unable to exercise.

While several methods are used to score treadmill tests using the Bruce protocol, the Duke treadmill score remains the most validated and generalizable way to assess risk and prognosis (7, 8). The Duke treadmill score equals the exercise time in minutes minus (5 times the ST-segment deviation, during or after exercise, in millimeters) minus 4 if angina occurs and 8 if angina is the reason for stopping the test. Among outpatients with suspected CAD, the 62% who had scores indicating low risk (Duke treadmill score $\geq$ 5) had a 4-year survival rate of 99% (average annual mortality rate, 0.25%). The 4% who had scores indicating high risk (Duke treadmill score ≤ -10) had a 4-year survival rate of 79% (average annual mortality rate, 5%) (**Table 4**). The Duke treadmill score performs well for both inpatients and outpatients, and preliminary data suggest that it is equally effective in men and women (7, 9, 10). Limited data suggest that the score does not work well in elderly persons, particularly those older than 75 years of age (11).

Risk Stratification with Stress Imaging Studies (Radionuclide Angiography and Echocardiography) in Symptomatic Patients

Recommendation 4: For patients with chronic stable angina who are able *to exercise,* do not *have left bundle-branch*

Table 3—**Continued**

Typical Angina			
Men with CAD, without Diabetes, Smoking, or Hyperlipidemia	Men with CAD, with Diabetes, Smoking, or Hyperlipidemia	Women with CAD, without Diabetes, Smoking, or Hyperlipidemia	Women with CAD, with Diabetes, Smoking, or Hyperlipidemia
← % →			
30	88	10	78
51	92	20	79
80	95	38	82
93	97	56	84

block or an electronically paced ventricular rhythm, and have *abnormal results on resting ECG or are using digoxin, exercise perfusion imaging or exercise echocardiography is recommended as the initial test for risk stratification (level of evidence: B).*

Recommendation 5: For patients who are unable *to exercise and* do not *have left bundle-branch block or an electronically paced ventricular rhythm, dipyridamole or adenosine myocardial perfusion imaging (level of evidence: B) or dobutamine echocardiography (level of evidence: B) is recommended as the initial test for risk stratification.*

Recommendation 6: For patients with *left bundle-branch block or electronically paced ventricular rhythm, dipyridamole or adenosine myocardial perfusion imaging is recommended regardless of ability to exercise (level of evidence: B).*

Recommendation 7: For patients with left bundle-branch block or electronically paced ventricular rhythm, exercise or dobutamine echocardiography (level of evidence: C) and exercise myocardial perfusion imaging (level of evidence: C) are not *recommended.*

The ACP agrees with the consensus of the writing committee of the ACC/AHA to recommend the use of stress imaging (not exercise ECG) for risk stratification in the following cases: 1) patients who have had previous cardiac catheterization to identify ischemia in the distribution of a coronary lesion of borderline severity and 2) patients who have had previous revascularization and have a significant change in anginal pattern suggestive of ischemia (level of evidence for both cases: C). The ACP also agrees with the consensus of the writing committee of the ACC/AHA to recommend against the use of any testing (exercise imaging or pharmacologic imaging) for patients with severe comorbid conditions that are likely to limit life expectancy or prevent revascularization (level of evidence: C).

Whenever possible, exercise should be used as the most appropriate form of stress. Exercise imaging testing should be used in patients who are able to exercise but who have confounding factors on their resting ECG or are taking digoxin. For patients who are unable to exercise, however, various types of pharmacologic stress are useful for risk stratification. It is important to note that the inability to perform an exercise test is itself a negative prognostic factor. Cardiac stress imaging consists of echocardiography or myocardial perfusion imaging. In both procedures, images are obtained at rest and during stress. Since the patients cannot exercise, the stress is induced pharmacologically. Dobutamine produces stress through increased cardiac contractility and heart rate, which will provoke wall-motion abnormalities in areas supplied by obstructed arteries. Dipyridamole and adenosine dilate normal coronary arteries more than obstructed ones, producing regional differences in perfusion. The most commonly used tracers for perfusion imaging are ^{201}thallium and ^{99m}technetium (sestamibi and tetrofosmin are technetium-labeled agents). The images are either 3 conventional planar views or multiple tomographic slices in 3 planes (single-photon emission computed tomography, or SPECT).

Normal results on a post-stress thallium scan are highly predictive of an excellent prognosis, even in patients with known coronary disease (12). On the basis of a synthesis of 16 studies involving 3594 patients (13), normal results on stress myocardial perfusion scanning indicate such a low likelihood of significant CAD that coronary arteriography is usually not indicated as a subsequent test. Although the published data are limited, patients with high-risk treadmill scores and normal images appear to be an exception to this rule (13).

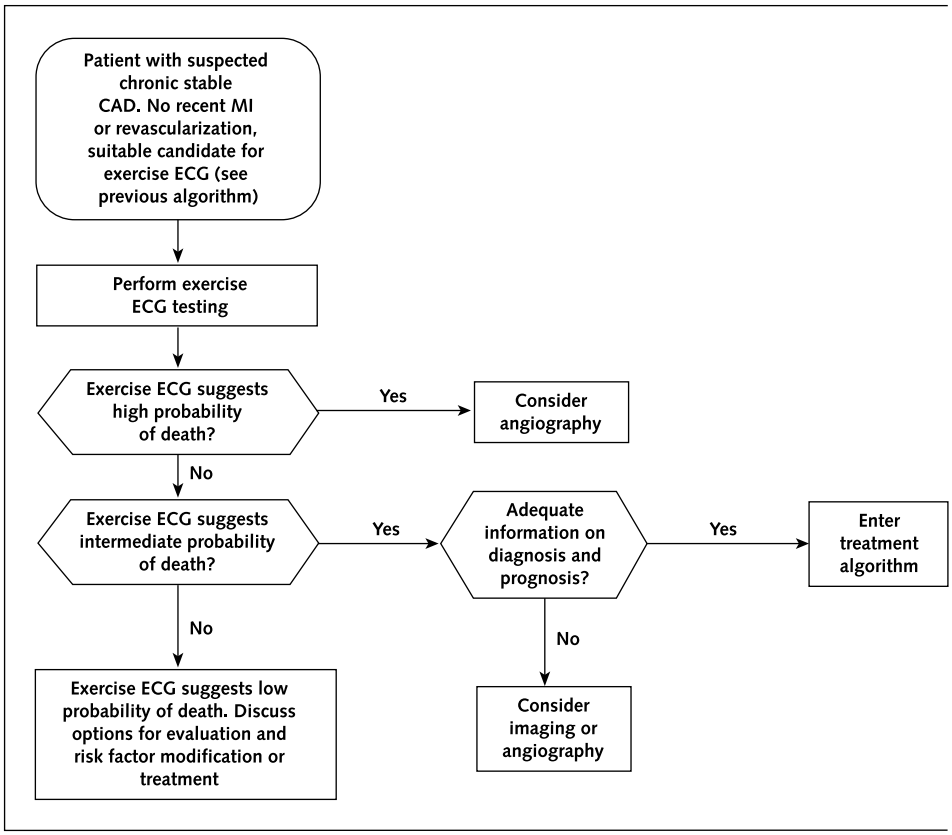
More recently, stress echocardiography has been used to assess patients with chronic stable angina (14). The presence or absence of inducible myocardial wall-motion abnormalities has useful predictive value in patients undergoing exercise or pharmacologic stress echocardiography. Negative results on stress echocardiography also denote a low cardiovascular event rate during follow up (15–23).

Left bundle-branch block, or an electronically paced ventricular rhythm, reduces the accuracy and specificity of exercise myocardial perfusion imaging, exercise echocardiography, and dobutamine echocardiography. Adenosine or dipyridamole myocardial perfusion imaging is preferred in such patients for diagnosis (24–32) and risk stratification (33–36).

Risk Stratification in Asymptomatic Patients

As mentioned previously, the ACC/AHA recommends against "screening" asymptomatic outpatients for coronary disease (3). However, the ACP recognizes the clinical reality that primary care physicians and subspecialists are being consulted by asymptomatic patients who may have been inappropriately screened and present with "abnormal" results on ambulatory ECG monitoring, electron-beam computed tomography, or other tests. Most of the recommendations in this section are based on level C evidence, which denotes expert opinion from the ACC/AHA guideline. As a matter of policy, the ACP seldom makes clinical policy recommendations on the basis of expert opinion. However,

Figure 2. **Algorithm for exercise electrocardiography (*ECG*) and angiography.**



CAD = coronary artery disease; MI = myocardial infarction.

this clinical situation has become a particularly important problem for ACP membership. Therefore, in the absence of any high-grade evidence (level A or B), the ACP has chosen to endorse the recommendations from the ACC/AHA document, which in this case were developed by using expert opinion.

Exercise ECG

Although it is often necessary to assess prognosis in asymptomatic patients who have abnormalities suggestive of CAD on ambulatory ECG monitoring or electron-beam computed tomography, it should be recognized that the risk for adverse cardiovascular events in this group is generally low because they have no symptoms. Moreover, decisions about therapy are not usually influenced by the results of these tests; primary prevention is usually warranted regardless of the test results, and antianginal therapy is not indicated. Thus, the main potential benefit of further testing is to identify the very small proportion of patients whose anatomic and functional characteristics indicate revascularization to prolong survival. In 1 large study dominated by asymptomatic patients, the Duke treadmill score predicted subsequent cardiac events. However, the absolute event rate was low, even in patients with high-risk scores. Patients with low-risk Duke treadmill scores can be reassured about their low risk for subsequent cardiac events. Thus, asymptomatic patients who are able to exercise can usually be evaluated with exercise ECG. In this case, the recommendations for exercise stress testing for risk stratification in asymptomatic patients would be the same as for symptomatic patients and would depend on patients' ability to exercise and the presence of abnormalities on resting ECG (see Recommendations 2 and 3).

Table 4. **Survival according to Risk Groups Based on Duke Treadmill Scores***

Risk Group (Duke Treadmill Score)	Proportion of Total	4-Year Survival Rate	Annual Mortality Rate
	← % →		
Low (≥5)	62	99	0.25
Moderate (−10 to 4)	34	95	1.25
High (<−10)	4	79	5

* Modified with permission from reference 2.

Stress Imaging Studies (Radionuclide Angiography and Echocardiography)

The recommendations for the use of stress imaging (exercise or pharmacologic) in asymptomatic patients with abnormalities on ambulatory ECG monitoring or electron-beam computed tomography are the same as for symptomatic patients. They depend on whether the patient is able

to exercise or whether abnormalities on resting ECG are present. In this case, the ACP recommends, on the basis of the opinion of the ACC/AHA, several options for further workup of asymptomatic patients.

Recommended options for cardiac stress imaging after exercise ECG for risk stratification in asymptomatic patients are as follows. Exercise myocardial perfusion imaging or exercise echocardiography may be performed in asymptomatic patients with an intermediate-risk or high-risk Duke treadmill score on exercise ECG (level of evidence: C). Adenosine or dipyridamole myocardial perfusion imaging or dobutamine echocardiography may be performed in asymptomatic patients with a previously inadequate exercise ECG (level of evidence: C). Asymptomatic patients with a low-risk Duke treadmill score on exercise ECG should not have exercise myocardial perfusion imaging, exercise echocardiography, adenosine or dipyridamole myocardial perfusion imaging, or dobutamine echocardiography (level of evidence: C).

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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.

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