ACC/AHA/ACP–ASIM Guidelines for the Management of Patients With Chronic Stable Angina: Executive Summary and Recommendations

A Report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (Committee on Management of Patients With Chronic Stable Angina)

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I. Introduction

A. Organization of Committee and Evidence Review

The American College of Cardiology/American Heart Association (ACC/AHA) Task Force on Practice Guidelines was formed to make recommendations regarding the diagnosis and treatment of patients with known or suspected cardiovascular disease. Ischemic heart disease is the single leading cause of death in the United States. The most common manifestation of this disease is chronic stable angina. Recognizing the importance of the management of this common entity and the absence of national clinical practice guidelines in this area, the task force formed the Committee on Management of Patients With Chronic Stable Angina to develop guidelines for the management of stable angina. Because this problem is frequently encountered in the practice of internal medicine, the task force invited the American College of Physicians–American Society of Internal Medicine (ACP–ASIM) to serve as a partner in this effort by identifying 3 general internists to serve on the committee.

The guidelines are arbitrarily divided into 4 sections: diagnosis, risk stratification, treatment, and patient follow-up. Experienced clinicians will quickly recognize that the distinctions between these sections may be arbitrary and unrealistic for individual patients. However, for most clinical decision making, these divisions are helpful and facilitate the presentation and analysis of the available evidence. Detailed evidence was developed whenever possible.

The weight of the evidence was ranked highest (A) if the data were derived from multiple randomized clinical trials involving large numbers of patients and intermediate (B) if the data were derived from a limited number of randomized trials involving small numbers of patients or careful analyses of nonrandomized studies or observational registries. A low rank (C) was given when expert consensus was the primary basis for the recommendation.
The customary ACC/AHA classifications I, II, and III are used in tables that summarize both the evidence and expert opinion and provide final recommendations for both patient evaluation and therapy:

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

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

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

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

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

The full text of the guidelines is published in the June 1999 issue of the *Journal of the American College of Cardiology*; the executive summary is published in the June 1, 1999, issue of *Circulation*. This document was approved for publication by the governing bodies of the American College of Cardiology, the American Heart Association, and the American College of Physicians–American Society of Internal Medicine.

### B. Scope of the Guidelines

These guidelines are intended to apply to adult patients with stable chest pain syndromes and known or suspected ischemic heart disease. Patients who have “ischemic equivalents,” such as dyspnea on exertion or arm pain with exertion, are included in these guidelines. Some patients with ischemic heart disease may become asymptomatic with appropriate therapy. As a result, the follow-up sections of the guidelines may apply to patients who were previously symptomatic. However, the diagnosis, risk stratification, and treatment sections of the guidelines are intended to apply to symptomatic patients. Asymptomatic patients with “silent ischemia” or known coronary artery disease (CAD) that has been detected in the absence of symptoms are beyond the scope of these guidelines. Pediatric patients are also beyond the scope of these guidelines because ischemic heart disease is unusual in such patients and is primarily related to the presence of coronary artery anomalies. These guidelines also do not apply to patients with chest pain syndromes following cardiac transplantation or early after revascularization or to those with acute ischemic syndromes such as myocardial infarction (MI) or unstable angina.

The 3 flow diagrams that follow summarize the management of stable angina in 3 algorithms: clinical assessment (Figure 1), stress testing/angiography (Figure 2), and treatment (Figure 3). The treatment mnemonic (Figure 4) is intended to highlight the 10 treatment elements that the committee considered most important.

### C. Magnitude of the Problem

Ischemic heart disease remains a major public health problem. Chronic stable angina is the initial manifestation of ischemic heart disease in approximately one half of patients. The magnitude of the problem can be easily summarized: chronic stable angina affects many millions of Americans, with associated annual costs that are measured in tens of billions of dollars.

### II. Diagnosis

#### A. History and Physical

**Recommendations**

**Class I**

In patients presenting with chest pain, a detailed symptom history, focused physical examination, and directed risk factor assessment should be performed. With this information, the clinician should estimate the probability of significant CAD (ie, low, intermediate, high). *(Level of Evidence: B)*

**Definition of Angina**

Angina is 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 usually occurs in patients with CAD involving ≥1 large epicardial artery. However, angina can also occur in individuals with valvular heart disease, hypertrophic cardiomyopathy, and uncontrolled hypertension. It can be present in patients with normal coronaries and myocardial ischemia related to spasm or endothelial dysfunction.

After the history of the pain is obtained, the physician should classify the symptom complex. One classification scheme for chest pain in many studies uses 3 groups—typical angina, atypical angina, or noncardiac chest pain (Table 1). Patients with noncardiac chest pain are generally at lower risk for ischemic heart disease. As indicated on the flow diagram, the history and appropriate diagnostic tests will usually focus on noncardiac causes of chest pain.

After a detailed chest pain history is taken, the presence of risk factors for CAD should be determined. Hyperlipidemia, diabetes, hypertension, cigarette smoking, and a family history of premature CAD are all important. Past history of cerebrovascular or peripheral vascular disease increase the likelihood that CAD will be present.

**TABLE 1. Clinical Classification of Chest Pain**

<table>
<thead>
<tr>
<th>Typical angina (definite)</th>
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<tr>
<td>(1) Subternal chest discomfort with a characteristic quality and duration that is (2) provoked by exertion or emotional stress and (3) relieved by rest or nitroglycerin</td>
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<table>
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<tr>
<th>Atypical angina (probable)</th>
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<tbody>
<tr>
<td>Meets 2 of the above characteristics</td>
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<table>
<thead>
<tr>
<th>Noncardiac chest pain</th>
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<tr>
<td>Meets ≤1 of the typical angina characteristics</td>
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B. Associated Conditions

Recommendations for Initial Laboratory Tests for Diagnosis

Class I
1. Hemoglobin. (Level of Evidence: C)
2. Fasting glucose. (Level of Evidence: C)
3. Fasting lipid panel, including total cholesterol, HDL cholesterol, triglycerides, and calculated LDL cholesterol. (Level of Evidence: C)

C. Noninvasive Testing

1. ECG/Chest X-Ray

Recommendations for Electrocardiography, Chest X-Ray, or Electron Beam Computed Tomography in the Diagnosis of Chronic Stable Angina

Class I
1. Rest ECG in patients without an obvious noncardiac cause of chest pain. (Level of Evidence: B)
2. Rest ECG during an episode of chest pain. (Level of Evidence: B)

Class IIa
Chest x-ray in patients with signs or symptoms of pulmonary disease. (Level of Evidence: B)

Class IIb
1. Chest x-ray in other patients. (Level of Evidence: C)
2. Electron beam computed tomography. (Level of Evidence: B)

A rest 12 lead ECG should be recorded in all patients with symptoms suggestive of angina pectoris; however, it will be normal in ≤50% of patients with chronic stable angina. A normal rest ECG does not exclude severe CAD. Evidence of prior Q-wave MI on the ECG or ST-T wave changes consistent with myocardial ischemia favors the diagnosis of angina pectoris. ECG evidence of left ventricular (LV) hypertrophy increases the probability that chest discomfort is angina pectoris.

3. Chest x-ray in patients with signs or symptoms of congestive heart failure, valvular heart disease, pericardial disease, or aortic dissection/aneurysm. (Level of Evidence: B)
The chest roentgenogram is often normal in patients with stable angina pectoris. Its usefulness as a routine test is not well established. It is more likely to be abnormal in patients with previous MI, those with a noncoronary artery cause of chest pain, and those with noncardiac chest discomfort.

2. Exercise ECG for Diagnosis

Recommendations for the Diagnosis of Obstructive CAD With Exercise ECG Testing Without an Imaging Modality

Class I
Patients with an intermediate pretest probability of CAD based on age, gender, and symptoms, including those with complete right bundle-branch block or <1 mm of rest ST depression (exceptions are listed below in classes II and III). *(Level of Evidence: B)*

Class IIa
Patients with suspected vasospastic angina. *(Level of Evidence: C)*

Class IIb

1. Patients with a high pretest probability of CAD by age, gender, and symptoms. *(Level of Evidence: B)*

2. Patients with a low pretest probability of CAD by age, gender, and symptoms. *(Level of Evidence: B)*

3. Patients taking digoxin with ECG baseline ST-segment depression <1 mm. *(Level of Evidence: B)*

4. Patients with ECG criteria for LV hypertrophy and <1 mm of baseline ST-segment depression. *(Level of Evidence: B)*

Class III

1. Patients with the following baseline ECG abnormalities:
   a. Preexcitation (Wolff-Parkinson-White) syndrome. *(Level of Evidence: B)*
   b. Electronically paced ventricular rhythm. *(Level of Evidence: B)*
   c. More than 1 mm of rest ST depression. *(Level of Evidence: B)*
   d. Complete left bundle-branch block. *(Level of Evidence: B)*

2. Patients with an established diagnosis of CAD due to prior MI or coronary angiography; however, testing can assess functional capacity and prognosis, as discussed in section III. *(Level of Evidence: B)*
Exercise testing is a well-established procedure that has been in widespread clinical use for many decades. Interpretation of the exercise test should include symptomatic response, exercise capacity, hemodynamic response, and ECG response. The occurrence of ischemic chest pain consistent with angina is important, particularly if it forces termination of the test. Abnormalities in exercise capacity, systolic blood pressure response to exercise, and heart rate response to exercise are important findings. The most important ECG findings are ST depression and elevation. The most commonly used definition for a positive exercise test is ≥1 mm of horizontal or downsloping ST-segment depression or elevation for ≥60 to 80 ms after the end of the QRS complex.

If the diagnosis remains uncertain after the history, physical examination, ECG, and chest x-ray, exercise ECG testing should be the next step in most patients. Diagnostic testing is most valuable when the pretest probability of obstructive CAD is intermediate: for example, when a 50-year-old man has atypical angina and the probability of CAD is 50% (see Table 2). In these conditions, the test result has the largest effect on the posttest probability of disease and thus on clinical decisions. The exact definition of the upper and lower boundaries of intermediate probability (eg, 10% and 90%, 20% and 80%, or 30% and 70%) is a matter of physician judgment in an individual situation. When the probability of obstructive CAD is high, a positive test result only confirms the high probability of disease, and a negative test result may
not decrease the probability of disease enough to make a clinical difference. When the probability of obstructive CAD is very low, a negative test result only confirms the low probability of disease, and a positive test result may not increase the probability of disease enough to make a clinical difference.

The exercise ECG has a number of limitations in symptomatic patients after coronary bypass surgery. Rest ECG abnormalities are frequent, and if an imaging test is not incorporated in the study, more reliance must be paid to symptom status, hemodynamic response, and exercise capacity. Because of these considerations, together with the need to document the site of ischemia, stress imaging tests are preferred in this group.

Restenosis is the 1 major limitation of percutaneous coronary interventions and remains a major consideration in patients with recurrent symptoms between 6 and 12 months later. Unfortunately, symptom status is an unreliable index to development of restenosis. The exercise ECG is an insensitive predictor of restenosis, with sensitivities ranging from 40% to 55%, significantly less than those obtainable with single photon emission computed tomography (SPECT) or exercise echocardiography. The lower sensitivity of exercise ECG (compared with imaging techniques) as well as its inability to localize disease limits its utility in the management of symptomatic patients after percutaneous interventions.

3. Echocardiography (Rest)

Recommendations for Echocardiography for Diagnosis of Cause of Chest Pain in Patients With Suspected Chronic Stable Angina Pectoris

Class I

1. Patients with a systolic murmur suggestive of aortic stenosis and/or hypertrophic cardiomyopathy. (Level of Evidence: C)
2. Evaluation of extent (severity) of ischemia (eg, LV segmental wall motion abnormality) when the echocardiogram can be obtained during pain or within 30 minutes after its abatement. (Level of Evidence: C)

Class IIb
Patients with a click and/or murmur to diagnose mitral valve prolapse. (Level of Evidence: C)

Class III
Patients with a normal ECG, no history of MI, and no signs or symptoms suggestive of heart failure, valvular heart disease, or hypertrophic cardiomyopathy. (Level of Evidence: C)

Echocardiography can be a useful tool for diagnosing CAD. However, most patients undergoing a diagnostic evaluation for angina do not need an echocardiogram.

Transthoracic echocardiographic imaging and Doppler recording are useful when there is a murmur or other evidence of conditions such as aortic stenosis or hypertrophic cardiomyopathy coexisting with CAD. Routine estimation of parameters of global LV function such as LV ejection fraction are unnecessary for diagnosis of chronic angina pectoris. For example, in patients with suspected angina and a normal ECG, no history of MI, and no physical signs or symptoms suggestive of heart failure, echocardiography (and radionuclide imaging for LV function) are not indicated.

4. Stress Imaging Studies: Echocardiographic and Nuclear

Recommendations for Cardiac Stress Imaging as the Initial Test for Diagnosis in Patients With Chronic Stable Angina Who Are Able to Exercise

Class I

1. Exercise myocardial perfusion imaging or exercise echocardiography in patients with an intermediate pretest probability of CAD who have 1 of the following baseline ECG abnormalities:
   a. Preexcitation (Wolff-Parkinson-White) syndrome. (Level of Evidence: B)
   b. More than 1 mm of ST depression. (Level of Evidence: B)

2. Exercise myocardial perfusion imaging or exercise echocardiography in patients with prior revascularization (either percutaneous transluminal coronary angioplasty [PTCA] or coronary artery bypass graft [CABG]). (Level of Evidence: B)

3. Adenosine or dipyridamole myocardial perfusion imaging in patients with an intermediate pretest probability of CAD and 1 of the following baseline ECG abnormalities:
   a. Electronically paced ventricular rhythm. (Level of Evidence: C)
   b. Left bundle-branch block. (Level of Evidence: B)

Class IIb

1. Exercise myocardial perfusion imaging and exercise echocardiography in patients with a low or high probability of CAD who have 1 of the following baseline ECG abnormalities:
   a. Preexcitation (Wolff-Parkinson-White) syndrome. (Level of Evidence: B)
   b. More than 1 mm of ST depression. (Level of Evidence: B)

2. Exercise myocardial perfusion imaging or exercise echocardiography in patients with an intermediate probability of CAD who have 1 of the following:
   a. Digoxin use with <1 mm ST depression on their baseline ECG. (Level of Evidence: B)
   b. LV hypertrophy with <1 mm ST depression on their baseline ECG. (Level of Evidence: B)

3. Exercise myocardial perfusion imaging or exercise echocardiography in patients with a normal rest ECG who is not taking digoxin. (Level of Evidence: B)

4. Exercise myocardial perfusion imaging, exercise echocardiography, adenosine or dipyridamole myocardial perfusion imaging, or dobutamine echocardiography as the initial stress test in a patient with a normal rest ECG who is not taking digoxin. (Level of Evidence: B)

5. Exercise or dobutamine echocardiography in patients with left bundle-branch block. (Level of Evidence: C)
Recommendations for Cardiac Stress Imaging as the Initial Test for Diagnosis in Patients With Chronic Stable Angina Who Are Unable to Exercise

Class I

1. Adenosine or dipyridamole myocardial perfusion imaging or dobutamine echocardiography in patients with an intermediate pretest probability of CAD. *(Level of Evidence: B)*

2. Adenosine or dipyridamole stress myocardial perfusion imaging or dobutamine echocardiography in patients with prior revascularization (either PTCA or CABG). *(Level of Evidence: B)*

Class IIb

1. Adenosine or dipyridamole stress myocardial perfusion imaging or dobutamine echocardiography in patients with a low or high probability of CAD in the absence of electronically paced ventricular rhythm or left bundle-branch block. *(Level of Evidence: B)*

2. Adenosine or dipyridamole myocardial perfusion imaging in patients with a low or high probability of CAD and 1 of the following baseline ECG abnormalities:
   a. Electronically paced ventricular rhythm. *(Level of Evidence: C)*
   b. Left bundle-branch block. *(Level of Evidence: B)*

Patients who are good candidates for cardiac stress testing with imaging, as opposed to routine treadmill and bicycle stress ECG, include those in the following categories (see also section II.C.3): (1) complete left bundle-branch block, electronically paced ventricular rhythm, preexcitation (Wolff-Parkinson-White) syndrome and other similar ECG conduction abnormalities; (2) patients who have >1 mm of rest ST-segment depression, including those with LV hypertrophy or taking drugs such as digitalis; (3) patients who are unable to exercise to a level high enough to give meaningful results on routine stress ECG; these patients should be considered for pharmacological stress imaging tests; and (4) patients with angina who have undergone prior revascularization or in whom considerations of functional significance of lesions or myocardial viability are important.

A summary of comparative advantages of stress nuclear perfusion imaging and stress echocardiographic techniques is provided in Table 3. Echocardiographic and radionuclide stress imaging have complementary roles, and both add value to routine stress ECG under the circumstances outlined above. The choice of which test to perform depends greatly on issues of local expertise and available facilities as well as those factors listed in Table 3.

Because of its lower cost and generally greater portability, stress echocardiography is more likely to be performed in the physician's office than stress radionuclide imaging; the availability of stress imaging in the office setting has both advantages and disadvantages. The quality of local expertise and facilities should be important considerations when the referring physician recommends a cardiac stress imaging test for a patient.

### TABLE 3. Comparative Advantages of Stress Echocardiography and Stress Radionuclide Perfusion Imaging in Diagnosis of CAD

<table>
<thead>
<tr>
<th>Advantages of Stress Echocardiography</th>
<th>Advantages of Stress Radionuclide Perfusion Imaging</th>
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<tbody>
<tr>
<td>1. Higher specificity</td>
<td>1. Higher technical success rate</td>
</tr>
<tr>
<td>2. Versatility: more extensive evaluation of cardiac anatomy and function</td>
<td>2. Higher sensitivity, especially for 1-vessel coronary disease</td>
</tr>
<tr>
<td>3. Greater convenience/efficacy/availability</td>
<td>3. Better accuracy in evaluating possible ischemia when multiple rest LV wall motion abnormalities are present</td>
</tr>
<tr>
<td>4. Lower cost</td>
<td>4. More extensive published database, especially in evaluation of prognosis</td>
</tr>
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D. Invasive Testing: Coronary Angiography

Recommendations for Coronary Angiography to Establish a Diagnosis in Patients With Suspected Angina, Including Those With Known CAD Who Have a Significant Change in Anginal Symptoms

Class I

Patients with known or possible angina pectoris who have survived sudden cardiac death. *(Level of Evidence: B)*

Class IIa

1. Patients with an uncertain diagnosis after noninvasive testing in whom the benefit of a more certain diagnosis outweighs the risk and cost of coronary angiography. *(Level of Evidence: C)*

2. Patients who cannot undergo noninvasive testing due to disability, illness, or morbid obesity. *(Level of Evidence: C)*

3. Patients with an occupational requirement for a definitive diagnosis. *(Level of Evidence: C)*

4. Patients who by virtue of young age at onset of symptoms, noninvasive imaging, or other clinical parameters are suspected of having a nonatherosclerotic cause of myocardial ischemia (coronary artery anomaly, Kawasaki disease, primary coronary artery dissection, radiation-induced vasculopathy). *(Level of Evidence: C)*

5. Patients in whom coronary artery spasm is suspected and provocative testing may be necessary. *(Level of Evidence: C)*

6. Patients with a high pretest probability of left main or 3-vessel CAD. *(Level of Evidence: C)*

Class IIb

1. Patients with recurrent hospitalization for chest pain in whom a definite diagnosis is judged necessary. *(Level of Evidence: C)*

2. Patients with an overriding desire for a definitive diagnosis and a greater-than-low probability of CAD. *(Level of Evidence: C)*

Class III

1. Patients with significant comorbidity in whom the risk of coronary arteriography outweighs the benefit of the procedure. *(Level of Evidence: C)*
2. Patients with an overriding personal desire for a definitive diagnosis and a low probability of CAD. 

(Level of Evidence: C)

This invasive technique for imaging the coronary artery lumen remains the most accurate for the diagnosis of clinically important obstructive coronary atherosclerosis and less common nonatherosclerotic causes of possible chronic stable angina pectoris, such as coronary artery spasm, coronary anomaly, Kawasaki disease, primary coronary artery dissection, and radiation-induced coronary vasculopathy.

Direct referral for diagnostic coronary angiography may be indicated in patients with chest pain possibly attributable to myocardial ischemia when noninvasive testing is contraindicated or unlikely to be adequate due to illness, disability, or physical characteristics.

The diagnosis may be established in patients whose noninvasive testing result is abnormal but not clearly diagnostic by using either stress imaging or coronary angiography. A stress imaging test may be recommended for a low-likelihood patient with an intermediate-risk treadmill result. Coronary angiography is usually more appropriate for a patient with a high-risk treadmill result.

In patients with symptoms suggestive but not characteristic of stable angina, direct referral to coronary angiography may be indicated if their occupation or activities could pose a risk to themselves or others. In certain patients with typical or atypical symptoms suggestive of stable angina and a high pretest probability of severe CAD, direct referral to coronary angiography may be indicated and prove cost-effective.

III. Risk Stratification

A. Clinical Assessment

Useful information that is relevant to prognosis can be obtained from the history. This information includes demographic characteristics such as age and gender as well as a medical history with a focus on hypertension, diabetes, hypercholesterolemia, smoking, peripheral arterial disease, and previous MI.

Several studies have examined the value of clinical parameters for identifying the presence of severe (3-vessel or left main) CAD. One study developed a 5-point cardiac risk score based on clinical parameters that were independently predictive of severe (3-vessel or left main) CAD: age, typical angina, diabetes, gender, and prior MI by history and ECG (Figure 5). Some patients have a high likelihood (>1 chance in 2) of severe disease on the basis of clinical parameters alone. Such patients should be considered for direct referral to angiography.

Risk stratification of patients with stable angina by use of clinical parameters may facilitate development of clearer indications of referral for exercise testing and cardiac catheterization.

B. ECG/Chest X-Ray

Patients with chronic stable angina who have rest ECG abnormalities are at greater risk than those with normal ECGs. The prognosis of patients with a normal ECG (which

implies normal rest LV function) and low clinical risk for severe CAD is excellent.

On the chest roentgenogram, the presence of cardiomegaly, an LV aneurysm, or pulmonary venous congestion is associated with a poorer long-term prognosis than normal chest x-ray findings.

C. Noninvasive Testing

1. Rest LV Function

(Echocardiographic/Radionuclide Imaging)

Recommendations for Measurement of Rest LV Function by Echocardiography or Radionuclide Angiography in Patients With Chronic Stable Angina

Class I

1. Echocardiography or radionuclide angiography (RNA) in patients with a history of prior MI, pathological Q waves, or symptoms or signs suggestive of heart failure to assess LV function. (Level of Evidence: B)

2. Echocardiography in patients with a systolic murmur suggesting mitral regurgitation to assess its severity and etiology. (Level of Evidence: C)

3. Echocardiography or RNA in patients with complex ventricular arrhythmias to assess LV function. (Level of Evidence: B)

Class III

1. Routine periodic reassessment of stable patients for whom no new change in therapy is contemplated. (Level of Evidence: C)

2. Patients with a normal ECG, no history of MI, and no symptoms or signs suggestive of heart failure. (Level of Evidence: B)

In the chronic stable angina patient who has a history of documented MI and/or Q waves on ECG, measurement of
global LV systolic function (eg, ejection fraction) may be important in choosing appropriate medical or surgical therapy and making recommendations about activity level, rehabilitation, and work status. Similarly, in patients who, in addition to chronic stable angina, have clinical signs or symptoms of heart failure, cardiac imaging may be helpful in establishing pathophysiological mechanisms and guiding therapy. For example, a patient with heart failure might have predominantly systolic LV dysfunction, predominantly diastolic dysfunction, mitral or aortic valve disease, some combination of these abnormalities, or a noncardiac cause for symptoms. The best treatment for the patient can be planned more rationally knowing the status of LV systolic and diastolic function (by echocardiography or radionuclide imaging), valvular function, and pulmonary artery pressure (by transthoracic echocardiographic techniques).

LV global systolic function and volumes have been well documented as important predictors of prognosis in patients with cardiac disease, including those with chronic stable angina. An important measure of LV global systolic function is LV ejection fraction, which is the fraction (or percent) of LV diastolic volume ejected by the heart on each beat.

2. Exercise Testing for Risk Stratification and Prognosis

Recommendations for Risk Assessment and Prognosis in Patients With an Intermediate or High Probability of CAD

Class I

1. Patients undergoing initial evaluation. (Exceptions are listed below in classes IIb and III.) (Level of Evidence: B)
2. Patients after a significant change in cardiac symptoms. (Level of Evidence: C)

Class IIb

1. Patients with the following ECG abnormalities:
   a. Preexcitation (Wolff-Parkinson-White) syndrome. (Level of Evidence: B)
   b. Electronically paced ventricular rhythm. (Level of Evidence: B)
   c. More than 1 mm of rest ST depression. (Level of Evidence: B)
   d. Complete left bundle-branch block. (Level of Evidence: B)
2. Patients who have undergone cardiac catheterization to identify ischemia in the distribution of a coronary lesion of borderline severity. (Level of Evidence: C)
3. Postvascularization patients who have a significant change in anginal pattern suggesting ischemia. (Level of Evidence: C)

Class III

Patients with severe comorbidity likely to limit life expectancy or prevent revascularization. (Level of Evidence: C)

Unless cardiac catheterization is indicated, patients with suspected or known CAD who present with new or changing symptoms suggestive of ischemia should undergo stress testing to assess the risk of future cardiac events. Furthermore, documentation of exercise-induced ischemia is desirable for most patients who are being evaluated for revascularization. The results of exercise testing may also be used to titrate medical therapy to the desired level of effectiveness.

The choice of stress test should be based on the patient’s rest ECG, physical ability to perform exercise, local expertise, and available technologies. Risk assessment in patients with a normal ECG who are not taking digoxin usually should start with the exercise test. In contrast, a stress-imaging technique should be used for patients with widespread rest ST depression (>1 mm), complete left bundle-branch block, ventricular paced rhythm, or preexcitation. Patients unable to exercise because of physical limitations such as reduced exercise capacity, arthritis, amputations, severe peripheral vascular disease, or severe chronic obstructive pulmonary disease should undergo pharmacological stress testing in combination with imaging.

One of the strongest and most consistent prognostic markers is the maximum exercise capacity. Exercise capacity is measured by maximal exercise duration, maximum MET level achieved (1 MET is the standard basal oxygen uptake of 3.5 mL kg\(^{-1}\) min\(^{-1}\)), maximum workload achieved, maximum heart rate, and double product. The specific variable used to measure exercise capacity is less important than the inclusion of exercise capacity in the assessment. The translation of exercise duration or workload into METs provides a standard measure of performance regardless of the type of exercise test or protocol used.

A second group of prognostic markers is related to exercise-induced ischemia. ST-segment depression and elevation (in leads without pathological Q waves and not in aVR) best summarize the prognostic information related to ischemia. Other variables are less powerful, including angina, the number of leads with ST-segment depression, the configuration of ST depression (downsloping, horizontal, or upsloping), and the duration of ST deviation into the recovery phase.

The Duke Treadmill Score combines this information and provides a way to calculate risk. 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 times the angina index, which has a value of 0 if there is no angina, 1 if angina occurs, and 2 if angina is the reason for stopping the test).

The Duke Treadmill Score may be used to predict average annual cardiac mortality (Table 4). Patients with a predicted average annual cardiac mortality rate ≤1% per year can be managed medically without the need for cardiac catheterization. Patients with a predicted average annual cardiac mortality rate ≥3% per year should be referred for cardiac catheterization. Patients with a predicted average annual cardiac mortality rate of 1% to 3% per year, including those with suspected LV dysfunction, should have either cardiac

| TABLE 4. Survival According to Risk Groups Based on Duke Treadmill Scores |
|-----------------------------|--------|----------------|----------------|
| Risk Group, Score          | % of Total | 4-Year Survival | Annual Mortality, % |
| Low (≤5)                   | 62     | 0.99           | 0.25            |
| Moderate (6 to 4)          | 34     | 0.95           | 1.25            |
| High (>5)                  | 4      | 0.79           | 5.0             |
catheterization or an exercise imaging study. Those with known LV dysfunction should have cardiac catheterization.

3. Stress Imaging Studies (Radionuclide and Echocardiography)

Recommendations for Cardiac Stress Imaging for Risk Stratification of Patients With Chronic Stable Angina Who Are Unable to Exercise

Class I

1. Exercise myocardial perfusion imaging or exercise echocardiography to identify the extent, severity, and location of ischemia in patients who do not have left bundle-branch block or an electronically paced ventricular rhythm and have either an abnormal rest ECG or are using digoxin. (Level of Evidence: B)

2. Dipyridamole or adenosine myocardial perfusion imaging in patients with left bundle-branch block or electronically paced ventricular rhythm. (Level of Evidence: B)

3. Exercise myocardial perfusion imaging or exercise echocardiography to assess the functional significance of coronary lesions (if not already known) in planning PTCA. (Level of Evidence: B)

Class IIb

1. Exercise or dobutamine echocardiography in patients with left bundle-branch block. (Level of Evidence: C)

2. Exercise, dipyridamole, adenosine myocardial perfusion imaging, or exercise or dobutamine echocardiography as the initial test in patients who have a normal rest ECG and are not taking digoxin. (Level of Evidence: B)

Class III

1. Exercise myocardial perfusion imaging in patients with left bundle-branch block. (Level of Evidence: C)

2. Exercise, dipyridamole, adenosine myocardial perfusion imaging, or exercise or dobutamine echocardiography in patients with severe comorbidity likely to limit life expectation or prevent revascularization. (Level of Evidence: C)

Recommendations for Cardiac Stress Imaging as the Initial Test for Risk Stratification of Patients With Chronic Stable Angina Who Are Unable to Exercise

Class I

1. Dipyridamole or adenosine myocardial perfusion imaging or dobutamine echocardiography to identify the extent, severity, and location of ischemia in patients who do not have left bundle-branch block or electronically paced ventricular rhythm. (Level of Evidence: B)

2. Dipyridamole or adenosine myocardial perfusion imaging in patients with left bundle-branch block or electronically paced ventricular rhythm. (Level of Evidence: B)

3. Dipyridamole or adenosine myocardial perfusion imaging or dobutamine echocardiography to assess the functional significance of coronary lesions (if not already known) in planning PTCA. (Level of Evidence: B)

Class IIb

Dobutamine echocardiography in patients with left bundle-branch block. (Level of Evidence: C)

Class III

Dipyridamole or adenosine myocardial perfusion imaging or dobutamine echocardiography in patients with severe comorbidity likely to limit life expectation or prevent revascularization. (Level of Evidence: C)

Stress imaging studies employing radionuclide myocardial perfusion imaging techniques or 2-dimensional echocardiography at rest and during stress are useful for risk stratification and determination of the most beneficial management strategy for patients with chronic stable angina. Whenever possible, treadmill or bicycle exercise should be used as the most appropriate form of stress because it provides the most information concerning patient symptoms, cardiovascular function, and hemodynamic response during usual forms of activity. In fact, the inability to perform a bicycle or exercise treadmill test is a strong negative prognostic factor for patients with chronic CAD.

In patients who cannot perform an adequate amount of bicycle or treadmill exercise, various types of pharmacological stress are useful for risk stratification. The selection of the type of pharmacological stress will depend on specific patient factors such as the patient’s heart rate and blood pressure, the presence or absence of bronchospastic disease, the presence of left bundle-branch block or a pacemaker, and the likelihood of ventricular arrhythmias.

Normal poststress thallium scan results are highly predictive of a benign prognosis even in patients with known coronary disease. A collation of 16 studies involving 3954 patients followed up for a mean of 29 months indicated a rate of cardiac death and MI of 0.9% per year, which is nearly as low as that of the general population. In a recent prospective study of 5183 consecutive patients who underwent myocardial perfusion studies during stress and later at rest, patients with normal scans were at low risk (<0.5% per year) for cardiac death and MI during 642±226 days of mean follow-up, and rates of both outcomes increased significantly with worsening scan abnormalities. The presence of a normal thallium stress test result indicates such a low likelihood of significant CAD that coronary arteriography is usually not indicated as a subsequent test unless the patient has a high-risk Duke treadmill score.

Stress echocardiography (with the aid of digital acquisition and storage of quad-screen images) is both sensitive and specific for detecting inducible myocardial ischemia in patients with chronic stable angina (see section II.C.4). In comparison with standard exercise treadmill testing, stress echocardiography provides additional clinical value for detecting and localizing myocardial ischemia. The results of stress echocardiography may provide important prognostic value. Several studies indicate that patients at low, interme-
Coronary Angiography for Risk Stratification in Patients With Chronic Stable Angina

Recommendations

**Class I**

1. Patients with disabling (Canadian Cardiovascular Society [CCS] classes III and IV) chronic stable angina despite medical therapy. *(Level of Evidence: B)*
2. Patients with high-risk criteria on noninvasive testing regardless of anginal severity. *(Level of Evidence: B)*
3. Patients with angina who have survived sudden cardiac death or serious ventricular arrhythmia. *(Level of Evidence: B)*
4. Patients with angina and symptoms and signs of congestive heart failure. *(Level of Evidence: C)*
5. Patients with clinical characteristics that indicate a high likelihood of severe CAD. *(Level of Evidence: C)*

**Class IIa**

1. Patients with significant LV dysfunction (ejection fraction <45%), CCS class I or II angina, and demonstrable ischemia but less than high-risk criteria on noninvasive testing. *(Level of Evidence: C)*
2. Patients with inadequate prognostic information after noninvasive testing. *(Level of Evidence: C)*

**Class IIb**

Patients with CCS class I or II angina, preserved LV function (ejection fraction >45%), and less than high-risk criteria on noninvasive testing. *(Level of Evidence: C)*

**Class III**

1. Patients with CCS class I or II angina who respond to medical therapy and have no evidence of ischemia on noninvasive testing. *(Level of Evidence: C)*
2. Patients who prefer to avoid revascularization. *(Level of Evidence: C)*

Patients identified as having increased risk on the basis of an assessment of clinical data and noninvasive testing are generally referred for coronary arteriography even if their symptoms are not severe. Noninvasive testing that is used appropriately is less costly than coronary angiography and has an acceptable predictive value for adverse events. This is most true when the pretest probability of severe CAD is low. When the pretest probability of severe CAD is high, direct referral for coronary angiography without noninvasive testing is probably most cost-effective because the total number of tests is reduced.

Coronary angiography, the traditional “gold standard” for clinical assessment of coronary atherosclerosis, has limitations. It is not a reliable indicator of the functional significance of a coronary stenosis and is insensitive in detection of a thrombus (an indicator of disease activity). More importantly, coronary angiography is ineffective in determining which plaques have characteristics likely to lead to acute coronary events, that is, the vulnerable plaque with large lipid core, thin fibrous cap, and increased macrophages. Serial angiographic studies performed before and after acute events and early after MI suggest that plaques resulting in unstable angina and MI commonly produced <50% stenosis before the acute event and were therefore angiographically “silent.” Despite these limitations of coronary angiography, the extent and severity of coronary disease and LV dysfunction identified on angiography are the most powerful predictors of long-term patient outcome. Several prognostic indexes have been used to relate disease severity to the risk of subsequent cardiac events; the simplest and most widely used is the classification of disease into 1-, 2-, or 3-vessel or left main coronary artery disease. In the Coronary Artery Surgery Study (CASS) registry of medically treated patients, the 12-year survival rate of patients with normal coronary arteries was 91% compared with 74% for those with 1-vessel disease, 59% for those with 2-vessel disease, and 40% for those with 3-vessel disease. It has been known for many years that patients with significant stenosis of the left main coronary artery have a poor prognosis when treated medically. The impact of LV dysfunction on survival was quite dramatic. In the CASS registry, the 12-year survival rate was 73% for patients with an ejection fraction between 50% and 100%, 54% for those with an ejection fraction between 35% and 49%, and only 21% for those with an ejection fraction <35%.

**IV. Treatment**

Recommendations for Pharmacotherapy to Prevent MI and Death and Reduce Symptoms

**Class I**

1. Aspirin in the absence of contraindications. *(Level of Evidence: A)*
2. ß-Blockers as initial therapy in the absence of contraindications in patients with prior MI. *(Level of Evidence: A)*
3. ß-Blockers as initial therapy in the absence of contraindications in patients without prior MI. *(Level of Evidence: B)*
4. Calcium antagonists* and/or long-acting nitrates as initial therapy when ß-blockers are contraindicated. *(Level of Evidence: B)*
5. Calcium antagonists* and/or long-acting nitrates in combination with ß-blockers when initial treatment with ß-blockers is not successful. *(Level of Evidence: B)*
6. Calcium antagonists* and/or long-acting nitrates as a substitute for ß-blockers if initial treatment with ß-blockers leads to unacceptable side effects. *(Level of Evidence: C)*
7. Sublingual nitroglycerin or nitroglycerin spray for the immediate relief of angina. *(Level of Evidence: C)*

8. Lipid-lowering therapy in patients with documented or suspected CAD and LDL cholesterol >130 mg/dL with a target LDL of <100 mg/dL. *(Level of Evidence: A)*

*Short-acting dihydropyridine calcium antagonists should be avoided.

**Class IIa**

1. Clopidogrel when aspirin is absolutely contraindicated. *(Level of Evidence: B)*

2. Long-acting nondihydropyridine calcium antagonists* instead of β-blockers as initial therapy. *(Level of Evidence: B)*

3. Lipid-lowering therapy in patients with documented or suspected CAD and LDL cholesterol 100 to 129 mg/dL, with a target LDL of 100 mg/dL. *(Level of Evidence: B)*

*Short-acting dihydropyridine calcium antagonists should be avoided.

**Class IIb**

Low-intensity anticoagulation with warfarin in addition to aspirin. *(Level of Evidence: B)*

**Class III**

1. Dipyridamole. *(Level of Evidence: B)*

2. Chelation therapy. *(Level of Evidence: B)*

**A. Overview of Treatment**

The treatment of stable angina has 2 major purposes. The first is to prevent MI and death (and thereby increase the “quantity” of life). The second is to reduce the symptoms of angina and the occurrence of ischemia, which should improve the quality of life.

Therapy directed toward preventing death has the highest priority. When 2 therapeutic strategies are compared, the one with a definite or very likely advantage in preventing MI and death should usually be selected. For example, coronary artery bypass surgery is the preferred therapy for patients with significant left main CAD because it prolongs life. Patient education and preference are important components in this decision-making process and are covered in subsequent sections.

Pharmacological therapy directed toward prevention of MI and death has expanded greatly in recent years with the emergence of evidence that demonstrates the efficacy of lipid-lowering agents for this purpose. The committee believes that the emergence of such medical therapy for the prevention of MI and death represents a new treatment paradigm that should be recognized by all health professionals involved in the care of patients with stable angina.

**Pharmacotherapy to Prevent MI and Death**

*Antiplatelet Agents*

Aspirin exerts its antithrombotic effect by inhibiting cyclooxygenase and synthesis of platelet thromboxane A<sub>2</sub>. It is effective in preventing first heart attacks. The use of aspirin in >3000 patients with stable angina was associated with a 33% reduction in the risk of adverse cardiovascular events. In patients with unstable angina, aspirin decreased the short- and long-term risk of fatal and nonfatal MI. In the Physician’s Health Study, aspirin (325 mg) given on alternate days to asymptomatic persons was associated with a decreased incidence of MI.

**Lipid-Lowering Agents**

In the Scandinavian Simvastatin Survival Study, treatment with HMG-coenzyme reductase inhibitors in patients with documented CAD (including stable angina) with a baseline total cholesterol level of 212 to 308 mg/dL was associated with a significant reduction in the risk of fatal and nonfatal MI and the need for revascularization. Other studies also have reported similar benefits of statins in patients with documented or suspected CAD, even with lower lipid levels. In general, modification of diet and exercise are less effective than statins in achieving the target levels of cholesterol and LDL; thus, lipid-lowering pharmacotherapy is usually required in patients with stable angina.

**β-Blockers**

All β-blockers appear to be equally effective in angina pectoris. In patients with chronic, stable, exertional angina, β-blockers decrease heart rate and blood pressure during exercise, and the onset of angina or the ischemic threshold is delayed or avoided. In the treatment of stable angina, it is conventional to adjust the dose of these drugs to reduce the rest heart rate to 55 to 60 beats per minute. In patients with more severe angina, the heart rate can be reduced below 50 beats per minute, provided that there are no symptoms associated with bradycardia and that heart block does not develop. β-Blocker therapy limits the increase in heart rate during exercise, which should not exceed 75% of the heart rate response associated with the onset of ischemia.

In the absence of contraindications, β-blockers are preferred as initial therapy. The evidence for this approach is strongest in the presence of prior MI, for which this class of drugs has been shown to reduce mortality.

**Calcium Antagonists**

Calcium antagonists, including the newer, second-generation vasoselective dihydropyridine agents and nondihydropyridine drugs such as verapamil and diltiazem, decrease coronary vascular resistance and increase coronary blood flow. All of these agents cause dilatation of the epicardial conduit vessels and the arteriolar resistance vessels. Dilatation of the epicardial coronary arteries is the principal mechanism that allows calcium antagonists to relieve vasospastic angina. Calcium antagonists also concurrently decrease myocardial oxygen demand, primarily by reduction of systemic vascular resistance and reduction in arterial pressure.

Short-acting dihydropyridine calcium antagonists have the potential to enhance the risk of adverse cardiac events and should be avoided. Long-acting calcium antagonists, including slow-release and long-acting dihydropyridines and nondihydropyridines, are effective in relieving symptoms. They are appropriate initial therapy in patients with contraindica-
tions to \( \beta \)-blockers, as a substitute for \( \beta \)-blockers in patients who develop unacceptable side effects to \( \beta \)-blockers, or in combination with \( \beta \)-blockers when initial therapy with \( \beta \)-blockers is not successful.

**Long-Acting Nitrates**

In patients with exertional stable angina, nitrates improve exercise tolerance, increase the time to onset of angina, and decrease ST-segment depression during the treadmill exercise test. Combined with \( \beta \)-blockers or calcium antagonists, nitrates produce greater antianginal and anti-ischemic effects in patients with stable angina.

**Selection of Pharmacological Therapy Versus Revascularization**

In patients with stable exertional angina, medical therapy appears to be as effective as angioplasty. In the Randomized Intervention Treatment of Angina (RITA-II) Trial, medical therapy in patients with CCS class II or III angina reduced the risk of nonfatal and fatal MI compared with angioplasty. However, angioplasty relieved symptoms more effectively than medical therapy. In the VA cooperative study, there was no difference in prognosis between patients treated with medical therapy compared with surgical therapy except in those with left main coronary artery stenosis. However, revascularization provided more relief of symptoms than medical therapy. The quality of life after revascularization appears to be better with surgery or angioplasty than with medical therapy. As discussed below in the revascularization section, if the patient is known to have left main coronary artery stenosis, 3-vessel CAD, or 2-vessel CAD with proximal left anterior coronary artery stenosis, revascularization by a catheter-based technique or surgery should be offered. The choice of therapy should be determined not only by the results of randomized trials but also by the patient’s preference.

**Definition of Successful Treatment of Chronic Stable Angina**

The treatment of chronic stable angina has 2 complementary objectives: to reduce the risk of mortality and morbid events and reduce symptoms. From the patient’s perspective, the latter is often of greater concern. The cardinal symptom of stable CAD is anginal chest pain or equivalent symptoms such as exertional dyspnea. Often the patient suffers not only from the discomfort of the symptom itself but also from accompanying limitations on activities and the associated anxiety that the symptoms may produce. Uncertainty about prognosis may be another source of anxiety. For some patients, the predominant symptoms may be palpitations or syncope caused by arrhythmias or fatigue, edema, or orthopnea caused by heart failure.

Because of the variation in symptom complexes among patients and their unique perceptions, expectations, and preferences, it is impossible to create a definition of treatment success that is universally accepted. For example, given an otherwise healthy, active patient, the treatment goal may be complete elimination of chest pain and a return to vigorous physical activity. Conversely, an elderly patient with more severe angina and several coexisting medical problems may be content with a reduction in symptoms that enables performance of only limited activities of daily living.

The committee agreed that for most patients the goal of treatment should be complete or near-complete elimination of anginal chest pain and a return to normal activities and a functional capacity of CCS class I angina. This goal should be accomplished with minimal side effects of therapy. This definition of successful therapy must be modified in light of the clinical characteristics and preferences of each patient.

**Initial Treatment**

The initial treatment of the patient should include all elements in the following mnemonic:

| A. Aspirin and Antianginal therapy |
| B. \( \beta \)-Blocker and Blood pressure |
| C. Cigarette smoking and Cholesterol |
| D. Diet and Diabetes |
| E. Education and Exercise |

In constructing a flow diagram to reflect the treatment process, the committee thought that it was clinically helpful to divide the entire treatment process into 2 subdivisions: antianginal treatment and education and risk factor modification. The assignment of each of the treatment elements to 1 of these 2 subdivisions is self-evident, with the possible exception of aspirin. Given the fact that aspirin clearly reduces the risk of subsequent heart attack and death but has no known benefit in preventing angina, the committee thought that it was best assigned to the education and risk factor subdivision as reflected in the flow diagram.

All patients with angina should receive a prescription for sublingual nitroglycerin and education about its proper use. It is particularly important for patients to recognize that this is a short-acting drug with no known long-term consequences so that they will not be reluctant to use it.

If the patient’s history has a prominent feature of rest and nocturnal angina suggesting vasoospasm, initiation of therapy with long-acting nitrates and calcium antagonists is appropriate.

As mentioned previously, medications or conditions that are known to provoke or exacerbate angina must be recognized and treated appropriately. On occasion, angina may resolve with the appropriate treatment of these conditions. If so, no further antianginal therapy is required. Most often, angina is improved but not relieved by the treatment of such conditions, and further therapy should then be initiated.

The committee favored the use of a \( \beta \)-adrenergoreceptor blocker as initial therapy in the absence of contraindications. The evidence for this approach is strongest in the presence of prior MI, for which this class of drugs has been shown to reduce mortality. Because these drugs have also been shown to reduce mortality in the treatment of patients with isolated hypertension who are at lower risk for mortality than patients with stable angina, the committee favored their use as initial therapy even in the absence of prior MI.

If serious contraindications with the \( \beta \)-adrenergoreceptor blockers exist, unacceptable side effects occur with their use,
or angina persists despite their use, calcium antagonists should then be administered. If serious contraindications to calcium antagonists exist, unacceptable side effects occur with their use, or angina persists despite their use, long-acting nitrate therapy should then be prescribed.

At any point, on the basis of coronary anatomy, severity of anginal symptoms, and patient preferences, it is reasonable to consider evaluation for coronary revascularization. As discussed earlier, certain categories of patients have a demonstrated survival advantage associated with revascularization, medical therapy should be attempted before angioplasty or surgery is considered. The extent of the effort that should be undertaken with medical therapy obviously depends on the individual patient. In general, the committee thought that low-risk patients should be treated with at least 2, and preferably all 3, of the available classes of drugs before medical therapy is considered a failure.

B. Education
Because the presentation of ischemic heart disease is often dramatic and because of impressive recent technological advances, healthcare providers tend to focus on diagnostic and therapeutic interventions, often overlooking critically important aspects of high quality care. Chief among these neglected areas is the education of patients. In the 1995 National Ambulatory Medical Care Survey, counseling about physical activity and diet occurred during only 19% and 23%, respectively, of general medical visits. This shortcoming was observed across specialties, including cardiology, internal medicine, and family practice.

Effective education is critical to enlisting patients’ full and meaningful participation in therapeutic and preventive efforts and in allaying their natural concerns and anxieties. This in turn is likely to lead to a patient who not only is better informed but who is also able to achieve a better quality of life and is more satisfied with his or her care. Education about what to do at the onset of symptoms of a possible acute MI is particularly important. A variety of principles should be followed to help ensure that educational efforts are successful.

1. Assess the patient’s baseline understanding.
2. Elicit the patient’s desire for information.
3. Use epidemiological and clinical evidence.
4. Use ancillary personnel and professional patient educators when appropriate.
5. Use professionally prepared resources when available.
6. Develop a plan with the patient.
7. Involve family members in educational efforts.
8. Remind, repeat, and reinforce.

In summary, patient education requires a substantial time investment by primary-care providers and specialists using an organized and thoughtful approach. The potential rewards for patients are also substantial in terms of improved quality of life, satisfaction, and adherence to medical therapy. As a result, many should also have improved physical function and survival.

C. Therapy of Associated Conditions
Coexisting medical conditions may affect the selection of pharmacological agents for the management of chronic stable angina. For the patient with aortic valve stenosis or hypertrophic obstructive cardiomyopathy, nitrates may induce hypotension and further compromise myocardial oxygen delivery. The coexistence of heart failure in patients with chronic stable angina poses a special therapeutic challenge. A growing body of evidence suggests potential benefits of β-blockers in patients with heart failure; however, because of negative inotropic properties, they must be used judiciously in this setting. There is little evidence of benefit of calcium antagonists in the setting of ischemic dilated cardiomyopathy.

In patients with asthma, β-blockers are contraindicated because of the likelihood of exacerbation of bronchospasm. In patients with heart block, β-blocking agents and heart-rate limiting calcium antagonists (diltiazem, verapamil) should be avoided because they decrease atrioventricular nodal conduction. In patients with severe peripheral vascular disease, β-blockers may worsen symptoms. For patients with migraines, β-blockers and calcium antagonists may be beneficial, whereas nitrates may worsen the headaches.

D. Coronary Disease Risk Factors and Evidence That Treatment Can Reduce the Risk for Coronary Disease Events

Recommendations for Treatment of Risk Factors

\textbf{Class I}

1. Treatment of hypertension according to Joint National Conference VI guidelines. (Level of Evidence: A)
2. Smoking cessation therapy. (Level of Evidence: B)
3. Management of diabetes. (Level of Evidence: C)
4. Exercise training program. (Level of Evidence: B)
5. Lipid-lowering therapy in patients with documented or suspected CAD and LDL \( \geq 130 \) mg/dL, with a target LDL \(< 100 \) mg/dL. (Level of Evidence: A)
6. Weight reduction in obese patients in the presence of hypertension, hyperlipidemia, or diabetes mellitus. (Level of Evidence: C)

\textbf{Class IIa}

Lipid-lowering therapy in patients with documented or suspected CAD and LDL cholesterol 100 to 129 mg/dL, with a target LDL of \(< 100 \) mg/dL. (Level of Evidence: B)

\textbf{Class IIb}

1. Hormonal replacement therapy in postmenopausal women in the absence of contraindications. (Level of Evidence: B)
2. Weight reduction in obese patients in the absence of hypertension, hyperlipidemia, or diabetes mellitus. (Level of Evidence: C)
3. Folate therapy in patients with elevated homocysteine levels. (Level of Evidence: C)
4. Vitamin C and E supplementation. (Level of Evidence: B)
5. Identification and appropriate treatment of clinical depression. (Level of Evidence: C)
6. Intervention directed at psychosocial stress reduction. (Level of Evidence: C)

Class III

1. Chelation therapy. (Level of Evidence: C)
2. Garlic. (Level of Evidence: C)
3. Acupuncture. (Level of Evidence: C)

Categorization of Coronary Disease Risk Factors

The 27th Bethesda Conference proposed that CAD risk factors be categorized both on the strength of evidence for causation and the evidence that risk factor modification can reduce risk for clinical CAD events. Category I risk factors were clearly associated with an increase in coronary disease risk, for which interventions have been shown to reduce the incidence of coronary disease events.

Such risk factors must be identified and, when present, treated as part of an optimal secondary prevention strategy in patients with chronic stable angina. They are common in this patient group and readily amenable to modification, and their treatment can affect clinical outcome favorably. For these reasons, they are discussed in these guidelines in greater detail than other risk factors. Lipid-lowering therapy has already been discussed because definitive evidence from randomized trials has shown that it is highly beneficial.

Smoking Cessation

Randomized clinical trials of smoking cessation have not been performed in patients with chronic stable angina. Three randomized smoking cessation trials have been performed in a primary prevention setting. Smoking cessation was associated with a reduction in cardiac event rates of 7% to 47% in these trials. The rapidity of risk reduction after smoking cessation is consistent with known adverse effects of smoking on fibrinogen levels and platelet adhesion. Other rapidly reversible effects of smoking include increased blood carboxyhemoglobin levels, reduced HDL cholesterol, and coronary artery vasoconstriction.

Patients with symptomatic coronary disease form the group most receptive to treatments directed to smoking cessation. Taylor and coworkers have shown that ≈32% of patients will stop smoking at the time of a cardiac event and that this rate can be significantly enhanced to 61% by a nurse-managed smoking cessation program. New behavioral and pharmacological approaches to smoking cessation are available for use by trained healthcare professionals. Few physicians are adequately trained in smoking cessation techniques. Identification of experienced allied healthcare professionals who can implement smoking cessation programs for patients with coronary disease is a priority. The importance of a structured approach cannot be overemphasized. The rapidity and magnitude of risk reduction, as well as the other health-enhancing benefits of smoking cessation, argue for the incorporation of smoking cessation in all programs of secondary prevention of coronary disease.

Hypertension

The first and second Veterans Affairs Cooperative studies were the first to definitively demonstrate the benefits of hypertension treatment. By 1993, there were 17 randomized trials of therapy in >47,000 patients of both sexes, all races, and a wide spectrum of blood pressures. The beneficial effects of hypertension treatment on cardiovascular disease risk have been confirmed in individual trials and meta-analyses. More recent trials in older patients with systolic hypertension have underscored the benefits to be derived from blood pressure lowering in the elderly. A recent meta-analysis found that the absolute reduction of coronary events in older subjects (2.7/1000 person-years) was more than twice as great as that in younger subjects (1.0/1000 person-years). This finding contrasts with clinical practice in which hypertension is often less aggressively treated in older persons.

Hypertensive patients with chronic stable angina are at high risk for cardiovascular disease morbidity and mortality. The benefits and safety of hypertension treatment in such patients have been established. Treatment begins with non-pharmacological means. When lifestyle modifications and dietary alterations adequately reduce blood pressure, pharmacological intervention is unnecessary. The modest benefit of antihypertensive therapy for coronary event reduction in clinical trials may underestimate the efficacy of this therapy in hypertensive patients with established coronary disease because in general, the higher the absolute risk of the population, the greater the magnitude of response to therapy.

Diabetes Mellitus

Although better metabolic control in persons with type I diabetes has been shown to lower the risk for microvascular complications, there is little information about the benefits of tighter metabolic control in type I or II diabetes with regard to reducing the risk for coronary disease in either primary or secondary prevention settings. At present, it is worthwhile to pursue strict glycemic control in diabetic persons with chronic stable angina in the belief that this approach will prevent some microvascular complications and may also reduce the risk for other cardiovascular disease complications, but convincing data from clinical trials are lacking.

The common coexistence of other modifiable factors in the diabetic patient contributes to increased coronary disease risk and must be managed aggressively. These risk factors include hypertension, obesity, and increased LDL-cholesterol levels. Elevated triglyceride levels and low HDL-cholesterol levels are also common in persons with diabetes.

Obesity

Obesity is a common condition associated with increased risk for coronary disease and mortality. Obesity is associated with and contributes to other coronary disease risk factors, including high blood pressure, glucose intolerance, low levels of HDL cholesterol, and elevated triglyceride levels. Hence, much of the increased CAD risk associated with obesity is mediated by these risk factors. It is likely that weight reduction in obese patients with coronary disease can reduce the risk for future coronary events because weight reduction will improve these other modifiable risk factors and reduce the increased myocardial oxygen demand imposed by obesity. Therefore, weight reduction is indicated in all obese patients with chronic stable angina, although no clinical trials have specifically examined the effect of weight loss on risk.
for coronary disease events. Referral to a dietitian is often necessary to maximize the likelihood of success of a dietary weight loss program.

Inactive Lifestyle: Exercise Training
Any discussion of exercise training must acknowledge that it will not only usually be incorporated into a multifactorial intervention program but will have multiple effects. It is very difficult to separate the effects of exercise training from the multiple secondary effects that it may have on confounding variables. For example, exercise training may lead to changes in weight, sense of well-being, and use of antianginal medication.

Multiple randomized, controlled trials comparing exercise training with a “no-exercise” control group have demonstrated a statistically significant improvement in exercise tolerance in the exercise group versus the control group. Four randomized trials have examined the potential benefit of exercise training on objective measures of ischemia. Three of those studies demonstrated a reduction in objective measures of ischemia in patients randomized to the exercise group compared with the control group.

Multiple randomized trials have examined the potential benefit of exercise training in the management of lipids. Some of these trials have examined exercise training alone; others have studied exercise training as part of a multifactorial intervention. The preponderance of evidence clearly suggests that exercise training is beneficial and associated with a reduction in total cholesterol, LDL cholesterol, and triglycerides in comparison with controlled therapy but has little effect on HDL cholesterol. Not surprisingly, these reductions in lipids have been associated with less disease progression using angiographic follow-up. However, exercise training alone is unlikely to be sufficient in patients with a lipid disorder.

Considering its effects on lipid levels and disease progression, it is attractive to hypothesize that exercise training will reduce the subsequent risk of cardiac events. However, only 1 clinical trial has examined the impact of exercise training on subsequent cardiac events in patients with stable angina. Although this trial suggested a favorable effect of exercise training on patient outcome, it was not definitive.

E. Revascularization for Chronic Stable Angina
Recommendations for Revascularization With PTCA (or Other Catheter-Based Techniques) and CABG in Patients With Stable Angina

Class I

1. CABG for patients with significant left main coronary disease. (Level of Evidence: A)
2. CABG for patients with 3-vessel disease. The survival benefit is greater in patients with abnormal LV function (ejection fraction <50%), (Level of Evidence: A)
3. CABG for patients with 2-vessel disease with significant proximal left anterior descending CAD and either abnormal LV function (ejection fraction <50%) or demonstrable ischemia on noninvasive testing. (Level of Evidence: A)

4. PTCA for patients with 2- or 3-vessel disease with significant proximal left anterior descending CAD, who have anatomy suitable for catheter-based therapy, normal LV function, and who do not have treated diabetes. (Level of Evidence: B)
5. PTCA or CABG for patients with 1- or 2-vessel CAD without significant proximal left anterior descending CAD but with a large area of viable myocardium and high-risk criteria on noninvasive testing. (Level of Evidence: B)
6. CABG for patients with 1- or 2-vessel CAD without significant proximal left anterior descending CAD who have survived sudden cardiac death or sustained ventricular tachycardia. (Level of Evidence: C)
7. In patients with prior PTCA, CABG or PTCA for recurrent stenosis associated with a large area of viable myocardium and/or high-risk criteria on noninvasive testing. (Level of Evidence: C)
8. PTCA or CABG for patients who have not been successfully treated (see text) by medical therapy and can undergo revascularization with acceptable risk. (Level of Evidence: B)

Class IIa

1. Repeat CABG for patients with multiple saphenous vein graft stenoses, especially when there is significant stenosis of a graft supplying the left anterior descending coronary artery. PTCA may be appropriate for focal saphenous vein graft lesions or multiple stenoses in poor candidates for reoperative surgery. (Level of Evidence: C)
2. PTCA or CABG for patients with 1- or 2-vessel CAD without significant proximal left anterior descending CAD but with a moderate area of viable myocardium and demonstrable ischemia on noninvasive testing. (Level of Evidence: B)
3. PTCA or CABG for patients with 1-vessel disease with significant proximal left anterior descending CAD. (Level of Evidence: B)

Class IIb

1. Compared with CABG, PTCA for patients with 3- or 2-vessel disease with significant proximal left anterior descending CAD who have anatomy suitable for catheter-based therapy and who have treated diabetes or abnormal LV function. (Level of Evidence: B)
2. PTCA for patients with significant left main coronary disease who are not candidates for CABG. (Level of Evidence: C)
3. PTCA for patients with 1- or 2-vessel CAD without significant proximal left anterior descending CAD who have survived sudden cardiac death or sustained ventricular tachycardia. (Level of Evidence: C)

Class III

1. PTCA or CABG for patients with 1- or 2-vessel CAD without significant proximal left anterior descending CAD who
   a. Have mild symptoms that are unlikely due to myocardial ischemia or have not received an adequate trial of medical therapy and
1) Have only a small area of viable myocardium or
2) Have no demonstrable ischemia on noninvasive testing. (Level of Evidence: C)

2. PTCA or CABG for patients with borderline coronary stenoses (50% to 60% diameter in locations other than the left main) and no demonstrable ischemia on noninvasive testing. (Level of Evidence: C)

3. PTCA or CABG for patients with insignificant coronary stenosis (<50% diameter). (Level of Evidence: C)

4. PTCA in patients with significant left main CAD who are candidates for CABG. (Level of Evidence: B)

Note: PTCA is used in these recommendations to indicate PTCA and/or other catheter-based techniques such as stents, atherectomy, and laser therapy.

Currently, there are 2 well-established revascularization approaches to treatment of chronic stable angina caused by coronary atherosclerosis. One is CABG, in which segments of autologous arteries and/or veins are used to reroute blood around relatively long segments of the proximal coronary artery. The second is PTCA, a technique that uses catheter-borne mechanical or laser devices to open a (usually) short area of stenosis from within the coronary artery.

CABG Versus Medical Management

The goals of coronary bypass surgery are to improve symptoms and prolong life expectancy. Early in the history of CABG, it became clear that successful bypass surgery relieved or improved angina. To investigate the question of whether bypass surgery prolonged survival, 3 large multicenter randomized trials, the Veterans Administration Cooperative Study (VA Study), the European Coronary Surgery Study (ECSS), and the Coronary Artery Surgery Study (CASS), were undertaken. These trials compared the strategy of initial bypass surgery with that of initial medical management in regard to long-term survival and symptom status for patients with mild or moderate symptoms.

Recently, a meta-analysis of these 3 major randomized trials of initial surgery versus medical management as well as other smaller trials has confirmed the survival benefit achieved by surgery at 10 postoperative years for patients with 3-, 2-, or even 1-vessel disease that included a stenosis of the proximal LAD coronary artery. The survival rate of these patients was improved by surgery whether they had normal or abnormal LV function. For patients without a proximal LAD stenosis, bypass surgery improved the mortality rate only for those with 3-vessel disease or left main stenosis.

PTCA

PTCA for CAD was introduced in 1977 as balloon angioplasty, a strategy in which a catheter-borne balloon was inflated at the point of coronary stenosis. Alternative mechanical devices for percutaneous treatments have been developed and have included rotating blades or burrs designed to remove atheromatous material, lasers to achieve photoablation of lesions, and metal intracoronary stents designed to structurally maintain lumen size.

PTCA Versus Medical Treatment

The initial randomized study that compared PTCA with medical management alone for the treatment of chronic stable angina was the Veterans Affairs Angioplasty Compared to Medicine (ACME) Trial, which involved patients with 1-vessel disease and exercise-induced ischemia. In a 6-month follow-up, the death rate was expectedly low for both the PTCA and medically treated groups, and 64% of the PTCA group were free of angina versus 46% of the medically treated group (P<0.01).

A second randomized trial comparing initial PTCA versus initial medical management (RITA-II) included a majority of patients with 1-vessel disease (60%) and some angina (only 20% without angina) monitored over a 2.7-year median follow-up interval. There was a slightly greater risk of death or MI for the PTCA group (P=0.02), although those risks were low for both groups. The PTCA patients had less angina 3 months after randomization, although by 2 years, the differences between the 2 groups were small (7.6% more medically treated patients had angina).

PTCA Versus CABG

Multiple trials have compared the strategy of initial PTCA versus initial CABG for the treatment of multivessel CAD. In general, the goal of these trials has been to try to answer the question of whether or not there are subsets of patients who pay a penalty in terms of survival for initial treatment with PTCA. The 2 US trials of PTCA versus CABG are the multicenter Bypass Angioplasty Revascularization Investigation (BARI) Trial and the 1-center Emory Angioplasty versus Bypass Surgery Trial (EAST).

The results of both of these trials at an ∼5-year follow-up interval have shown that early and late survival rates have been equivalent for the PTCA and CABG groups. In the BARI trial, the subgroup of patients with treated diabetes had significantly better survival rates with CABG. That survival advantage for CABG was focused in the group of diabetic patients with multiple severe lesions. In the EAST trial, diabetics had equivalent survival rates with CABG or PTCA at 3 years. Longer-term follow-up data from the BARI and EAST trials have not yet been published.

Recommendations for Revascularization for Patients With Native-Vessel CAD

Advances have been made in medical therapy that reduce MI and death and decrease the rate of progression of coronary stenoses. However, there is still no evidence that medical treatment alone sufficiently improves the life expectancy of the high-risk subgroups defined by the trials of medical treatment versus bypass surgery.

The randomized trials of initial medical treatment versus initial surgery showed that patients with left main stenoses ≥70% and those with multivessel CAD with a proximal LAD stenosis ≥70% have a better late survival rate if they have coronary bypass surgery. Because the randomized trials of PTCA versus bypass surgery included an inadequate number of patients in these high-risk subsets, it cannot be assumed that the alternative strategy of PTCA produces equivalent late survival in such patients.
Meta-analysis of the randomized trials of medical management versus CABG have further indicated that patients without severe symptoms but with a proximal left anterior descending artery lesion have a better survival rate with surgery, even if they have normal LV function and only 1-vessel disease. For these patients, data from the PTCA versus CABG trials appear to show that, at least for the first 5 years, the alternative revascularization strategy of PTCA does not compromise survival for patients who are good angiographic candidates for PTCA.

Caution should be used in treating diabetic patients with PTCA, particularly in the setting of multivessel, multilesson, severe CAD.

V. Patient Follow-Up: Monitoring of Symptoms and Antianginal Therapy

Recommendations for Echocardiography, Treadmill Exercise Testing, Stress Imaging Studies, and Coronary Angiography During Patient Follow-Up

Class I

1. Chest x-ray for patients with evidence of new or worsening congestive heart failure. (Level of Evidence: C)
2. Assessment of LV ejection fraction and segmental wall motion in patients with new or worsening congestive heart failure or evidence of intervening MI by history or ECG. (Level of Evidence: C)
3. Echocardiography for evidence of new or worsening valvular heart disease. (Level of Evidence: C)
4. Treadmill exercise test for patients without prior revascularization who have a significant change in clinical status, are able to exercise, and do not have any of the ECG abnormalities listed below in number 5. (Level of Evidence: C)
5. Stress imaging procedures for patients without prior revascularization who have a significant change in clinical status and are unable to exercise or have 1 of the following ECG abnormalities:
   a. Preexcitation (Wolff-Parkinson-White) syndrome. (Level of Evidence: C)
   b. Electronically paced ventricular rhythm. (Level of Evidence: C)
   c. More than 1 mm of rest ST depression. (Level of Evidence: C)
   d. Complete left bundle-branch block. (Level of Evidence: C)
6. Stress imaging procedures for patients who have a significant change in clinical status and required a stress imaging procedure on their initial evaluation because of equivocal or intermediate-risk treadmill results. (Level of Evidence: C)
7. Stress imaging procedures for patients with prior revascularization who have a significant change in clinical status. (Level of Evidence: C)
8. Coronary angiography in patients with marked limitation of ordinary activity (CCS class III) despite maximal medical therapy. (Level of Evidence: C)

Class IIb

Annual treadmill exercise testing in patients who have no change in clinical status, can exercise, have none of the ECG abnormalities listed in number 5 above, and have an estimated annual mortality of >1%. (Level of Evidence: C)

Class III

1. Echocardiography or radionuclide imaging for assessment of LV ejection fraction and segmental wall motion in patients with a normal ECG, no history of MI, and no evidence of congestive heart failure. (Level of Evidence: C)
2. Repeat treadmill exercise testing in <3 years in patients who have no change in clinical status and an estimated annual mortality <1% on their initial evaluation as demonstrated by 1 of the following:
   a. Low-risk Duke treadmill score (without imaging). (Level of Evidence: C)
   b. Low-risk Duke treadmill score with negative imaging. (Level of Evidence: C)
   c. Normal LV function and a normal coronary angiogram. (Level of Evidence: C)
   d. Normal LV function and insignificant CAD. (Level of Evidence: C)
3. Stress imaging procedures for patients who have no change in clinical status and a normal rest ECG, are not taking digoxin, are able to exercise, and did not require a stress imaging procedure on their initial evaluation because of equivocal or intermediate-risk treadmill results. (Level of Evidence: C)
4. Repeat coronary angiography in patients with no change in clinical status, no change on repeat exercise testing or stress imaging, and insignificant CAD on initial evaluation. (Level of Evidence: C)

The committee believes that the patient with successfully treated chronic stable angina should have a follow-up evaluation every 4 to 12 months. A more precise interval cannot be recommended because many factors influence the length of the follow-up period. During the first year of therapy, annual evaluations every 4 to 6 months are recommended. After the first year of therapy, annual evaluations are recommended if the patient is stable and reliable enough to call or make an appointment when anginal symptoms become worse or other symptoms occur. Patients who are comanaged by their primary-care physician and cardiologist may alternate these visits, provided that communication among physicians is excellent and all appropriate issues are addressed at each visit. Annual office visits can be supplemented by telephone or other types of contact between the patient and the physicians caring for him or her. Patients who cannot reliably identify and report changes in their status or who need more support with their treatment or risk factor reduction should be seen more frequently.

Five questions must be answered regularly during the follow-up of the patient who is receiving treatment for chronic stable angina:

1. Has the patient decreased the level of physical activity since the last visit?
2. Have the patient’s anginal symptoms increased in frequency and become more severe since the last visit? If the symptoms have worsened or the patient has de-
creased physical activity to avoid precipitating angina, then he or she should be evaluated and treated according to either the unstable angina or chronic stable angina guidelines, as appropriate.

3. How well is the patient tolerating therapy?
4. How successful has the patient been in reducing modifiable risk factors and improving knowledge about ischemic heart disease?
5. Has the patient developed any new comorbid illnesses or has the severity or treatment of known comorbid illnesses worsened the patient’s angina?

In patients who have been successfully treated as previously defined and who have had no change in clinical status, the rationale for follow-up noninvasive stress testing is to identify patients in whom further evaluation and revascularization might be appropriate to improve prognosis. Such a strategy can only be successful if the patient’s prognosis on medical therapy is sufficiently poor that it can potentially be improved. Previous experience in the randomized trials of coronary artery bypass surgery demonstrated that patients randomized to initial CABG had a lower mortality rate than those treated with medical therapy only if they were at substantial risk. Low-risk patients who did not have a lower mortality with CABG had a 5-year survival rate with medical therapy of $\approx 95\%$. This is equivalent to an annual mortality rate of $1\%$. As a result, follow-up testing to identify patients whose prognosis can be improved is inappropriate when the patient’s estimated annual mortality rate is $\leq 1\%$. In contrast, patients with a survival advantage with CABG, such as those with 3-vessel disease, have an annual mortality rate $\geq 3\%$. Follow-up testing is more appropriate in patients whose risk is in this range. The strategy for performance of additional testing at any point during a patient’s follow-up is analogous to the strategy for performance of angiography after initial treadmill testing. It is appropriate in high-risk situations, a matter of clinical judgment in intermediate-risk situations, and not required in low-risk situations.

The choice of stress test to be used in patient follow-up testing should be dictated by considerations similar to those outlined earlier for the initial evaluation of the patient. In patients with interpretable exercise ECGs who are capable of exercise, treadmill exercise testing remains the first choice. Whenever possible, follow-up testing should be done using the same stress and imaging techniques to permit the most valid comparison to the original study. When different modes of stress and imaging are used, it is much more difficult to judge whether an apparent change in results is due to differences in the modality or a change in the patient’s underlying status.

**Key Words:** AHA Scientific Statements □ angina □ coronary artery disease □ myocardial infarction
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