

Coronary Artery Disease Guideline

These clinical guidelines are designed to assist clinicians by providing an analytical framework for the evaluation and treatment of patients. They are not intended to replace a clinician’s judgment or to establish a protocol for all patients with a particular condition. A guideline will rarely establish the only approach to a problem.

GUIDELINE HISTORY and APPROVAL

ACTION	SEED GUIDELINE and/or MAIN INFORMATION & GROUP SOURCE(S)	DATE	ORGANIZATION
Guideline Reviewed, Revised, and Approved	American College of Cardiology/ American Heart Association 2002 Guideline Update for the Management of Patients with Chronic Stable Angina. (<i>J Am Coll Cardiol</i> , 2003;107:149-158). Located at www.acc.org and www.americanheart.org	July 02, 2003	Geisinger Health Plan Guideline Review Conference/ Coronary Artery Disease Team
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OVERVIEW

Each year, approximately 1,200,000 Americans have a heart attack. 650,000 (approximately 60%) are first time heart attacks and about 38 percent of people who experience a coronary attack in a given year die from it. Sixteen million Americans have a history of a myocardial infarction, angina pectoris or both (1,2). Among members of the Geisinger Health Plan, an average of 91 members per month are hospitalized with heart attack, unstable angina or undergo invasive cardiac procedures including stent placement, angioplasty or open heart surgery. Numerous studies have shown the risk of cardiac events can be diminished by treatment with platelet inhibitors, beta blockers, lipid lowering therapy and modification of significant cardiac risk factors, such as diabetes, tobacco use and hypertension. The purpose of this guideline is to help physicians manage their patients with coronary syndromes for maximum benefit. It is anticipated this guideline will be used in the context of disease management for coronary artery disease.

Hochman JS, Tamis JE, Thompson TD, Weaver WD, White HD. *New Engl J Med* 1999;341:226-2232.

AHA 2004 Heart Attack and Angina Statistics.

<http://www.americanheart.org/presenter.jhtml?identifier=4591>

SEED GUIDELINE

American College of Cardiology/American Heart Association 2002 Guideline Update for the Management of Patients with Chronic Stable Angina. (*J Am Coll Cardiol*, 2003;107:149-158).

Located at www.acc.org and www.americanheart.org

2007 Chronic Angina Focused Update of the ACC/AHA 2002 Guidelines for the Management of Patients with Chronic Stable Angina *J Am Coll Cardiol* 2007;50(23):2264-2274

GOALS

1. To increase the rate of beta blocker, aspirin and lipid lowering therapy use among GHP members with CAD.
2. To increase the evaluation of lipid levels among GHP members with CAD.
3. To increase ASCVD risk factor control among GHP members with CAD.

FAST FACTS

1. In considering the impact of beta-blockers, platelet inhibitors, and lipid lowering therapy, consider the “number needed to treat.”
2. Beta blockers: Based on 31 clinical trials reported in the medical literature, approximately 84 patients need to be treated for one year to avoid one death, and 107 patients have to be treated to avoid one non-fatal re-infarction. (Freemantle N, Cleland JY, Mason J, Harrison J: Beta blockade after myocardial infarction: systematic review and meta regression analysis. *BMJ* 1999;318:1730-1737).
3. Anti-platelet agents are also recommended for secondary prevention. It has been estimated that the number needed to treat to prevent one cardiovascular death is 83. The NNT to prevent all cardiovascular morbidity has been reported to be as low as 45. (Miller DB: Secondary prevention of ischemic heart disease: relative numbers needed to treat with different therapies. *Arch Int Med*. 1997;157:2045-2052 and Weisman SM. Graham DY: Evaluation of the benefits and risks of low-dose aspirin in the secondary prevention of cardiovascular and cerebrovascular events. *Archives of Int Med* 162(19):2197-202, 2002 Oct 28).
4. Lipid Lowering Therapy: Lipid lowering therapy is a mainstay of primary and secondary prevention. The number needed to treat reported in trials of primary prevention among individuals with multiple risk factors is 53 to prevent a nonfatal MI and 190 to prevent all cause death. In secondary prevention, based on 23 clinical trials, the number needed to treat is 37 to prevent death from any cause and as low as 43 to prevent one non-fatal heart attack. (Rembold CM: Number needed to treat analysis of the prevention of myocardial infarction and death by antidyslipidemic therapy. *J Family Practice* 1996;42:577-86. and Ross SD. Allen IE. Connelly JE. Korenblat BM. Smith ME. Bishop D. Luo D. Clinical outcomes in statin treatment trials: a meta-analysis. *Archives of Internal Medicine*. 159(15):1793-802, 1999 Aug 9-23).



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I. Introduction

The full text of the guidelines is available on the Web sites of the American College of Cardiology (www.acc.org) and the American Heart Association (www.americanheart.org). The summary article is published in the January 1, 2003 issue of the Journal of the American College of Cardiology and the January 7/14, 2003 issue of Circulation. The update is published in the Dec 4, 2007 issue of the Journal of the American College of Cardiology. This pocket guide provides rapid prompts for appropriate patient management that is outlined in much greater detail, along with caveats and levels of evidence, in those documents. Users of this guide should consult those documents for more information.

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. Subsection V describes the approach to the special group of asymptomatic patients with known or suspected coronary artery disease (CAD).

The customary ACC/AHA classifications I, II, and III are used in tables that summarize the recommendations:

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.

II. Clinical Assessment (Figure 1)

A. Recommendations for History and Physical Examination

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, i.e., low, intermediate, high.

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 one or more large epicardial arteries, but can also occur in individuals with other cardiac problems.

After the history is obtained, the physician should classify the symptom complex. One scheme uses 3 groups—typical angina, atypical angina, or noncardiac chest pain (Table 1). The term nonspecific chest pain might be preferable to noncardiac chest pain, as it is meant to imply a low probability of CAD. The patient's age, gender, and chest pain can be used to estimate the probability of significant CAD (Table 2).

Hyperlipidemia, diabetes, hypertension, cigarette smoking, a family history of premature CAD, and a past history of cerebrovascular or peripheral vascular disease increase the probability of CAD.

B. Recommendations for Initial Laboratory Tests, ECG, and Chest X-Ray for Diagnosis

- Class I**
1. Hemoglobin
 2. Fasting glucose
 3. Fasting lipid panel, including total cholesterol, HDL cholesterol, triglycerides, and calculated LDL cholesterol
 4. Rest electrocardiogram (ECG) in patients without an obvious noncardiac cause of chest pain
 5. Rest ECG during an episode of chest pain
 6. Chest X-ray in patients with signs or symptoms of congestive heart failure, valvular heart disease, pericardial disease, or aortic dissection/aneurysm

Class IIa Chest X-ray in patients with signs or symptoms of pulmonary disease

- Class IIb**
1. Chest X-ray in other patients
 2. Electron-beam computed tomography
-

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 or more with chronic stable angina. A normal rest ECG does not exclude severe CAD.

However, it does imply normal rest left ventricular (LV) function and therefore a favorable prognosis. Evidence of prior Q-wave myocardial infarction (MI), left ventricular hypertrophy (LVH), or ST-T wave changes consistent with myocardial ischemia on the ECG favors the diagnosis of angina pectoris and worsens the patient's prognosis.

The *chest X-ray* is often normal in patients with stable angina pectoris. Its usefulness as a routine test is not well established. The presence of cardiomegaly, an LV aneurysm or pulmonary venous congestion is associated with a poorer long-term prognosis.

Key questions after history and physical examination, initial laboratory tests, ECG, and chest X-ray:

1. Does the history suggest an intermediate to high probability of CAD? If not, history and appropriate diagnostic tests will usually focus on noncardiac causes of chest pain.
2. Does the patient have intermediate- or high-risk unstable angina? Such patients should be managed according to the recommendations outlined in the ACC/AHA Unstable Angina and Non-ST-Segment Elevation MI Guideline. *
3. Has the patient had a recent MI (less than 30 days) or has the patient recently (less than 6 months) undergone percutaneous coronary intervention (PCI) or coronary artery bypass graft surgery (CABG)? If so, the patient should be managed according to the appropriate ACC/AHA guidelines on these subjects.
4. Does the patient have a comorbid condition such as severe anemia that may precipitate myocardial ischemia in the absence of significant anatomic coronary obstruction? If such a condition is present, treatment should be initiated for it.

* Braunwald E, Antman EM, Beasley JW, et al. ACC/AHA 2002 guideline update for the management of patients with unstable angina and non-ST-segment elevation myocardial infarction: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (Committee to Update the 2000 Guidelines on the Management of the Patients with Unstable Angina). 2002 (available at www.acc.org and www.americanheart.org).

C. Recommendations for Echocardiography or Radionuclide Angiography in Patients with Suspected Chronic Stable Angina Pectoris

- Class I**
1. Echocardiography in patients with a systolic murmur suggestive of aortic stenosis, mitral regurgitation, and/or hypertrophic cardiomyopathy
 2. Echocardiography or radionuclide angiography (RNA) to assess LV function in patients with a history of prior MI, pathological Q waves, symptoms or signs suggestive of heart failure, or complex ventricular arrhythmias.
-

Class IIb Echocardiography in patients with a click and/or murmur to diagnose mitral valve prolapsed.

Class III Echocardiography or RNA in patients with a normal ECG, no history of MI, and no signs or symptoms suggestive of heart failure, valvular heart disease, or hypertrophic cardiomyopathy.

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 suggesting aortic stenosis, mitral regurgitation, and/or hypertrophic cardiomyopathy.

Routine estimation of global LV function is 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 is not indicated.

In contrast, for the patient who has a history of documented MI and/or Q waves on ECG, or clinical signs or symptoms of heart failure, measurement of global LV systolic function (e.g., ejection fraction) may be helpful.

After echocardiography is performed, the clinician must address two questions:

1. Is a severe primary valvular lesion present? If so, the patient should be managed according to the ACC/AHA Valvular Heart Disease Guideline recommendations. *
2. Is a left ventricular abnormality present that makes the diagnosis of CAD highly likely? If so, subsequent management is based on the patient's suitability for further prognostic/risk assessment.

*J Am Coll Cardiol 1998;32:1486-588

Completion of Clinical Assessment

The clinician should then assess the probability of CAD and the need for prognostic/risk assessment. Most patients will be managed according to the flow diagram on stress testing/angiography (*Figure 2*). However, if the patient has a high probability of CAD, but is not a candidate for prognostic/risk assessment because of comorbidity or patient preference, the patient should be managed according to the flow diagram on treatment without stress testing or angiography (*Figure 3*).

III. Stress Testing/Angiography (Figure 2)

A. Recommendations for Exercise ECG Testing Without an Imaging Modality

- Class I**
1. For diagnosis of obstructive CAD in patients with an intermediate pretest probability of CAD (based on age, gender, and symptoms), including those with complete right bundle-branch block or less than 1 mm of rest ST depression (exceptions are listed below in classes IIb and III).
 2. For risk assessment and prognosis in patients undergoing initial evaluation. (Exceptions are listed below in classes IIb and III.)
-

- Class IIb**
- For diagnosis of obstructive CAD in:
- a. Patients with a high pretest probability of CAD by age, gender, and symptoms.
 - b. Patients with a low pretest probability of CAD by age, gender, and symptoms.
 - c. Patients taking digoxin with ECG baseline ST-segment depression less than 1 mm.
 - d. Patients with ECG criteria for LV hypertrophy and less than 1 mm of baseline ST-segment depression.
-

- Class III**
1. For diagnosis of obstructive CAD in patients with the following baseline ECG abnormalities:
 - a. Pre-excitation (Wolff-Parkinson-White) syndrome.
 - b. Electronically paced ventricular rhythm.
 - c. More than 1 mm of rest ST depression.
 - d. Complete left bundle-branch block (LBBB).

(Exercise ECG testing is a class IIb for risk assessment and prognosis in such patients, as exercise capacity can still be assessed.)
 2. For risk assessment and prognosis in patients with severe comorbidity likely to limit life expectancy or prevent revascularization.
-

Direct referral for diagnostic coronary angiography may be indicated when noninvasive testing is contraindicated or unlikely to be adequate due to illness, disability, or physical characteristics; when a patient's occupation or activities could pose a risk to themselves or others; or when the pretest probability of severe CAD is high.

However, most patients will be candidates for a stress test prior to angiography. The choice of stress test should be based on the patient's rest ECG, physical ability to perform exercise, local expertise, and available technologies. In patients with a normal ECG who are not taking digoxin, testing usually should start with the exercise ECG. In contrast, stress imaging should be used for patients with widespread rest ST depression (more than 1 mm), complete LBBB, ventricular paced rhythm, or pre-excitation. Patients unable to exercise should undergo pharmacological stress testing in combination with imaging.

Interpretation of the exercise test should include symptomatic response, exercise capacity, hemodynamic response, and ECG response. The most important ECG findings are ST depression and elevation. The most commonly used definition for a positive exercise test is 1 mm or more of horizontal or downsloping ST-segment depression or elevation for at least 60 to 80 ms after the end of the QRS complex.

The exercise ECG has a number of limitations in symptomatic patients after CABG or PCI. Stress imaging tests are preferred in these groups. One of the strongest prognostic markers is the maximum exercise capacity. A second group of prognostic markers is related to exercise-induced ischemia. The Duke Treadmill Score combines this information (Table 3).

B. Recommendations for Cardiac Stress Imaging in Patients With Chronic Stable Angina Who Are Able 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 LBBB or an electronically-paced ventricular rhythm and have either an abnormal rest ECG or are using digoxin.
2. Dipyridamole or adenosine myocardial perfusion imaging in patients with LBBB or electronically paced ventricular rhythm.
3. Exercise myocardial perfusion imaging or exercise echocardiography in patients with an intermediate pretest probability of CAD who have pre-excitation (Wolff-Parkinson-White) syndrome or more than 1 mm of rest ST depression.
4. Exercise myocardial perfusion imaging or exercise echocardiography in patients with prior revascularization (either PCI or CABG).

- Class IIb**
1. Exercise or dobutamine echocardiography in patients with LBBB.
 2. Exercise, dipyridamole, adenosine myocardial perfusion imaging, or exercise dobutamine echocardiography as the initial stress test in patients who have a normal rest ECG and are not taking digoxin.
-

- Class III**
1. Exercise myocardial perfusion imaging in patients with LBBB.
 2. Exercise, dipyridamole, or adenosine myocardial perfusion imaging, or exercise dobutamine echocardiography for risk stratification in patients with severe comorbidity likely to limit life expectation or prevent revascularization.
-

Echocardiographic and radionuclide stress imaging have complementary roles, and both add value to routine stress ECG for the specific patients listed in the recommendations, as well as for patients who are unable to exercise. The choice of which test to perform depends on local expertise, test availability, and the factors in Table 4.

Whenever possible, treadmill or bicycle exercise should be used as the most appropriate form of stress because it provides the most information. 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, including adenosine or dipyridamole myocardial perfusion imaging and dobutamine echocardiography. 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 LBBB or a pacemaker, and the likelihood of ventricular arrhythmias. Details are available in the executive summary or full text of the guideline.

C. Invasive Testing: Coronary Angiography

Recommendations for Coronary Angiography

- Class I**
1. Patients with disabling (Canadian Cardiovascular Society [CCS] classes III and IV) chronic stable angina despite medical therapy.
 2. Patients with high-risk criteria on clinical assessment or noninvasive testing regardless of anginal severity.
 3. Patients with angina who have survived sudden cardiac death or serious ventricular arrhythmia.
 4. Patients with angina and symptoms and signs of congestive heart failure.
-

- 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.
 2. Patients who cannot undergo noninvasive testing due to disability, illness, or morbid obesity.
 3. Patients with an occupational requirement for a definitive diagnosis.
 4. Patients with inadequate prognostic information after noninvasive testing.
-

- Class III**
1. Patients with significant comorbidity in whom the risk of coronary arteriography outweighs the benefit of the procedure.
 2. Patients with CCS class I or II angina who respond to medical therapy and have no evidence of ischemia on noninvasive testing.
 3. Patients who prefer to avoid revascularization.
-

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.

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 (Table 5). 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.

Either stress imaging (perfusion imaging or echocardiography) or coronary angiography may be employed in patients whose exercise ECG does not provide adequate diagnostic or prognostic information. A stress imaging test may be recommended for a low-likelihood patient with an intermediate-risk exercise ECG. Coronary angiography is usually more appropriate for a patient with a high-risk exercise ECG.

Coronary angiography 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. Serial angiographic studies performed before and after acute events and early after MI suggest that plaques resulting in unstable angina and MI commonly produced less than 50% stenosis before the acute event and were therefore angiographically “silent.”

Nevertheless, the extent and severity of coronary disease and LV dysfunction identified on angiography are currently 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 CAD.

IV. Treatment (Figure 3)

A. Recommendations for Pharmacotherapy to Prevent MI and Death and Reduce Symptoms

- Class I**
1. Aspirin in the absence of contraindications.
 2. Beta blockers as initial therapy in the absence of contraindications.
 3. ACE inhibitor in all patients with CAD* who also have diabetes and/or LV systolic dysfunction.
 4. Calcium antagonists** and/or long-acting nitrates as initial therapy for reduction of symptoms when beta blockers are contraindicated.
 5. Calcium antagonists** and/or long-acting nitrates in combination with beta blockers when initial treatment with beta blockers is not successful.
 6. Calcium antagonists** and/or long-acting nitrates as a substitute for beta blockers if initial treatment with beta blockers leads to unacceptable side effects.
 7. Sublingual nitroglycerin or nitroglycerin spray for the immediate relief of angina.
 8. Low-density lipoprotein-lowering therapy in patients with documented or suspected CAD and LDL cholesterol greater than 130 mg/dL with a target LDL of less than 100 mg/dL.
-
- Class IIa**
1. Clopidogrel when aspirin is absolutely contraindicated.
 2. Long-acting nondihydropyridine calcium antagonists** instead of beta blockers as initial therapy.
 3. In patients with documented or suspected CAD and LDL cholesterol 100 to 129 mg per dL, several therapeutic options are available:
 - a. Lifestyle and/or drug therapies to lower LDL to less than 100 mg per dL.
 - b. Weight reduction and increased physical activity in persons with the metabolic syndrome.
 - c. Institution of treatment of other lipid or nonlipid risk factors; consider use of nicotinic acid or fibric acid for elevated triglycerides or low HDL cholesterol.
 4. ACE inhibitor in patients with CAD* or other vascular disease who exhibit systolic dysfunction. Diuretics may be indicated in diastolic dysfunction.
-

Class IIb Low-intensity anticoagulation with warfarin in addition to aspirin.

Class III 1. Dipyridamole.

- * Significant CAD by angiography or previous myocardial infarction.
- ** Short-acting dihydropyridine calcium antagonists should be avoided.

Basic Treatment/Education

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

- A. Aspirin and Antianginal therapy
- B. Beta blocker and Blood pressure
- C. Cigarette smoking and Cholesterol
- D. Diet and Diabetes
- E. Education and Exercise

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 such as the education of patients.

Effective education 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.

B. Pharmacotherapy to Prevent MI and Death

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.

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. This represents a new treatment paradigm that should be recognized by all health professionals involved in the care of patients with stable angina. For that reason, lipid-lowering agents are highlighted on the treatment flow diagram (Figure 3).

Aspirin is effective in preventing heart attacks. 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.

In a randomized trial, the use of the ACE inhibitor ramipril (10 mg per day) reduced the cardiovascular death, MI, and stroke in patients who were at high risk for, or had, vascular disease in the absence of heart

failure. ACE inhibitors should be used in most patients as routine secondary prevention for patients with known CAD, particularly in patients with diabetes without severe renal disease.

C. Pharmacotherapy to Reduce Ischemia and Relieve Symptoms

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 vasospasm, initiation of therapy with long-acting nitrates and calcium antagonists is appropriate.

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.

A beta blocker is the preferred initial therapy in the absence of contraindications. All beta blockers appear to be equally effective in angina pectoris.

If serious contraindications to the beta-adrenoreceptor blockers exist, unacceptable side effects occur with their use, or angina persists despite their use, calcium antagonists should then be administered. 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.

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. Nitrates add to the antianginal and anti-ischemic effects of either beta blockers or calcium antagonists.

Coexisting medical conditions may affect the selection of pharmacological agents for the management of chronic stable angina. For example, for the patient with aortic valve stenosis or hypertrophic obstructive cardiomyopathy, nitrates may induce hypotension and further compromise myocardial oxygen delivery.

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 to reduce symptoms. From the patient's perspective, the latter is often of greater concern.

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 most patients, the goal of treatment should be complete or near-complete elimination of anginal chest pain, 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.

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. The extent of medical therapy obviously depends on the individual patient. In general, 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.

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

Recommendations for Treatment of Risk Factors

- Class I**
1. Treatment of hypertension according to *NHLBI Joint National Conference VII Report on Prevention, Detection, and Treatment of High Blood Pressure*
 2. Smoking cessation therapy
 3. Management of diabetes
 4. Comprehensive cardiac rehabilitation program (including exercise)
 5. Low-density lipoprotein-lowering therapy in patients with documented or suspected CAD and LDL cholesterol greater than 130 mg/dL with a target LDL of less than 100 mg/dL
 6. Weight reduction in obese patients in the presence of hypertension, hyperlipidemia, or diabetes mellitus.
-
- Class IIa**
1. In patients with documented or suspected CAD and LDL cholesterol 100 to 129 mg/dL, several therapeutic options are available:
 - a. Lifestyle and/or drug therapies to lower LDL to less than 100 mg/dL.
 - b. Weight reduction and increased physical activity in persons with the metabolic syndrome.
 - c. Institution of treatment of other lipid or nonlipid risk factors; consider use of nicotinic acid or fibric acid for elevated triglycerides or low HDL cholesterol.
 2. Therapy to lower non-HDL cholesterol in patients with documented or suspected CAD and triglycerides of greater than 200, with a target non-HDL cholesterol of less than 130 mg/dL.
 3. Weight reduction in obese patients in the absence of hypertension, hyperlipidemia or diabetes mellitus.
-
- Class IIb**
1. Folate therapy in patients with elevated homocysteine levels.
 2. Identification and appropriate treatment of clinical depression in order to improve CAD outcomes.
 3. Intervention directed at psychosocial stress reduction.
-

The most important risk factors are those that are clearly associated with an increase in CAD, for which interventions have been shown to reduce the incidence of CAD 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. Lipid-lowering therapy has already been discussed because definitive evidence from randomized trials has shown that it is highly beneficial in reducing death and MI.

Smoking Cessation

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.

Hypertension

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.

Diabetes Mellitus

Strict glycemic control in diabetic persons with chronic stable angina will prevent some microvascular complications and may also reduce the risk for other cardiovascular disease complications, but convincing data from clinical trials are lacking.

Obesity

Obesity is a common condition associated with increased risk for CAD 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. Risk is particularly raised in the presence of abdominal obesity, which can be identified by a waist circumference greater than 102 cm (40 inches) in men or 88 cm (35 inches) in women. Because weight reduction in overweight and obese people is a method to reduce multiple other risk factors, it is an important component of secondary prevention of CHD.

Inactive Lifestyle: Exercise Training

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.

E. Revascularization for Chronic Stable Angina

Recommendations for Revascularization With PCI (Percutaneous Coronary Intervention) and CABG in Patients With Stable Angina

- Class I
1. CABG for patients with significant left main coronary disease
 2. CABG for patients with 3-vessel disease. The survival benefit is greater in patients with abnormal LV function (ejection fraction less than 50%).
 3. CABG for patients with 2-vessel disease with significant proximal left anterior descending CAD and either abnormal LV function (ejection fraction less than 50%) or demonstrable ischemia on noninvasive testing.
 4. PCI 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.
 5. PCI 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.
 6. In patients with prior PCI, CABG or PCI for recurrent stenosis associated with a large area of viable myocardium and/or high-risk criteria on noninvasive testing.
 7. PCI or CABG for patients who have not been successfully treated (see text) by medical therapy and can undergo revascularization with acceptable risk.
-
- 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. PCI may be appropriate for focal saphenous vein graft lesions or multiple stenoses in poor candidates for reoperative surgery.
 2. PCI or CABG for patients with 1-vessel disease with significant proximal left anterior descending CAD.
-
- Class IIb
- Compared with CABG, PCI 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.

Class III

1. PCI or CABG for patients with 1- or 2-vessel CAD without significant proximal left anterior descending CAD who 1) have mild symptoms that are unlikely due to myocardial ischemia or 2) 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.
 2. PCI 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.
 3. PCI or CABG for patients with insignificant coronary stenosis (less than 50% diameter).
 4. PCI in patients with significant left main CAD who are candidates for CABG.
-

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

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 PCI, a technique that uses catheter-borne mechanical or laser devices to open a (usually) short area of stenosis from within the coronary artery.

The randomized trials of initial medical treatment versus initial surgery showed that patients with left main stenoses greater than 70% and those with multivessel CAD with a proximal LAD stenosis greater than 70% have a better late survival rate if they have coronary bypass surgery. Because the randomized trials of PCI versus bypass surgery included an inadequate number of patients in these high-risk subsets, it cannot be assumed that the alternative strategy of PCI produces equivalent late survival in such patients. Caution should be used in treating diabetic patients with PCI, particularly in the setting of multi-vessel, multi-lesion, severe CAD. In elderly patients, revascularization appears to improve quality of life and morbidity compared to medical therapy.

V. Asymptomatic Patients With Known or Suspected Coronary Artery Disease

This update outlines the approach to asymptomatic patients with known or suspected CAD on the basis of a history and/or ECG evidence of previous MI, coronary angiography, or an abnormal noninvasive test. The inclusion of asymptomatic patients with abnormal noninvasive tests does not constitute an endorsement of such tests for the purposes of screening, but simply acknowledges the clinical reality that such patients often present for evaluation after such tests have been performed. Multiple ACC/AHA guidelines and scientific statements have discouraged the use of ambulatory monitoring, treadmill testing, stress echocardiography, stress myocardial perfusion imaging, and electron-beam computed tomography (EBCT) as routine screening tests in asymptomatic individuals.

A. Recommendations for Noninvasive Testing for the Diagnosis of Obstructive CAD and Risk Stratification in Asymptomatic Patients

Class IIb

1. Exercise ECG testing without an imaging modality* in asymptomatic patients with possible myocardial ischemia on ambulatory ECG monitoring or with severe coronary calcification** on EBCT in the absence of one of the following ECG abnormalities:
 - a. Pre-excitation (Wolff-Parkinson-White) syndrome
 - b. Electronically-paced ventricular rhythm
 - c. More than 1 mm of ST depression at rest
 - d. Complete left bundle-branch block

**Note: In females with a positive exercise ECG test, an imaging study should be considered due to increased risk of false positive findings.*
2. Exercise perfusion imaging or exercise echocardiography in asymptomatic patients with possible myocardial ischemia on ambulatory ECG monitoring or with severe coronary calcification on EBCT who are able to exercise and have one of the following baseline ECG abnormalities:
 - a. Pre-excitation (Wolff-Parkinson-White) syndrome
 - b. More than 1 mm of ST depression at rest
3. Adenosine or dipyridamole myocardial perfusion imaging in patients with severe coronary calcification on EBCT, but with one of the following baseline ECG abnormalities:
 - a. Electronically-paced ventricular rhythm
 - b. Left bundle-branch block
4. Adenosine or dipyridamole myocardial perfusion imaging or dobutamine echocardiography in patients with possible myocardial ischemia on ambulatory ECG monitoring or with severe coronary calcification on EBCT, who are unable to exercise.
5. Exercise myocardial perfusion imaging or exercise echocardiography after exercise ECG testing in asymptomatic patients with an intermediate-risk or high-risk Duke treadmill score.

** Severe coronary calcification=calcium score more than 75th percentile for age- and gender-matched populations

6. Adenosine or dipyridamole myocardial perfusion imaging or dobutamine echocardiography after exercise ECG testing in asymptomatic patients with an inadequate exercise ECG.
-

Class III

1. Exercise ECG testing without an imaging modality in asymptomatic patients with possible myocardial ischemia on ambulatory ECG monitoring or with severe coronary calcification on EBCT, but with the baseline ECG abnormalities listed under Class IIb (1) above.
2. Exercise ECG testing without an imaging modality in asymptomatic patients with an established diagnosis of CAD due to prior MI or coronary angiography; however, testing can assess functional capacity and prognosis.
3. Exercise or dobutamine echocardiography in asymptomatic patients with left bundle-branch block.
4. Adenosine or dipyridamole myocardial perfusion imaging or dobutamine echocardiography in asymptomatic patients who are able to exercise and do not have left bundle-branch block or electronically paced ventricular rhythm.
5. Exercise myocardial perfusion imaging, exercise echocardiography, adenosine or dipyridamole myocardial perfusion imaging, or dobutamine echocardiography after exercise ECG testing in asymptomatic patients with a low-risk Duke treadmill score.

In asymptomatic patients, risk stratification and prognosis are more important considerations than diagnosis. Since the treatment of asymptomatic patients cannot improve their symptoms, the principal goal of evaluation and treatment is the improvement of patient outcome by reducing the rate of death and nonfatal MI. In one 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, suggesting that the ability to improve outcome with revascularization in such patients is limited.

B. Recommendations for Coronary Angiography for Risk Stratification in Asymptomatic Patients

Class IIa Patients with high-risk criteria suggesting ischemia on noninvasive testing.

Class IIb Patients with inadequate prognostic information after noninvasive testing.

Class III Patients who prefer to avoid revascularization.

The noninvasive test findings that identify high-risk patients are based on studies in symptomatic patients. These findings are probably also applicable to asymptomatic patients, but associated with a lower level of absolute risk in the absence of symptoms.

C. Recommendations for Pharmacotherapy to Prevent MI and Death in Asymptomatic Patients

-
- Class I**
1. Aspirin in the absence of contraindication in patients with prior MI.
 2. Beta blockers as initial therapy in the absence of contraindications in patients with prior MI.
 3. Low-density lipoprotein-lowering therapy in patients with documented CAD and LDL cholesterol greater than 130 mg/dL, with a target LDL of less than 100 mg/dL.
 4. ACE inhibitor in patients with CAD₁ who also have diabetes and/or systolic dysfunction.
-
- Class IIa**
1. Aspirin in the absence of contraindications in patients without prior MI.
 2. Beta blockers as initial therapy in the absence of contraindications in patients without prior MI.
 3. Low-density lipoprotein-lowering therapy in patients with documented CAD and LDL cholesterol 100 to 129 mg/dL, with a target LDL of 100 mg/dL.
 4. ACE inhibitor in all patients with CAD₁ or other vascular disease.
-

¹ Significant CAD by angiography or previous myocardial infarction

Even in asymptomatic patients, aspirin and beta blockers are recommended in patients with prior MI. In the absence of prior MI, patients with documented CAD on the basis of noninvasive testing or coronary angiography probably also benefit from aspirin, although the data on this specific subset of patients are limited. Several studies have investigated the potential role of beta blockers in patients with asymptomatic ischemia demonstrated on exercise testing and/or ambulatory monitoring. The data generally demonstrate a benefit from beta-blocker therapy, but not all trials have been positive. Lipid-lowering therapy in asymptomatic patients with documented CAD decreases the rate of adverse ischemic events.

Treatment of Risk Factors

In asymptomatic patients with documented CAD on the basis of noninvasive testing or coronary angiography, the treatment of risk factors outlined above is clearly appropriate. In the absence of documented CAD, asymptomatic patients should also undergo treatment of risk factors according to primary prevention standards.

Revascularization

In asymptomatic patients, revascularization cannot improve symptoms. The only appropriate indication for revascularization with either PCI or CABG is therefore to improve prognosis. Most of the recommendations for revascularization for patients with stable angina also apply to asymptomatic patients, as their underlying rationale is to improve prognosis. However, the level of evidence in support of these recommendations in asymptomatic patients is clearly weaker than in symptomatic patients.

Figure 1. Clinical Assessment

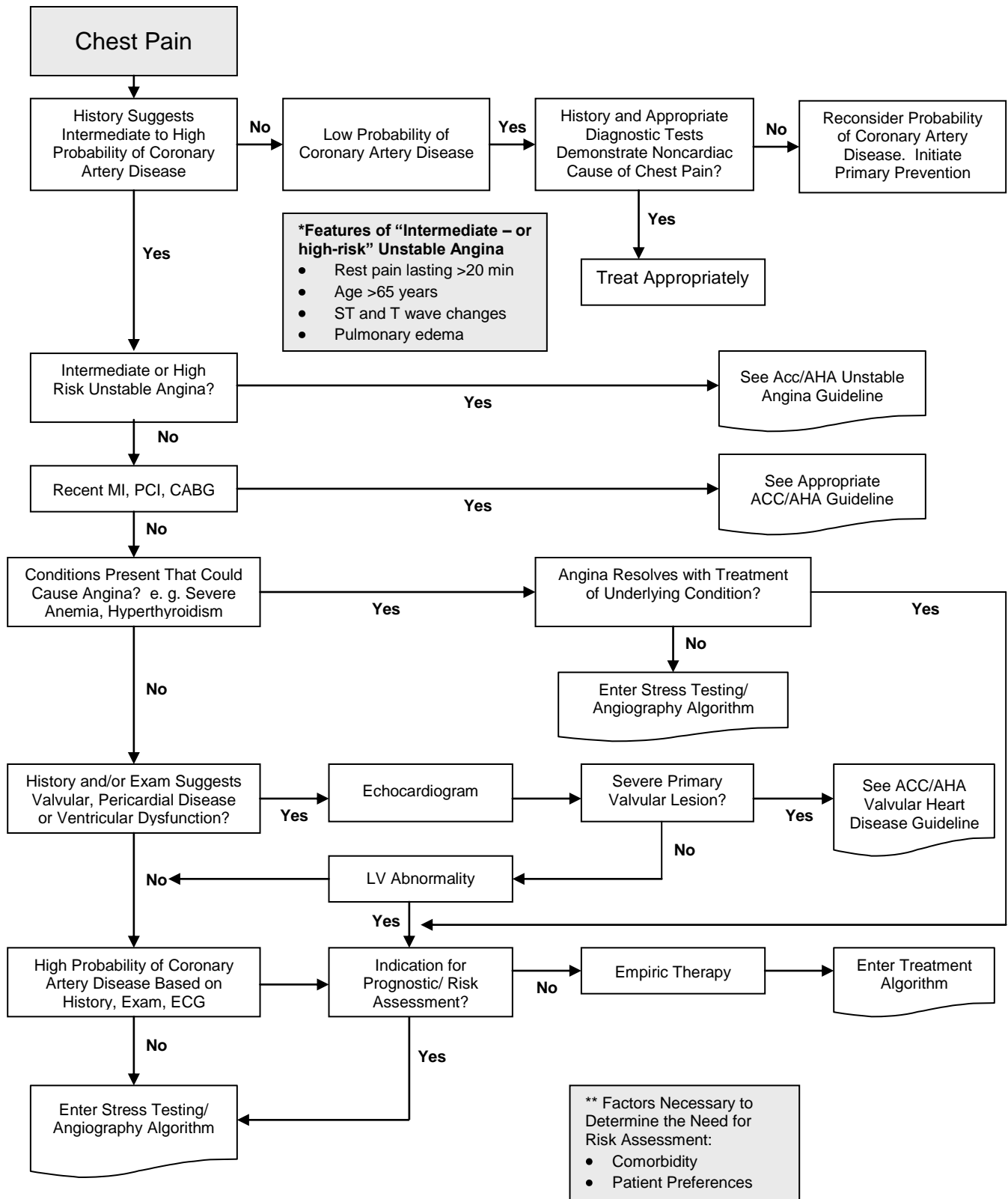


Figure 2. Stress Testing/Angiography

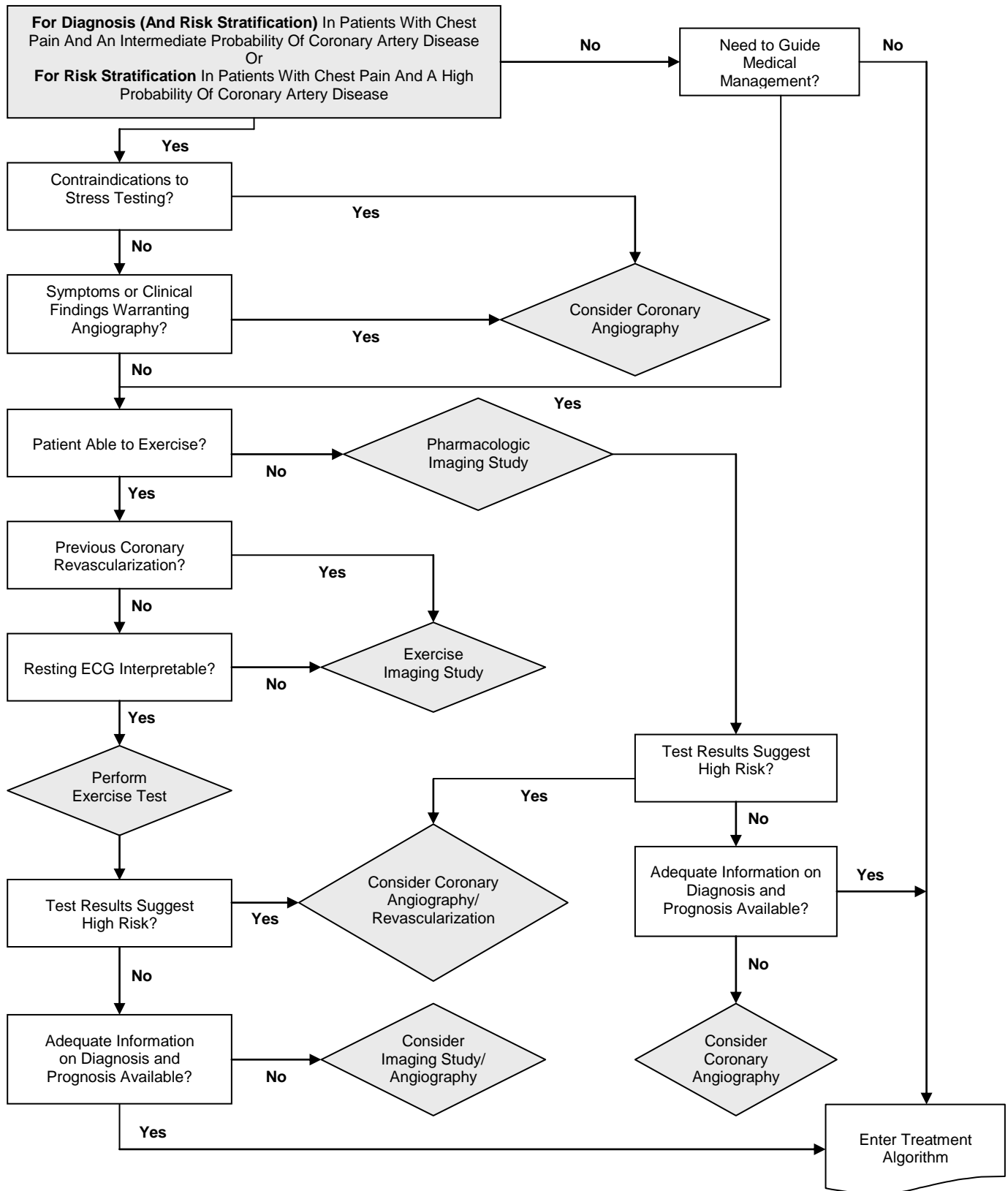
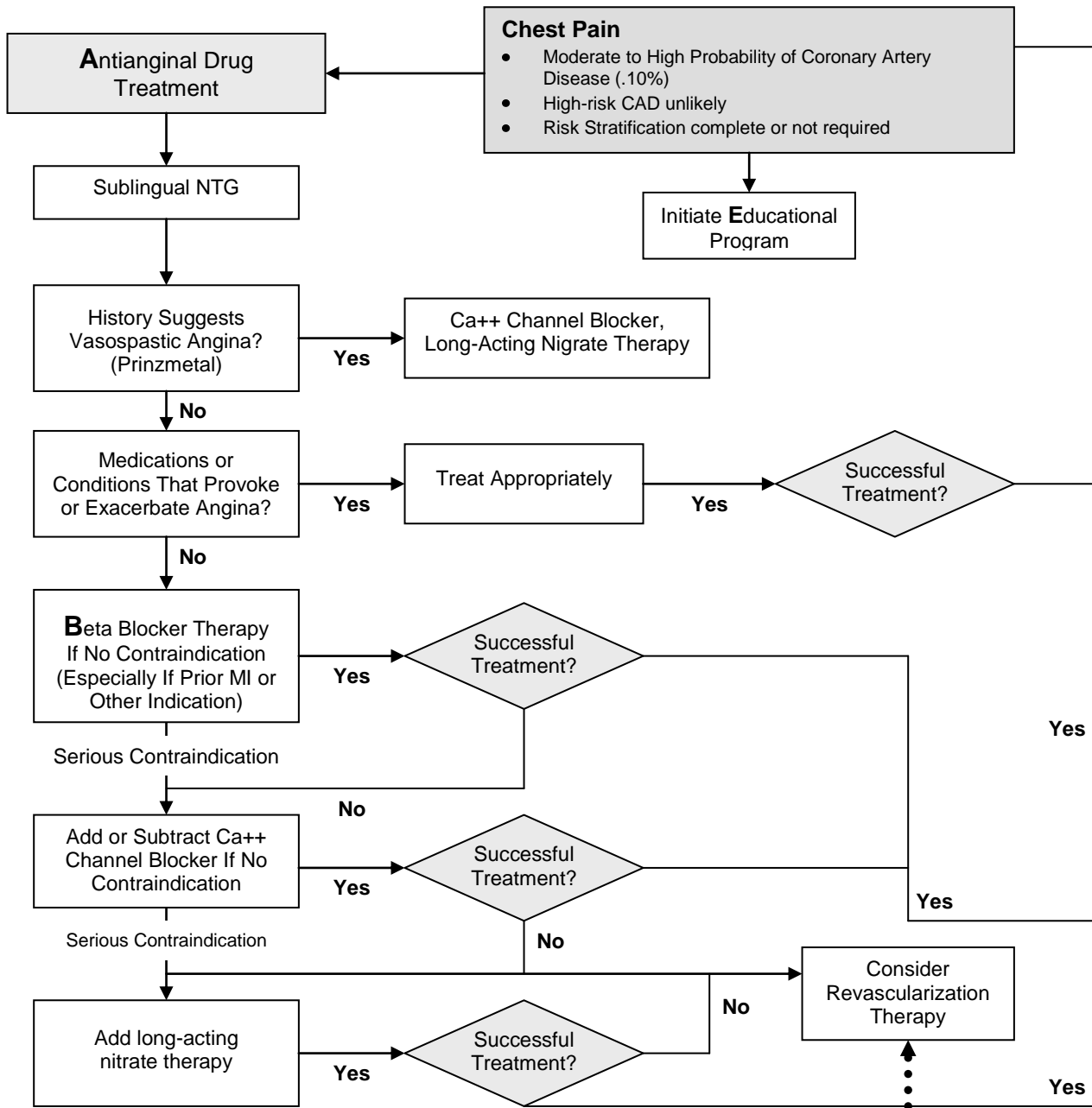


Figure 3. Treatment

NTG indicates nitroglycerin; LDL, low-density lipoprotein; ACE, angiotensin converting enzyme; NCEP, National Cholesterol Education Program; JNC, Joint National Committee; and AS, aortic stenosis.



Conditions That Exacerbate or Provoke Angina:

Medications:

- Vasodilators
- Excessive Thyroid Replacement
- Vasoconstrictors

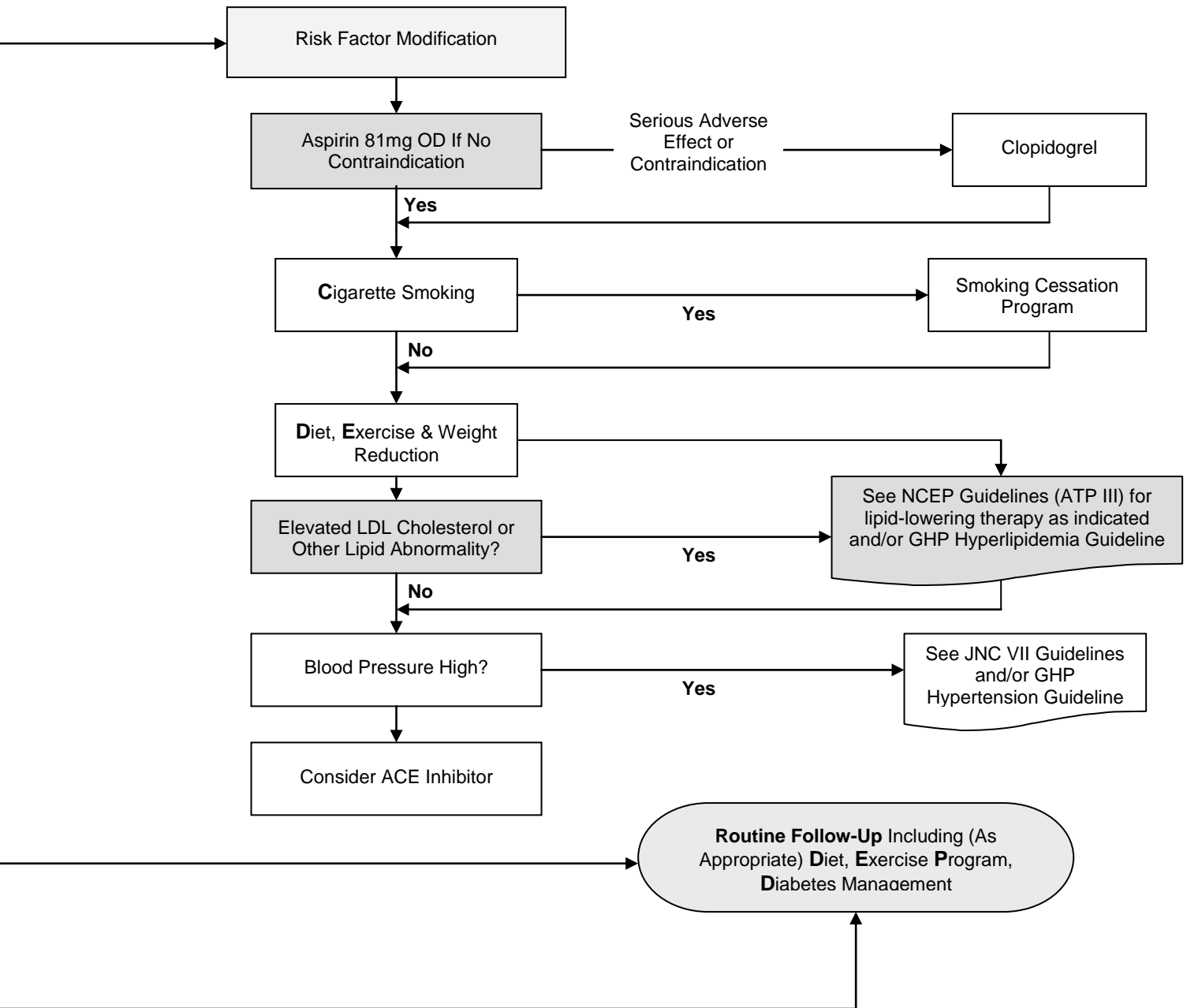
Other Medical Problems:

- Profound Anemia
- Uncontrolled Hypertension
- Hyperthyroidism
- Hypoxemia

Other Cardiac Problems:

- Tachyarrhythmias
- Bradyarrhythmias
- Valvular Heart Disease (especially AS)
- Hypertrophic Cardiomyopathy

Figure 3. Treatment (Continued)



** At any point in this process, based on coronary anatomy, severity of anginal symptoms and patient preferences, it is reasonable to consider evaluation for coronary revascularization. Unless a patient is documented to have left main, three-vessel, or two-vessel coronary artery disease with significant stenosis of the proximal left anterior descending coronary artery, there is no demonstrated survival advantage associated with revascularization in low-risk patients with chronic stable angina; thus, medical therapy should be attempted in most patients before considering PCI or CABG.

Table 1. Clinical Classification of Chest Pain

Typical angina (definite)

(1) Substernal chest discomfort with a characteristic quality and duration that is (2) provoked by exertion or emotional stress and (3) relieved by rest or nitroglycerin

Atypical angina (probable)

Meets 2 of the above characteristics

Noncardiac chest pain

Meets ≥ 1 of the typical angina characteristics

Table 2: Pretest Likelihood of CAD in Symptomatic Patients According to Age and Sex*

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

*Each Value represents percent with significant CAD on catheterization.

Table 3. Duke Treadmill Score: Calculation and Interpretation

Time in minutes on Bruce protocol	=
-5 x amount of depression (in mm)	= -
-4 x angina index, which is	0= no angina on test 1= angina, not limiting 2= limiting angina = -
Total score	
=	

Score	Risk Group	Annual Mortality
≥5	Low	0.25%
-10 to +4	Intermediate	1.25%
≤-11	High	5.25%

Table 4. Comparative Advantages of Stress Echocardiography and Stress Radionuclide Perfusion Imaging in Diagnosis of CAD

Advantages of Stress Echocardiography

1. Higher specificity
2. Versatility: more extensive evaluation of cardiac anatomy and function
3. Greater convenience/efficacy/availability
4. Lower cost

Advantages of Stress Perfusion Imaging

1. Higher technical success rate
2. Higher sensitivity, especially for 1-vessel coronary disease
3. Better accuracy in evaluating possible ischemia when multiple rest LV wall motion abnormalities are present
4. More extensive published database, especially in evaluation of prognosis

Table 5. Noninvasive Risk Stratification

High-Risk (Greater Than 3% Annual Mortality Rate)

1. Severe resting left ventricular dysfunction (LVEF < 35%)
2. High-risk treadmill score (score \leq -11)
3. Severe exercise left ventricular dysfunction (exercise LVEF <35%)
4. Stress-induced large perfusion defect (particularly if anterior)
5. Stress-induced multiple perfusion defects of moderate size
6. Large, fixed perfusion defect with LV dilation or increased lung uptake (thallium-201)
7. Stress-induced moderate perfusion defect with LV dilation or increased lung uptake (thallium-201)
8. Echocardiographic wall motion abnormality (involving greater than two segments) developing at low dose of dobutamine (\leq 10 mg/kg/min) or at a low heart rate (<120 beats/min)
9. Stress echocardiographic evidence of extensive ischemia

Intermediate-Risk (1%-3% annual mortality rate)

1. Mild/moderate resting left ventricular dysfunction (LVEF = 35% to 49%)
2. Intermediate-risk treadmill score (-11 < score < 5)
3. Stress-induced moderate perfusion defect without LV dilation or increased lung intake (thallium-201)
4. Limited stress echocardiographic ischemia with a wall motion abnormality only at higher doses of dobutamine involving less than or equal to two segments

Low-Risk (less than 1% annual mortality rate)

1. Low-risk treadmill score (score \geq 5)
2. Normal or small myocardial perfusion defect at rest or with stress*
3. Normal stress echocardiographic wall motion or no change of limited resting wall motion abnormalities during stress*

**Although the published data are limited, patients with these findings will probably not be at low-risk in the presence of either a high-risk treadmill score or severe resting left ventricular dysfunction (LVEF < 35%).*

Figure 4. Treatment Mnemonic

Aspirin and antianginals

Beta blocker and blood pressure

Cholesterol and cigarettes

Diet and diabetes

Education and Exercise

MEASURES

- Percent of members with LDL < 100
- Percent of members with LDL < 70
- Percent of members with anterior MI, diabetes or heart failure on ACE/ARB
 - Admits/1000
 - Inpatient days/1000
 - ER days/1000