Chronic Stable Angina

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Introduction

Angina pectoris is a clinical syndrome characterized by discomfort in the chest, jaw, back or arm typically aggravated by exertion or emotional stress and relieved by rest or nitroglycerin. Angina pectoris is usually associated with epicardial coronary artery disease including one or more obstructions of greater than 70%, but it can also occur in patients with valvular heart disease, hypertrophic cardiomyopathy, or uncontrolled hypertension. Symptoms are thought to result from regional or global myocardial ischemia due to mismatch between myocardial oxygen supply and demand (Table 1.1). In women, angina pectoris can be seen in the absence of obvious epicardial coronary artery obstruction or other cardiac pathology, presumably due to coronary artery endothelial dysfunction or other factors. Chronic stable angina refers to anginal symptoms that occur daily, weekly or less frequently and are typically predictable and reproducible [1–4].

Classification of angina pectoris

Chest discomfort can be described as typical angina, atypical angina or non-anginal chest pain, depending upon whether or not symptoms occur with increased myocardial oxygen demand and are relieved by rest or nitroglycerin. Typical angina is usually described as a sensation of chest tightness, heaviness, pressure, burning or squeezing sometimes accompanied by radiation to the inner arm, jaw, back or epigastrium. What makes the discomfort "typical" is the predictable relationship to increased activity (implying increased myocardial

Table 1.1 Conditions provoking or exacerbating ischemia

Increased oxygen demand	Decreased oxygen supply
Noncardiac	*Noncardiac*
Hyperthermia	Anemia
Hyperthyroidism	Hypoxemia
Sympathomimetic toxicity (e.g., cocaine use)	Pneumonia
Hypertension	Asthma
Anxiety	Chronic obstructive pulmonary disease
Arteriovenous fistulae	Pulmonary hypertension
	Interstitial pulmonary fibrosis
Cardiac	Obstructive sleep apnea
Hypertrophic cardiomyopathy	Sickle cell disease
Aortic stenosis	Sympathomimetic toxicity (e.g., cocaine use)
Dilated cardiomyopathy	Hyperviscosity
Tachycardia	Polycythemia
Ventricular	Leukemia
Supraventricular	Thrombocytosis
	Hypergammaglobulinemia
	Cardiac
	Aortic stenosis
	Hypertrophic cardiomyopathy

oxygen consumption) and subsequent relief with rest or NTG (Table 1.2).

The severity of angina pectoris is customarily described using the Canadian Cardiovascular Society Classification System (Table 1.3).

Table 1.2 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 NTG.

Atypical angina (probable)
Meets two of the above characteristics.

Noncardiac chest pain
Meets one or none of the typical anginal characteristics.

Modified from Diamond, IACC, 1983.

Demographics of angina pectoris

Coronary artery disease, the principal cause of angina pectoris, is thought to be present in 13,200,000 American adults, about half of whom (6,500,000 or 3.8% of the population) have angina pectoris or chest pain [4]. The incidence of stable angina is about 400,000 persons per year and there are an estimated 63,000 hospital discharges per year (2003) [4]. The annual mortality rate is hard to assess in the US since angina pectoris is rarely listed on death certificates as the cause of death. Data from the European Society of Cardiology estimates the annual mortality rate ranges from 0.9–1.4 % and the annual incidence of non-fatal MI ranges from 0.5–2.6% [3]. Only about 20% of cardiac events are preceded by long-standing angina [4].

Table 1.3 Grading of angina pectoris by the Canadian Cardiovascular Society Classification System

Class I
Ordinary physical activity does not cause angina, such as walking, climbing stairs. Angina (occurs) with strenuous, rapid or prolonged exertion at work or recreation.

Class II
Slight limitation of ordinary activity. Angina occurs on walking or climbing stairs rapidly, walking uphill, walking or stair climbing after meals, or in cold, or in wind, or under emotional stress, or only during the few hours after awakening. Angina occurs on walking more than 2 blocks on the level and climbing more than one flight of ordinary stairs at a normal pace and in normal condition.

Class III
Marked limitations of ordinary physical activity. Angina occurs on walking one to two blocks on the level and climbing one flight of stairs in normal conditions at a normal pace.

Class IV
Inability to carry on any physical activity without discomfort – anginal symptoms may be present at rest.

Source: Campeau L. Grading of angina pectoris [letter]. Circulation, 1976;54:522–523. Copyright © 1976. American Heart Association. Inc. Reprinted with permission.

Patients with new onset or changing anginal symptoms

Patients who present with a history of angina that has recently started or has changed in frequency, severity or pattern are often classified as having unstable angina. These patients can be subdivided by their short-term risk of death (Table 1.4). Patients at high or moderate risk often have an acute coronary syndrome caused by coronary artery plaques that have ruptured. Their risk of death is intermediate, between that of patients with acute MI and patients with stable angina. The initial evaluation of high- or moderate-risk patients with unstable angina is best carried out in the inpatient setting. However, low-risk patients with unstable angina have a short-term risk similar to that of patients with stable angina. Their evaluation can be accomplished safely and expeditiously in an outpatient setting. The recommendations made in these guidelines do not apply to patients with high- or moderate-risk unstable angina but are applicable to the low-risk unstable angina group.

The development of practice guidelines

The American College of Cardiology/American Heart Association Task Force on Practice Guidelines met in 2001 and 2002 to update the 1999 Guidelines for the Management of Patients with Chronic Stable Angina. This guideline was published in 2003. In 2007, a subgroup of the writing committee updated the 2002 Chronic Stable Guideline to be consistent with the AHA/ACC Guidelines for Secondary Prevention for Patients with Coronary and Other Atherosclerotic Vascular Disease. In 2006, the European Society of Cardiology [3] published its own guideline which differs somewhat from the ACC/AHA guideline. Both sets of guidelines will be considered in this chapter.

The Classification of Recommendations (COR) and Level of Evidence (LOE) are expressed in the ACC/AHA/ESC format (see table in front of book). These recommendations are evidence-based from published data where applicable.

Asymptomatic individuals

This chapter and the recommendations that follow are intended to apply to symptomatic patients. These were the focus of the original 1999 guideline. The 2002 update included additional sections and recommendations for asymptomatic patients with known or suspected coronary artery disease (CAD). Such individuals are often identified on the basis of evidence of a previous myocardial infarction by history and/or electrocardiographic changes, coronary angiography, or an abnormal noninvasive test, including coronary calcification on computed tomography (CT). Multiple ACC/AHA guidelines, scientific statements and expert consensus documents have discouraged the use of noninvasive tests, including ambulatory monitoring, treadmill testing, stress echocardiography, stress myocardial perfu-

Table 1.4 Short-term risk of death or nonfatal myocardial infarction in patients with unstable angina

High risk	Intermediate risk	Low risk
At least one of the following features must be present:	No high-risk features but must have any of the following:	No high- or intermediate-risk feature but may have any of the following:
Prolonged ongoing (>20 min) rest pain	Prolonged (>20 min) rest angina, now resolved, with moderate or high likelihood of CAD	Increased angina frequency, severity, or duration
Pulmonary edema, most likely related to ischemia	Rest angina (>20 min or relieved with sublingual nitroglycerin)	Angina provoked at a lower threshold
Angina at rest with dynamic ST changes ≥1 mm	Nocturnal angina	New onset angina with onset 2 weeks to 2 months prior to presentation
Angina with new or worsening MR murmur	Angina with dynamic T-ware changes	Normal or unchanged ECG
Angina with S_3 or new/worsening rales	New onset CCSC III or IV angina in the past 2 weeks with moderate or high likelihood of CAD	
Angina with hypotension	Pathologic Q waves or resting ST depression ≤1 mm in multiple lead groups (anterior, inferior, lateral)	
	Age >65 years	

CCSC indicates Canadian Cardiovascular Society Classification.

Note: Estimation of the short-term risks of death and nonfatal MI in unstable angina is a complex multivariable problem that cannot be fully specified in a table such as this. Therefore, the table is meant to offer general guidance and illustration rather than rigid algorithms.

sion, and CT, in asymptomatic individuals. Their inclusion in the 2002 guideline did not represent an endorsement of such tests for the purposes of screening, but rather an acknowledgment of the clinical reality that asymptomatic patients may present for further evaluation after abnormal tests. In general, the recommendations that appeared in the 2002 update for asymptomatic individuals were qualitatively similar to those that appear here for symptomatic patients. In some cases, either the class of the recommendation or the level of evidence, or both, were lower for asymptomatic patients. Interested readers may consult the 2002 guideline update on either the ACC or AHA website (www.americanheart.org or www.acc.org).

Recommendations for the management of patients with chronic stable angina

Note: Recommendations in **black** are from the ACC/AHA guideline and recommendations in **purple** are from the European Society of Cardiology guideline.

Diagnosis

A. History and physical examination

Recommendation

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 (i.e., ≤5%), intermediate (>5% and <90%), or high [≥90%]) (Tables 1.5 and 1.6). *(Level of Evidence: B)*

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; B)*

3 Fasting lipid panel, including total cholesterol, high density lipoprotein (HDL) cholesterol, triglycerides, and calculated low-density lipoprotein (LDL) cholesterol. *(Level of Evidence: C; B)*

Table 1.5 Pretest likelihood of CAD in symptomatic patients according to age and sex* (combined Diamond/Forrester and CASS Data)

	Nonanginal Chest pain		Atypical angina		Typical angina	
Age (years)	**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 the percent with significant CAD on catheterization.

Table 1.6 Comparing pretest likelihoods of CAD in low-risk symptomatic patients with high-risk symptomatic patients – Duke Database

	Nonanginal Chest pain		Atypical angina		Typical angina	
Age (years)	**Men**	**Women**	**Men**	**Women**	**Men**	**Women**
35 y	3–35	1–19	8–59	2–39	30–88	10–78
45 y	9–47	2–22	21–70	5–43	51–92	20–79
55 y	23–59	4–25	45–79	10–47	80–95	38–82
65 y	49–69	9–29	71–86	20–51	93–97	56–84

Each value represents the percent with significant CAD. The first is the percentage for a low-risk, mid-decade patient without diabetes, smoking, or hyperlipidemia. The second is that of the same age patient with diabetes, smoking, and hypelipidemia. Both high- and low-risk patients have normal resting ECGs. If ST-T-wave changes or Q waves had been present, the likelihood of CAD would be higher in each entry of the table.

4 Full blood count including Hb and white cell count *(Level of Evidence: B)*
5 Creatinine *(Level of Evidence: C)*
6 Markers of myocardial damage if evaluation suggests clinical instability or acute coronary syndrome *(Level of Evidence: A)*
7 Thyroid function if clinically indicated *(Level of Evidence: C)*

Class IIa
Oral glucose tolerance test *(Level of Evidence: B)*

Class IIb
1 Hs C-reactive protein *(Level of Evidence: B)*
2 Lipoprotein a, ApoA, and ApoB *(Level of Evidence: B)*
3 Homocysteine *(Level of Evidence: B)*
4 HbA1c *(Level of Evidence: B)*
5 NT-BNP *(Level of Evidence: B)*

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 A rest ECG in patients without an obvious noncardiac cause of chest pain is recommended. *(Level of Evidence: B)*
2 A rest ECG during an episode of chest pain is recommended. *(Level of Evidence: B)*
3 A chest X-ray in patients with signs or symptoms of congestive heart failure (CHF), valvular heart disease, pericardial disease, or aortic dissection/aneurysm is recommended. *(Level of Evidence: B)*
4 A resting ECG is recommended while the patient is pain-free. *(Level of Evidence: C)*

Class IIa

A chest X-ray in patients with signs or symptoms of pulmonary disease is reasonable. *(Level of Evidence: B)*

Class IIb

1 A chest X-ray in other patients may be considered. *(Level of Evidence: C)*

2 Electron-beam computed tomography may be considered. *(Level of Evidence: B)*

3 A routine periodic ECG in the absence of clinical change may be considered. *(Level of Evidence: C)*

2. Recommendations for diagnosis of obstructive CAD with exercise ECG testing without an imaging modality

Class I

Exercise ECG is recommended in patients with an intermediate pretest probability of CAD (>5% and <90%) based on age, gender, and symptoms, including those with complete right bundle-branch block or less than 1 mm of ST depression at rest (exceptions are listed below in classes II and III). *(Level of Evidence: B)* (See Tables 1.5 and 1.6).

Class IIa

Exercise ECG is reasonable in patients with suspected vasospastic angina. *(Level of Evidence: C)*

Class IIb

1 Exercise ECG may be considered in patients with a high pretest probability of CAD by age, gender, and symptoms. *(Level of Evidence: B)*

2 Exercise ECG may be considered in patients with a low pretest probability of CAD by age, gender, and symptoms. *(Level of Evidence: B)*

3 Exercise ECG may be considered in patients taking digoxin whose ECG has less than 1 mm of baseline ST-segment depression. *(Level of Evidence: B)*

4 Exercise ECG may be considered in patients with ECG criteria for LVH and less than 1 mm of baseline ST-segment depression. *(Level of Evidence: B)*

5 Routine periodic exercise ECG may be reasonable in the absence of clinical change. *(Level of Evidence: C)*

Class III

1 Exercise ECG is not recommended in patients with the following baseline ECG abnormalities.

a. Pre-excitation (Wolff–Parkinson–White) syndrome. *(Level of Evidence: B)*

b. Electronically paced ventricular rhythm. *(Level of Evidence: B)*

c. More than 1 mm of ST depression at rest. *(Level of Evidence: B)*

d. Complete left bundle-branch block. *(Level of Evidence: B)*

2 Exercise ECG is not recommended in patients with an established diagnosis of CAD owing to prior MI or coronary angiography; however, testing can assess functional capacity and prognosis, as discussed in Section III. *(Level of Evidence: B)*

3. Echocardiography: Recommendations for echocardiography for diagnosis of cause of chest pain in patients with suspected chronic stable angina pectoris

Class I

1 Echocardiography is recommended for patients with systolic murmur suggestive of aortic stenosis or hypertrophic cardiomyopathy *(Level of Evidence: C, B)*

2 Echocardiography is recommended for evaluation of extent (severity) of ischemia (e.g., LV segmental wall-motion abnormality) when the echocardiogram can be obtained during pain or within 30 min after its abatement. *(Level of Evidence: C)*

3 Echocardiography is recommended for patients with suspected heart failure *(Level of Evidence: B).*

4 Echocardiography is recommended for patients with prior MI *(Level of Evidence: B).*

5 Echocardiography is recommended for patients with LBBB, Q waves or other significant pathological changes on ECG, including electrocardiographic left anterior hemiblock *(Level of Evidence: C).*

Class IIb

Echocardiography may be considered in patients with a click or murmur to diagnose mitral valve prolapse [15]. *(Level of Evidence: C)*

Table 1.7 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 single vessel coronary disease involving the left circumflex
3. Better accuracy in evaluating possible ischemia when multiple resting IV wall motion abnormalities are present
4. More extensive published database – especially in evaluation of prognosis

Class III

Echocardiography is not recommended 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. *(Level of Evidence: C)*

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

See Table 1.7.

Class I

1 Exercise myocardial perfusion imaging or exercise echocardiography is recommended in patients with an intermediate pretest probability of CAD who have one of the following baseline ECG abnormalities:

a. Pre-excitation (Wolff–Parkinson–White) syndrome. *(Level of Evidence: B)*

b. More than 1 mm of ST depression at rest. *(Level of Evidence: B)*

2 Exercise myocardial perfusion imaging or exercise echocardiography is recommended in patients with prior revascularization (either PCI or CABG). *(Level of Evidence: B)*

3 Adenosine or dipyridamole myocardial perfusion imaging is recommended in patients with an intermediate pretest probability of CAD and one of the following baseline ECG abnormalities:

a. Electronically paced ventricular rhythm. *(Level of Evidence: C)*

b. Left bundle-branch block. *(Level of Evidence: B)*

4 Exercise myocardial perfusion imaging or exercise echocardiography is recommended in patients with a non-conclusive exercise ECG but reasonable exercise tolerance, who do not have a high probability of significant coronary disease and in whom the diagnosis is still in doubt. *(Level of Evidence: B)*

Class IIa

Exercise myocardial perfusion imaging or exercise echocardiography is reasonable in the following circumstances:

1 Patients with prior revascularization (PCI or CABG) in whom localization of ischaemia is important. *(Level of evidence: B)*

2 As an alternative to exercise ECG in patients where facilities, costs, and personnel resources allow. *(Level of evidence: B)*

3 As an alternative to exercise ECG in patients with a low pre-test probability of disease such as women with atypical chest pain. *(Level of Evidence: B)*

4 To assess functional severity of intermediate lesions on coronary arteriography. *(Level of Evidence: C)*

5 To localize ischaemia when planning revascularization options in patients who have already had arteriography. *(Level of Evidence: B)*

6 Pharmacological stress imaging techniques [either echocardiography or perfusion] are reasonable with the same Class I indications outlined above, where local facilities favor pharmacologic rather than exercise stress. *(Level of Evidence: B)*

Class IIb

1 Exercise myocardial perfusion imaging or exercise echocardiography may be considered in patients with a low or high probability of CAD who have one of the following baseline ECG abnormalities:

a. Pre-excitation (Wolff–Parkinson–White) syndrome. *(Level of Evidence: B)*

b. More than 1 mm of ST depression. *(Level of Evidence: B)*

2 Adenosine or dipyridamole myocardial perfusion imaging may be considered in patients with a low or high probability of CAD and one of the following baseline ECG abnormalities:

a. Electronically paced ventricular rhythm. *(Level of Evidence: C)*

b. Left bundle-branch block. *(Level of Evidence: B)*

3 Exercise myocardial perfusion imaging or exercise echocardiography may be considered in patients with an intermediate probability of CAD who have one of the following:

a. Digoxin use with less than 1 mm ST depression on the baseline ECG. *(Level of Evidence: B)*

b. LVH with less than 1 mm ST depression on the baseline ECG. *(Level of Evidence: B)*

4 Exercise myocardial perfusion imaging, exercise echocardiography, adenosine or dipyridamole myocardial perfusion imaging, or dobutamine echocardiography may be considered 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 may be considered in patients with left bundle-branch block. *(Level of Evidence: C)*

5. Recommendations for cardiac stress imaging as the initial test for diagnosis in patients with chronic stable angina who are unable to exercise

(Pharmacological stress with imaging techniques [either echocardiography or perfusion] is recommended in the initial assessment of angina with the same Class I, IIa and IIb indications outlined above, if the patient is unable to exercise adequately.)

Class I

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

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

Class IIb

1 Adenosine or dipyridamole stress myocardial perfusion imaging or dobutamine echocardiography may be considered 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 may be considered in patients with a low or a high probability of CAD and one of the following baseline ECG abnormalities:

a. Electronically paced ventricular rhythm. *(Level of Evidence: C)*

b. Left bundle-branch block. *(Level of Evidence: B)*

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

6. Recommendations for ambulatory ECG for initial diagnostic assessment of angina

Class I

An ambulatory ECG is recommended for angina with suspected arrhythmia. *(Level of Evidence: B)*

Class IIa

An ambulatory ECG may be reasonable for suspected vasospastic angina. *(Level of Evidence: C)*

7. Recommendations for the use of CT angiography in stable angina

Class IIb

CT angiography may be considered in patients with a low pre-test probability of disease, with a nonconclusive exercise ECG or stress imaging test. *(Level of Evidence: C)*

D. Invasive testing: value of 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

1 Coronary angiography is recommended in patients with known or possible angina pectoris who have survived sudden cardiac death. *(Level of Evidence: B)*

2 Coronary angiography is recommended in patients with severe stable angina (Class 3 or greater of Canadian Cardiovascular Society Classification, with a high pre-test probability of disease, particularly if the symptoms are inadequately responding to medical treatment.) *(Level of Evidence: B)*
3 Coronary angiography is recommended in patients with serious ventricular arrhythmias. *(Level of Evidence: C)*
4 Coronary angiography is recommended in patients previously treated by myocardial revascularization (PCI, CABG), who develop early recurrence of moderate or severe angina pectoris. *(Level of Evidence: C)*

Class IIa

1 Coronary angiography is reasonable in 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 Coronary angiography is reasonable in patients who cannot undergo noninvasive testing because of disability, illness, or morbid obesity. *(Level of Evidence: C)*
3 Coronary angiography is reasonable in patients with an occupational requirement for a definitive diagnosis. *(Level of Evidence: C)*
4 Coronary angiography is reasonable in patients who by virtue of young age at onset of symptoms, noninvasive imaging, or other clinical parameters are suspected of having a nonatherosclerotic cause for myocardial ischemia (coronary artery anomaly, Kawasaki disease, primary coronary artery dissection, radiation-induced vasculopathy). *(Level of Evidence: C)*
5 Coronary angiography is reasonable in patients in whom coronary artery spasm is suspected and provocative testing may be necessary. *(Level of Evidence: C)*
6 Coronary angiography is reasonable in patients with a high pretest probability of left main or three-vessel CAD. *(Level of Evidence: C)*
7 Coronary angiography is reasonable in patients with a high risk of restenosis after PCI, if PCI has been performed in a prognostically important site. *(Level of Evidence: C)*

Class IIb

1 Coronary angiography may be considered in patients with recurrent hospitalization for chest pain in whom a definite diagnosis is judged necessary. *(Level of Evidence: C)*
2 Coronary angiography may be considered in patients with an overriding desire for a definitive diagnosis and a greater-than-low probability of CAD. *(Level of Evidence: C)*

Class III

1 Coronary angiography is not recommended in patients with significant comorbidity in whom the risk of coronary arteriography outweighs the benefit of the procedure. *(Level of Evidence: C)*
2 Coronary angiography is not recommended in patients with an overriding personal desire for a definitive diagnosis and a low probability of CAD. *(Level of Evidence: C)*

Risk stratification

The recommendations that follow are for risk stratification by clinical evaluation, including ECG and laboratory tests, in stable angina.

A. Clinical evaluation

Class I

1 A detailed clinical history and physical examination is recommended including BMI and/or waist circumference in all patients, also including a full description of symptoms, quantification of functional impairment, past medical history, and cardiovascular risk profile. *(Level of Evidence: B)* (Figure 1.1).
2 Resting ECG in all patients is recommended. *(Level of Evidence: B)*

B. Noninvasive testing

Recommendations for measurement of rest LV function by echocardiography or radionuclide angiography in patients with chronic stable angina

Class I

1 Echocardiography or RNA is recommended in patients with a history of prior MI, pathologic Q waves, or symptoms or signs suggestive of heart

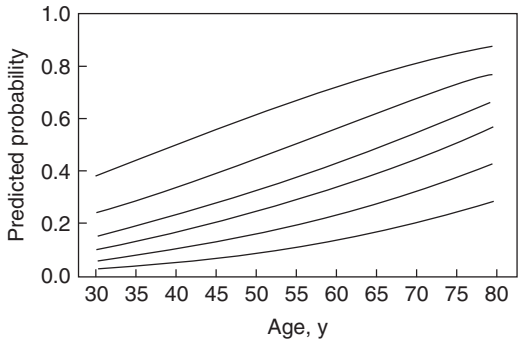

Fig. 1.1 Nomogram showing the probability of severe (three-vessel or left main) coronary disease based on a five-point score. One point is awarded for each of the following variables: male gender, typical angina, history and electrocardiographic evidence of myocardial infarction, diabetes and use of insulin. Each curve shows the probability of severe coronary disease as a function of age. From Hubbard *et al.* with permission.

failure to assess LV function. *(Level of Evidence: B)*

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

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

4 Resting echocardiography is recommended in patients with hypertension. *(Level of Evidence: B)*

5 Resting echocardiography is recommended in patients with diabetes. *(Level of Evidence: C)*

Class IIa

Resting echocardiography is recommended in patients with a normal resting ECG without prior MI who are not otherwise to be considered for coronary arteriography. *(Level of Evidence: C)*

Class III

1 Echocardiography or RNA is not recommended for routine periodic reassessment of stable patients for whom no new change in therapy is contemplated. *(Level of Evidence: C)*

2 Echocardiography or RNA is not recommended in patients with a normal ECG, no history of MI, and no symptoms or signs suggestive of CHF. *(Level of Evidence: B)*

Recommendations for exercise testing risk assessment and prognosis in patients with an intermediate or high probability of CAD

Class I

1 Exercise testing is recommended in patients undergoing initial evaluation. (Exceptions are listed below in Classes IIb and III) *(Level of Evidence: B)*

2 Exercise testing is recommended in patients after a significant change in cardiac symptoms. *(Level of Evidence: C)*. (Tables 1.8, 1.9 and 1.10).

Class IIa

Exercise testing is reasonable in patients post-revascularization with a significant deterioration in symptomatic status. *(Level of Evidence: B)*

Class IIb

1 Exercise testing may be considered in patients with the following ECG abnormalities:

a. Pre-excitation (Wolff-Parkinson-White) syndrome. *(Level of Evidence: B)*

b. Electronically paced ventricular rhythm. *(Level of Evidence: B)*

c. More than 1 mm of ST depression at rest. *(Level of Evidence: B)*

d. Complete left bundle-branch block. *(Level of Evidence: B)*

2 Exercise testing may be considered in patients who have undergone cardiac catheterization to identify ischemia in the distribution of coronary lesion of borderline severity. *(Level of Evidence: C)*

3 Exercise testing may be considered in post-revascularization patients who have a significant change in anginal pattern suggestive of ischemia. *(Level of Evidence: C)*

Class III

Exercise testing is not recommended in patients with severe comorbidity likely to limit life expectancy or prevent revascularization. *(Level of Evidence: C)*

Table 1.8 Survival according to risk groups based on Duke Treadmill Scores

Risk group (score)	Percentage of total	Four-year survival	Annual mortality (percent)
Low (≥+5)	62	0.99	0.25
Moderate (–10 to +4)	34	0.95	1.25
High (<–10)	4	0.79	5.0

The Duke treadmill score equals the exercise time in minutes minus (5 times the ST-segment deviation, during or after exercise, in millimeters).

Table 1.9 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 ≤–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 (≤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 ≥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%).

C. Use of exercise test results in patient management

Recommendation for exercise testing in patients with chest pain 6 months or more after revascularization

Class IIb

Exercise testing may be considered in patients with a significant change in anginal pattern suggestive of ischemia. *(Level of Evidence: B)*

Recommendations for cardiac stress imaging as the initial test for risk stratification of patients with chronic stable angina who are able to exercise

Class I

1 Exercise myocardial perfusion imaging or exercise echocardiography is recommended 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

Table 1.10 CAD Prognostic Index

Extent of CAD	Prognostic weight (0–100)	5-Year survival rate (%)*
1-vessel disease, 75%	23	93
>1-vessel disease, 50% to 74%	23	93
1-vessel disease, ≥95%	32	91
2-vessel disease	37	88
2-vessel disease, both ≥95%	42	86
1-vessel disease, ≥95% proximal LAD	48	83
2-vessel disease, ≥95% LAD	48	83
2-vessel disease, ≥95% proximal LAD	56	79
3-vessel disease	56	79
3-vessel disease, ≥95% m at least 1	63	73
3-vessel disease, 75% proximal LAD	67	67
3-vessel disease, ≥95% proximal LAD	74	59

*Assuming medical treatment only. CAD indicates coronary artery disease; LAD, left anterior descending artery. From Califf RM, Armstrong PW. Carver JR, *et al*: Task Force 5. Stratification of patients into high-, medium- and low-risk subgroups for purposes of risk factor management. J Am Coll Cardiol. 1996;27:964–1047.

who either have an abnormal rest ECG or are using digoxin. *(Level of Evidence: B)*

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

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

4 Exercise myocardial perfusion imaging or exercise echocardiography is recommended in patients with a non-conclusive exercise ECG, but intermediate or high probability of disease. *(Level of Evidence: B)*

Class IIa

1 Exercise myocardial perfusion imaging or exercise echocardiography is reasonable in patients with a deterioration in symptoms post-revascularization. *(Level of Evidence B)*

2 Exercise myocardial perfusion imaging or exercise echocardiography is reasonable as an alternative to exercise ECG in patients, in which facilities, cost, and personnel resources allow. *(Level of Evidence: B)*

3 Pharmacological stress imaging techniques [either echocardiography or perfusion] are reasonable with the same Class I indications outlined above, where local facilities favor pharmacologic rather than exercise stress *(Level of Evidence: B)*

Class IIb

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

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

Class III

1 Exercise myocardial perfusion imaging is not recommended in patients with left bundle-branch block. *(Level of Evidence: C)*

2 Exercise, dipyridamole, or adenosine myocardial perfusion imaging, or exercise or dobutamine echocardiography is not recommended 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 is recommended 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 is recommended 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 is recommended to assess the functional significance of coronary lesions (if not already known) in planning PCI. *(Level of Evidence: B)*

Class IIb

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

Class III

Dipyridamole or adenosine myocardial perfusion imaging or dobutamine echocardiography is not recommended in patients with severe comorbidity likely to limit life expectation or prevent revascularization. *(Level of Evidence: C)*

D. Coronary angiography and left ventriculography

Recommendations for coronary angiography for risk stratification in patients with chronic stable angina

See Figure 1.2.

Class I

1 Coronary angiography is recommended in patients with disabling (Canadian Cardiovascular Society [CCS] classes III and IV) chronic stable angina despite medical therapy. *(Level of Evidence: B)* (Table 1.11).

2 Coronary angiography is recommended in patients with high-risk criteria on noninvasive testing (Table 1.10) regardless of anginal severity. *(Level of Evidence: B)* (Table 1.11).

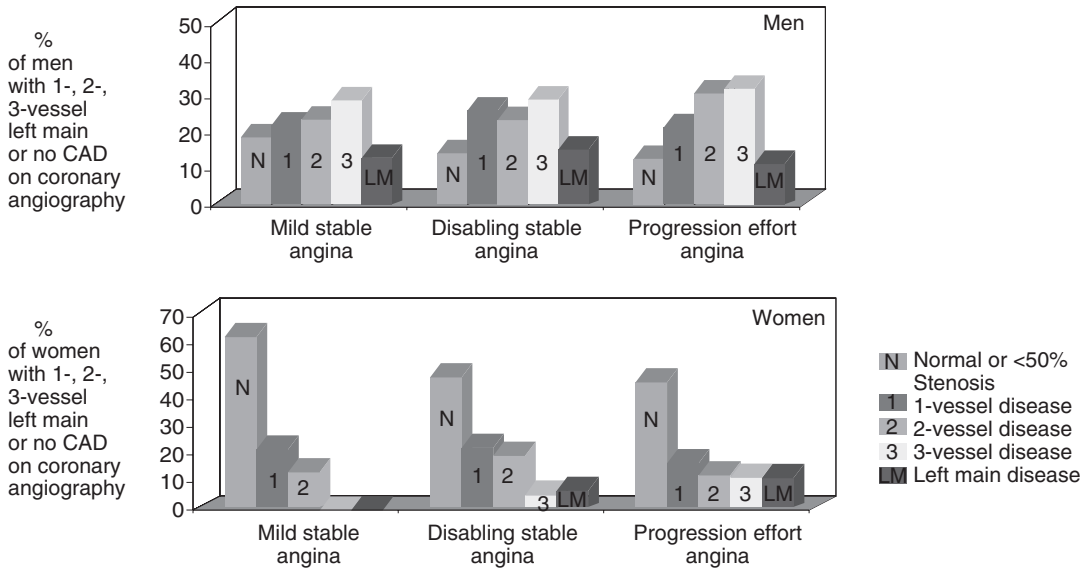

Fig. 1.2 Coronary angiography findings in patients with chronic effort-induced angina pectoris. Top: Percentage of men with one-vessel, two-vessel, three-vessel, left main or no coronary artery disease on coronary angioraphy. Bottom: Percentage of women with one-vessel, two-vessel, three-vessel, left main, or no coronary artery disease on coronary angiography. N indicates normal or <50% stenosis; 1, one-vessel disease; 2, two-vessel disease; 3, three-vessel disease; LM, left main disease. Data from Douglas and Hurst.

Table 1.11 Properties of beta-blockers in clinical use

Drugs	Selectivity	Partial agonist activity	Usual dose for angina
Propranolol	None	No	20–80 mg twice daily
Metoprolol	β_1	No	50–200 mg twice daily
Atenolol	β_1	No	50–200 mg/day
Nadolol	None	No	40–80 mg/day
Timolol	None	No	10 mg twice daily
Acebutolol	β_1	Yes	200–600 mg twice daily
Betaxolol	β_1	No	10–20 mg/day
Bisoprolol	β_1	No	10 mg/day
Esmolol (intravenous)	β_1	No	50–300 mcg/kg/min
Labetalol*	None	Yes	200–600 mg twice daily
Pindolol	None	Yes	2.5–7.5 mg 3 times daily

* Labetalol is a combined alpha- and β-blocker.

3 Coronary angiography is recommended in patients with angina who have survived sudden cardiac death or serious ventricular arrhythmia. *(Level of Evidence: B)*

4 Coronary angiography is recommended in patients with angina and symptoms and signs of CHF. *(Level of Evidence: C)*

5 Coronary angiography is recommended in patients with clinical characteristics that indicate a high likelihood of severe CAD. *(Level of Evidence: C)*

6 Coronary angiography is recommended in patients with stable angina in patients who are being considered for major noncardiac surgery, especially vascular surgery (repair of aortic aneurysm, femoral bypass, carotid endarterectomy) with intermediate or high risk features on noninvasive testing. *(Level of Evidence: B)*

Class IIa

1 Coronary angiography is reasonable in patients with significant LV dysfunction (ejection fraction less than 45%), CCS class I or II angina, and demonstrable ischemia but less than high-risk criteria on noninvasive testing. *(Level of Evidence: C)*

2 Coronary angiography is reasonable in patients with inadequate prognostic information after noninvasive testing. *(Level of Evidence: C)*

3 Coronary angiography is reasonable in patients with a high risk of restenosis after PCI, if PCI has been performed in a prognostically important site. *(Level of Evidence: C)*

Class IIb

1 Coronary angiography may be considered in patients with CCS class I or II angina, preserved LV function (ejection fraction greater than 45%), and less than high-risk criteria on noninvasive testing. *(Level of Evidence: C)*

2 Coronary angiography may be considered in patients with CCS class III or IV angina, which with medical therapy improves to class I or II. *(Level of Evidence: C)*

3 Coronary angiography may be considered in patients with CCS class I or II angina but intolerance (unacceptable side effects) to adequate medical therapy. *(Level of Evidence: C)*

Class III

1 Coronary angiography is not recommended in patients with CCS class I or II angina who respond to medical therapy and who have no evidence of ischemia on noninvasive testing. *(Level of Evidence: C)*

2 Coronary angiography is not recommended in patients who prefer to avoid revascularization. *(Level of Evidence: C)*

Recommendations for investigation in patients with the classical triad of Syndrome X

Class I

A resting echocardiogram is recommended in patients with angina and normal or non-obstructed

coronary arteries to assess for presence of ventricular hypertrophy and/or diastolic dysfunction. *(Level of Evidence: C)*

Class IIb

1 Intracoronary acetylcholine is reasonable during coronary arteriography, if the arteriogram is visually normal, to assess endothelium dependent coronary flow reserve, and exclude vasospasm. *(Level of Evidence: C)*

2 Intracoronary ultrasound, coronary flow reserve, or fractional flow reserve are reasonable measurements to exclude missed obstructive lesions, if angiographic appearances are suggestive of a non-obstructive lesion rather than completely normal, and stress imaging techniques identify an extensive area of ischaemia. *(Level of Evidence: C)*

Treatment

A. Pharmacologic therapy

Recommendations for pharmacotherapy to prevent MI and death and to reduce symptoms

Class I

1 Aspirin should be started at 75 to 162 mg per day (75 mg per day in ESC guideline) and continued indefinitely in all patients unless contraindicated. *(Level of Evidence: A)*

2 Beta-blockers as initial therapy is recommended to reduce symptoms in the absence of contraindications in patients with prior MI *(Level of Evidence: A)* or without prior MI. *(Level of Evidence: B)*

Test the effects of a beta-1 blocker, and titrate to full dose; consider the need for 24 h protection against ischemia. *(Level of Evidence: A)* (Table 1.12).

3 It is beneficial to start and continue beta-blocker therapy indefinitely in all patients who have had MI, acute coronary syndrome, or left ventricular dysfunction with or without heart failure symptoms, unless contraindicated. *(Level of Evidence: A)*

4 ACE inhibitors should be started and continued indefinitely in all patients with left ventricular ejection fraction less than or equal to 40% and in those with hypertension, diabetes, or chronic kidney disease unless contraindicated. *(Level of Evidence: A)*

5 ACE inhibitors should be started and continued indefinitely in patients who are not lower risk (lower risk defined as those with normal left ventricular ejection fraction in whom cardiovascular risk factors are well controlled and revascularization has been performed), unless contraindicated. *(Level of Evidence: B)*

Table 1.12 Nitroglycerin and nitrates in angina

Compound	Route	Dose	Duration of effect
Nitroglycerin	Sublingual tablets	0.3–0.6 mg up to 1.5 mg	$1^1/_2$–7 min
	Spray	0.4 mg as needed	Similar to sublingual tablets
	Ointment	2% 6 × 6 in., 15 × 15 cm 7.5–40 mg	Effect up to 7 h
	Transdermal	0.2–0.8 mg/h every 12 h	8–12 h during intermittent therapy
	Oral sustained release	2.5–13 mg	4–8 h
	Buccal	1–3 mg 3 times daily	3–5 h
	Intravenous	5–200 mcg/min	Tolerance in 7–8 h
Isosorbide dinitrate	Sublingual	2.5–15 mg	Up to 60 min
	Oral	5–80 mg, 2–3 times daily	Up to 8 h
	Spray	1.25 mg daily	2–3 min
	Chewable	5 mg	2–$2^1/_2$ h
	Oral slow release	40 mg 1–2 daily	Up to 8 h
	Intravenous	1.25–5.0 mg/h	Tolerance in 7–8 h
	Ointment	100 mg/24 h	Not effective
Isosorbide mononitrate	Oral	20 mg twice daily 60–240 mg once daily	12–24 h
Pentaerythritol tetranitrate	Sublingual	10 mg as needed	Not known
Erythritol tetranitrate	Sublingual	5–10 mg as needed	Not known
	Oral	10–30 3 times daily	Not known

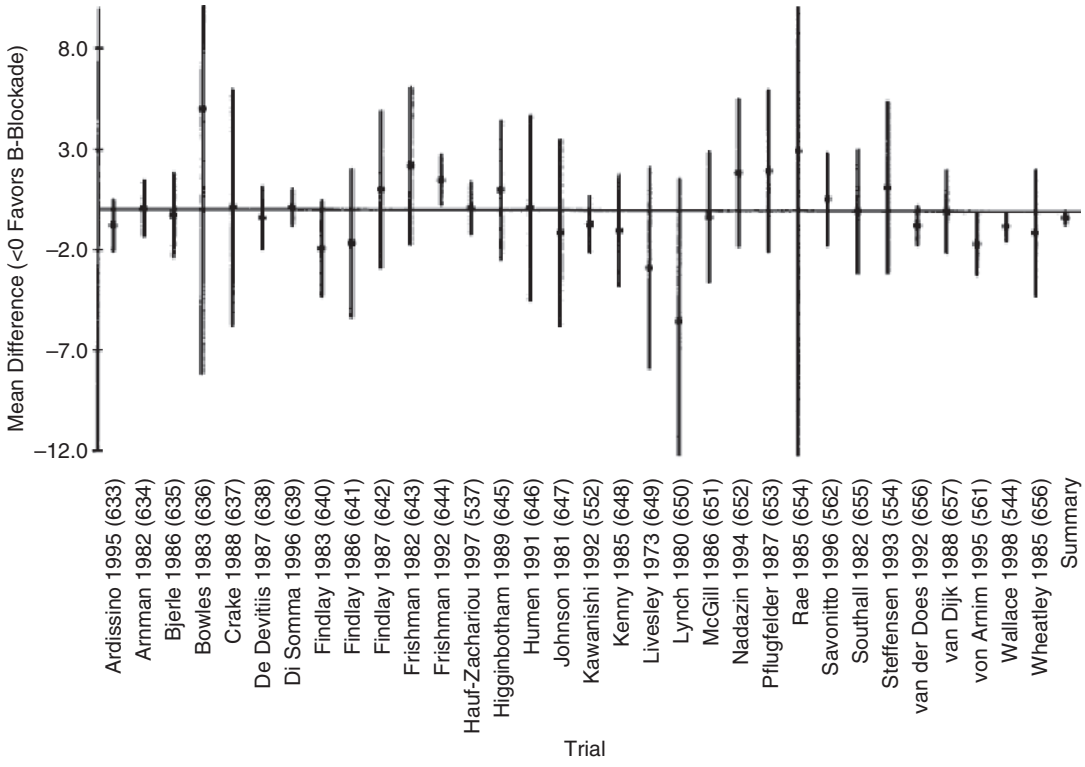

Fig. 1.3 Beta-blockers versus calcium antagonists: angina relief.
Source: Heidenreich PA, for the UCSF-Stanford Evidence-based Practice Center (AHCPR).

6 Sublingual nitroglycerin or nitroglycerin spray is recommended for the immediate relief of angina. *(Level of Evidence: B)*

7 Calcium antagonists or long-acting nitrates is recommended as initial therapy for reduction of symptoms when beta-blockers are contraindicated. *(Level of Evidence: B)* (Figure 1.3)

8 Calcium antagonists or long-acting nitrates is recommended in combination with beta-blockers when initial treatment with beta-blockers is not successful. *(Level of Evidence: B)* In case of beta-blocker intolerance or poor efficacy attempt monotherapy with a calcium channel blocker *(Level of Evidence: A)*, long acting nitrate *(Level of Evidence: C), or* nicorandil. *(Level of Evidence: C)* (Tables 1.13 and 1.14).

9 If the effects of beta-blocker monotherapy are insufficient, add a dihydropyridine calcium channel blocker. *(Level of Evidence: B)*

10 Calcium antagonists and long-acting nitrates are recommended as a substitute for beta-blockers if initial treatment with beta-blockers leads to unacceptable side effects. *(Level of Evidence: C)*

11 Angiotensin receptor blockers are recommended for patients who have hypertension, have indications for but are intolerant of ACE inhibitors, have heart failure, or have had a myocardial infarction with left ventricular ejection fraction less than or equal to 40%. *(Level of evidence: A)*

12 Aldosterone blockade is recommended for use in post-MI patients without significant renal dysfunction or hyperkalemia who are already receiving therapeutic doses of an ACE inhibitor and a beta blocker, have a left ventricular ejection fraction less than or equal to 40%, and have either diabetes or heart failure. (*Level of Evidence: A)*

Table 1.13 Recommended drug therapy (calcium antagonist vs. beta-blocker) in patients with angina and associated conditions

Condition	Recommended treatment (and alternative)	Avoid
Medical conditions		
Systemic hypertension	Beta-blockers (calcium antagonists)	
Migraine or vascular headaches	Beta-blockers (verapamil or diltiazem)	
Asthma or chronic obstructive pulmonary disease with bronchospasm	Verapamil or diltiazem	Beta-blockers
Hyperthyroidism	Beta-blockers	
Raynaud's syndrome	Long-acting slow-release calcium antagonists	Beta-blockers
Insulin-dependent diabetes mellitus	Beta-blockers (particularly if prior MI) or long-acting slow-release calcium antagonists	
Non-insulin–dependent diabetes mellitus	Beta-blockers or long-acting slow-release calcium antagonists	
Depression	Long-acting slow-release calcium antagonists	Beta-blockers
Mild peripheral vascular disease	Beta-blockers or calcium antagonists	
Severe peripheral vascular disease with rest ischemia	Calcium antagonists	Beta-blockers
Cardiac arrhythmias and conduction abnormalities		
Sinus bradycardia	Long-acting slow-release calcium antagonists that do not decrease heart rate	Beta-blockers, verapamil, diltiazem
Sinus tachycardia (not due to heart failure)	Beta-blockers	
Supraventricular tachycardia	Verapamil, diltiazem, or beta-blockers	
Atrioventricular block	Long-acting slow-release calcium antagonists that do not slow A-V conduction	Beta-blockers, verapamil, diltiazem
Rapid atrial fibrillation (with digitalis)	Verapamil, diltiazem, or beta-blockers	
Ventricular arrhythmias	Beta-blockers	
Left ventricular dysfunction		
Congestive heart failure		
Mild (LVEF $\geq$ 40%)	Beta-blockers	
Moderate to severe (LVEF $<$ 40%)	Amlodipine or felodipine (nitrates)	Verapamil, diltiazem
Left-sided valvular heart disease		
Mild aortic stenosis	Beta-blockers	
Aortic insufficiency	Long-acting slow-release dihydropyridines	
Mitral regurgitation	Long-acting slow-release dihydropyridines	
Mitral stenosis	Beta-blockers	
Hypertrophic cardiomyopathy	Beta-blockers, non-dihydropyridine calcium antagonist	Nitrates, dihydropyridine calcium antagonists

MI indicates myocardial infarction; LVEF, left ventricular ejection fraction.

Table 1.14 Randomized controlled trials examining the effects of exercise training on exercise capacity in patients with stable angina

First author	N	Men (%)	Setting	Intervention	F/C	Outcome
Ornish	46	N/A	Res	M	24 d	↑ ex. tolerance
Froelicher	146	100	OR	E	1 y	↑ ex. tolerance ↑ O_2 consumption
May	121	N/A	OR	E	10–12 mo	↑ O_2 consumption ↑ max HR-BP
Sebrechts	56	100	OR	E	1 y	↑ ex. duration
Oldridge	22	100	OR/H	E	3 mo	↑ O_2 consumption
Schuler	113	100	OR	M	1 y	↑ work capacity ↑ max HR-BP
Hambrecht	88	100	Hosp/H	M	1 y	↑ O_2 consumption ↑ ex. duration
Fletcher	88 Disabled	100	H	E	6 mo	NS (ex. duration or O_2 consumption)
Haskell	300	86	H	M	4 y	↑ ex. tolerance

Res indicates Residential facility. OR, Outpatient rehab; H, home; Hosp, Hospital; M, Multifactorial; E, Exercise training only; ↑, Statistically significant increase favoring intervention; NS, No significant difference between groups; N/A, Not available.

13 An annual influenza vaccination is recommended for patient with cardiovascular disease. (*Level of Evidence: B*)

14 Lipid management – see subsequent recommendations for treatment of risk factors.

Class IIa

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

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

3 It is reasonable to use ACE inhibitors among lower-risk patients with mildly reduced or normal left ventricular ejection fraction in whom cardiovascular risk factors are well controlled and revascularization has been performed. *(Level of Evidence: B)*

4 High-dose statin therapy is reasonable in high risk (>2% annual CV mortality) patients with proven coronary disease. *(Level of Evidence: B)*

5 In cases of beta-blocker intolerance try sinus node inhibitor *(Level of Evidence: B)*

6 If calcium channel blocker (CCB) monotherapy or combination therapy (CCB with beta-blocker) is unsuccessful, substitute the CCB with a long-acting nitrate or nicorandil. Be careful to avoid nitrate tolerance. *(Level of Evidence C)*

Class IIb

1 Low-intensity anticoagulation with warfarin may be considered in addition to aspirin. Use of warfarin in conjunction with aspirin and/or clopidogrel is associated with an increased risk of bleeding and should be monitored closely. *(Level of Evidence: B)*

2 Angiotensin receptor blockers may be considered in combination with ACE inhibitors for heart failure due to left ventricular systolic dysfunction. *(Level of Evidence: B)*

3 Fibrate therapy may be considered in patients with low HDL and high triglycerides who have diabetes or the metabolic syndrome. *(Level of Evidence: B)*

4 Fibrate or nicotinic acid as adjunctive therapy to statin may be considered in patients with low HDL and high triglycerides at high risk (>2% annual CV mortality). *(Level of Evidence: C)*

5 Metabolic agents may be used where available as add on therapy, or as substitution therapy when conventional drugs are not tolerated. *(Level of Evidence: B)*

Class III

1 Dipyridamole is not recommended. *(Level of Evidence: B)*

2 Chelation therapy (intravenous infusions of ethylenediamine tetraacetic acid of EDTA) is not recommended for the treatment of chronic angina or arteriosclerotic cardiovascular disease and may be harmful because of its potential to cause hypocalcemia. *(Level of Evidence: C)*

Recommendations for pharmacological therapy to improve symptoms in patients with Syndrome X

Class I

1 Therapy with nitrates, beta-blockers, and calcium antagonists alone or in combination are recommended. *(Level of Evidence: B)*

2 Statin therapy in patients with hyperlipidemia is recommended. *(Level of Evidence: B)*

3 ACE-inhibition in patients with hypertension is recommended. *(Level of Evidence: C)*

Class IIa

Trial of therapy with other anti-anginals including nicorandil and metabolic agents is reasonable. *(Level of Evidence: C)*

Class IIb

1 Aminophylline for continued pain despite Class I measures may be considered. *(Level of Evidence: C)*

2 Imipramine for continued pain despite Class I measures may be considered. *(Level of Evidence: C)*

Recommendations for pharmacological therapy of vasospastic angina

Class I

Treatment with calcium antagonists and if necessary nitrates in patients whose coronary arteriogram is normal or shows only non-obstructive lesions is recommended. *(Level of Evidence: B)*

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 Patients should initiate and/or maintain lifestyle modification-weight control; increased physical activity; moderation of alcohol consumption; limited sodium intake; and maintenance of a diet high in fresh fruits, vegetables, and low-fat dairy products. *(Level of Evidence: B)*

2 Blood pressure control according to Joint Nation Conference VII guidelines is recommended (i.e., blood pressure less than 140/90 mm Hg or less than 130/80 mm Hg for patients with diabetes or chronic kidney disease). *(Level of Evidence: A)*

3 For hypertensive patients with well established coronary artery disease, it is useful to add blood pressure medication as tolerated, treating initially with beta blockers and/or ACE inhibitors, with addition of other drugs as needed to achieve target blood pressure. *(Level of Evidence: C)*

4 Smoking cessation and avoidance of exposure to environmental tobacco smoke at work and home is recommended. Follow-up, referral to special programs, and/or pharmacotherapy (including nicotine replacement) is recommended, as is a stepwise strategy for smoking cessation (Ask, Advise, Assess, Assist, Arrange). *(Level of Evidence: B)*

5 Diabetes management should include lifestyle and pharmacotherapy measures to achieve a near-normal HbA_{1c}. (*Level of Evidence: B)*

6 Vigorous modification of other risk factors (e.g., physical activity, weight management, blood pressure control, and cholesterol management) as recommended should be initiated and maintained. *(Level of Evidence: B)*

7 Physical activity of 30 to 60 minutes, 7 days per week (minimum 5 days per week) is recommended. All patients should be encouraged to obtain 30 to 60 minutes of moderate-intensity aerobic activity, such as brisk walking, on most, preferably all, days of the week, supplemented by an increase in daily activities (such as walking breaks at work, gardening, or household work). *(Level of Evidence: B)*.

8 The patient's risk should be assessed with a physical activity history. Where appropriate, an exercise test is useful to guide the exercise prescription. *(Level of Evidence: B)*

9 Medically supervised programs (cardiac rehabilitation) are recommended for at-risk patients (e.g., recent acute coronary syndrome or revascularization, heart failure). *(Level of Evidence: B)*

10 Dietary therapy for all patients should include reduced intake of saturated fats (to less than 7% of

total calories), trans-fatty acids, and cholesterol (to less than 200 mg per day). *(Level of Evidence: B)*

11 Daily physical activity and weight management are recommended for all patients. *(Level of Evidence: B)*

12 Recommended lipid management includes assessment of a fasting lipid profile. *(Level of Evidence: A)*

13 LDL-C should be less than 100 mg per dL. *(Level of Evidence: A)*

14 If baseline LDL-C is greater than or equal to 100 mg per dL, LDL-lowering drug therapy should be initiated in addition to therapeutic lifestyle changes. When LDL-lowering medications are used in high-risk or moderately high-risk persons, it is recommended that intensity of therapy be sufficient to achieve a 30% to 40% reduction in LDL-C levels. *(Level of Evidence: A)*

15 If on treatment LDL-C is greater than or equal to 100 mg per dL, LDL-lowering drug therapy should be intensified. (*Level of Evidence: A)*

16 If TG are 200 to 499 mg per dL, non-HDL-C should be less than 130 mg per dL. *(Level of Evidence: A)*

17 BMI and waist circumference should be assessed regularly. On each patient visit, it is useful to consistently encourage weight maintenance/reduction through an appropriate balance of physical activity, caloric intake, and formal behavioral programs when indicated to achieve and maintain a BMI between 18.5 and 24.9 kg/m^2. *(Level of Evidence: B)*

18 If waist circumference is greater than or equal to 35 inches (89 cm) in women or greater than or equal to 40 inches (102 cm) in men it is beneficial to initiate lifestyle changes and consider treatment strategies for metabolic syndrome as indicated. Some male patients can develop multiple metabolic risk factors when the waist circumference is only marginally increased, e.g., 37 to 40 inches (94 to 102 cm). Such persons may have a strong genetic contribution to insulin resistance. They should benefit from changes in life habits, similarly to men with categorical increases in waist circumference. *(Level of Evidence: B)*

19 The initial goal of weight loss therapy should be to gradually reduce body weight by approximately 10% from baseline. With success, further weight loss can be attempted if indicated through further assessment. *(Level of Evidence: B)*

Class IIa

1 Adding plant stanol/sterols (2 g per day) and/or viscous fiber (greater than 10 g per day) is reasonable to further lower LDL-C. *(Level of Evidence: A)*

2 Reduction of LDL-C to less than 70 mg per dL or high-dose statin therapy is reasonable. *(Level of Evidence: A)*

3 If baseline LDL-C is 70 to 100 mg per dL, it is reasonable to treat LDL-C to less than 70 mg per dL. *(Level of Evidence: B)*

4 Further reduction of non-HDL-C to less than 100 mg per dL is reasonable.

5 If TG are greater than or equal to 200 to 499 mg per dL therapeutic options to reduce non-HDL-C are:

a. niacin can be useful as a therapeutic option to reduce non-HDL-C (after LDL-C-lowering therapy) or

b. fibrate therapy as a therapeutic option can be useful to reduce non-HDL-C (after LDL-C lowering therapy. *(Level of Evidence: B)*

6 The following lipid management strategies can be beneficial: If LDL-C less than 70 mg per dL is the chosen target, consider drug titration to achieve this level to minimize side effects and cost. When LDL-C less than 70 mg per dL is not achievable because of high baseline LDL-C levels, it generally is possible to achieve reductions of greater than 50% in LDL-C levels by either statins or LDL-C-lowering drug combinations.*(Level of Evidence: C)*

Class IIb

1 Folate therapy may be considered in patients with elevated homocysteine levels. *(Level of Evidence: C)*

2 Identification and appropriate treatment of clinical depression may be considered to improve CAD outcomes. *(Level of Evidence: C)*

3 Intervention directed at psychosocial stress reduction may be considered. *(Level of Evidence: C)*

4 Expanding physical activity to include resistance training on 2 days per week may be reasonable. *(Level of Evidence: C)*

5 For all patients, encouraging consumption of omega-T fatty acids in the form of fish or in capsule form (1 g per day) for risk reduction may be reasonable. For treatment of elevated TG, higher doses are usually necessary for risk reduction. *(Level of Evidence: B)*

Class III

1 Initiation of hormone replacement therapy in postmenopausal women is not recommended for the purpose of reducing cardiovascular risk. *(Level of Evidence: A)*

2 Vitamin C and E supplementation is not recommended. *(Level of Evidence: A)*

3 Chelation therapy (intravenous infusions of ethylenediamine tetraacetic acid of EDTA) is not recommended for the treatment of chronic angina or arteriosclerotic cardiovascular disease and may be harmful because of its potential to cause hypocalcemia. *(Level of Evidence: C)*

4 Garlic is not recommended. *(Level of Evidence: C)*

5 Acupuncture is not recommended. *(Level of Evidence: C)*

6 Coenzyme Q is not recommended. *(Level of Evidence: C)*

Recommendations for revascularization with PCI (or other catheter-based techniques) and CABG in patients with stable angina

Class I

1 Coronary artery bypass grafting is recommended for patients with significant left main coronary disease. *(Level of Evidence: A)*

2 Coronary artery bypass grafting is recommended for patients with three-vessel disease. The survival benefit is greater in patients with abnormal LV function (ejection fraction less than 50%). *(Level of Evidence: A)*

3 Coronary artery bypass grafting is recommended for patients with two-vessel disease with significant proximal LAD CAD and either abnormal LV function (ejection fraction less than 50%) or demonstrable ischemia on noninvasive testing. *(Level of Evidence: A)*

4 CABG is recommended for significant disease with impaired LV function and viability demonstrated by noninvasive testing. *(Level of Evidence: B)*

5 Percutaneous coronary intervention is recommended for patients with two- or three-vessel disease with significant proximal LAD CAD, who have anatomy suitable for catheter-based therapy and normal LV function and who do not have treated diabetes. *(Level of Evidence: B)*

6 Percutaneous coronary intervention or CABG is recommended for patients with one- or two-vessel CAD without significant proximal LAD CAD but with a large area of viable myocardium and high-risk criteria on noninvasive testing. *(Level of Evidence: B)*

7 Coronary artery bypass grafting is recommended for patients with one- or two-vessel CAD without significant proximal LAD CAD who have survived sudden cardiac death or sustained ventricular tachycardia. *(Level of Evidence: C)*

8 In patients with prior PCI, CABG or PCI is recommended for recurrent stenosis associated with a large area of viable myocardium or high-risk criteria on noninvasive testing. *(Level of Evidence: C)*

9 Percutaneous coronary intervention or CABG is recommended for patients who have not been successfully treated by medical therapy (see text) and can undergo revascularization with acceptable risk. *(Level of Evidence: B)*

Class IIa

1 Repeat CABG is reasonable for patients with multiple saphenous vein graft stenoses, especially when there is significant stenosis of a graft supplying the LAD. It may be appropriate to use PCI for focal saphenous vein graft lesions or multiple stenoses in poor candidates for reoperative surgery. *(Level of Evidence: C)*

2 Use of PCI or CABG is reasonable for patients with one- or two-vessel CAD without significant proximal LAD disease but with a moderate area of viable myocardium and demonstrable ischemia on noninvasive testing. *(Level of Evidence: B)*

3 Use of PCI or CABG is reasonable for patients with one-vessel disease with significant proximal LAD disease. *(Level of Evidence: B)*

4 CABG is reasonable for single- or two-vessel CAD without significant proximal LAD stenosis in patients who have survived sudden cardiac death or sustained ventricular tachycardia. *(Level of Evidence: B)*

5 CABG is reasonable for significant three vessel disease in diabetics with reversible ischaemia on functional testing. *(Level of Evidence: C)*

6 PCI or CABG is reasonable for patients with reversible ischaemia on functional testing and evidence of frequent episodes of ischaemia during daily activities. *(Level of Evidence: C)*

Class IIb

1 Compared with CABG, PCI may be considered for patients with two- or three-vessel disease with significant proximal LAD CAD, who have anatomy suitable for catheter-based therapy, and who have treated diabetes or abnormal LV function. *(Level of Evidence: B)*

2 Use of PCI may be considered for patients with significant left main coronary disease who are not candidates for CABG. *(Level of Evidence: C)*

3 PCI may be considered for patients with one- or two-vessel CAD without significant proximal LAD CAD who have survived sudden cardiac death or sustained ventricular tachycardia. *(Level of Evidence: C)*

Class III

1 Use of PCI or CABG is not recommended for patients with one- or two vessel CAD without significant proximal LAD CAD, who have mild symptoms that are unlikely due to myocardial ischemia, or who have not received an adequate trial of medical therapy and

a. have only a small area of viable myocardium or

b. have no demonstrable ischemia on noninvasive testing. *(Level of Evidence: C)*

2 Use of PCI or CABG is not recommended for patients with borderline coronary stenoses (50% to 60% diameter in locations other than the left main coronary artery) and no demonstrable ischemia on noninvasive testing. *(Level of Evidence: C)*

3 Use of PCI or CABG is not recommended for patients with insignificant coronary stenosis (less than 50% diameter). *(Level of Evidence: C)*

4 Use of PCI is not recommended in patients with significant left main coronary artery disease who are candidates for CABG. *(Level of Evidence: B)*

Recommendations for revascularization to improve symptoms in patients with stable angina

Class I

1 CABG for multi-vessel disease (MVD) technically suitable for surgical revascularization is recommended in patients with moderate to severe symptoms not controlled by medical therapy, in whom risks of surgery do not outweigh potential benefits. *(Level of Evidence: A)*

2 PCI for single vessel disease technically suitable for percutaneous revascularization is recommended in patients with moderate to severe symptoms not controlled by medical therapy, in whom procedural risks do not outweigh potential benefits. *(Level of Evidence: A)*

3 PCI for MVD without high risk coronary anatomy, technically suitable for percutaneous revascularization is recommended in patients with moderate to severe symptoms not controlled by medical therapy and in whom procedural risks do not outweigh potential benefits. *(Level of Evidence: A)*

Class IIa

1 PCI for single vessel disease technically suitable for percutaneous revascularization is reasonable in patients with mild to moderate symptoms which are nonetheless unacceptable to the patient, in whom procedural risks do not outweigh potential benefits. *(Level of Evidence: A)*

2 CABG for single vessel disease technically suitable for surgical revascularization is reasonable in patients with moderate to severe symptoms not controlled by medical therapy, in whom operative risk does not outweigh potential benefit. *(Level of Evidence: A)*

3 CABG in MVD technically suitable for surgical revascularization is reasonable in patients with mild to moderate symptoms, which are nonetheless unacceptable to the patient, in whom operative risk does not outweigh potential benefit. *(Level of Evidence: A)*

4 PCI for MVD technically suitable for percutaneous revascularization is reasonable in patients with mild to moderate symptoms, which are nonetheless unacceptable to the patient, in whom procedural risks do not outweigh potential benefits. *(Level of Evidence: A)*

Class IIb

CABG in single vessel disease technically suitable for surgical revascularization may be considered in patients with mild-to-moderate symptoms, which are nonetheless unacceptable to the patient, in whom operative risk is not greater than estimated annual mortality. *(Level of Evidence: B)*

Recommendations for alternative therapies for chronic stable angina in patients refractory to medical therapy who are not candidates for percutaneous intervention or surgical revascularization

Class IIa

Surgical laser transmyocardial revascularization is reasonable. *(Level of Evidence: A)*

Class IIb

1 Enhanced external counterpulsation may be considered. *(Level of Evidence: B)*

2 Spinal cord stimulation may be considered. *(Level of Evidence: B)*

Patient follow-up: monitoring of symptoms and anti-anginal therapy

Recommendations for echocardiography, treadmill exercise testing, stress radionuclide imaging, stress echocardiography studies, and coronary angiography during patient follow-up

Class I

1 A chest X-ray is recommended for patients with evidence of new or worsening CHF. *(Level of Evidence: C)*

2 Assessment of LV ejection fraction and segmental wall motion by echocardiography or radionuclide imaging is recommended in patients with new or worsening CHF or evidence of intervening MI by history or ECG. *(Level of Evidence: C)*

3 Echocardiography is recommended for evidence of new or worsening valvular heart disease. *(Level of Evidence: C)*

4 Treadmill exercise test is recommended 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 radionuclide imaging or stress echocardiography procedures are recommended for patients without prior revascularization who have a significant change in clinical status and are unable to exercise or have one of the following ECG abnormalities:

a. Pre-excitation (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 radionuclide imaging or stress echocardiography procedures are recommended 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 radionuclide imaging or stress echocardiography procedures are recommended for patients with prior revascularization who have a significant change in clinical status. *(Level of Evidence: C)*

8 Coronary angiography is recommended 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 may be considered in patients who have no change in clinical status, can exercise, have none of the ECG abnormalities listed in number 5, and have an estimated annual mortality rate greater than 1%. *(Level of Evidence: C)*

Class III

1 Echocardiography or radionuclide imaging is not recommended for assessment of LV ejection fraction and segmental wall motion in patients with a normal ECG, no history of MI, and no evidence of CHF. *(Level of Evidence: C)*

2 Repeat treadmill exercise testing is not recommended in less than three years in patients who have no change in clinical status and an estimated annual mortality rate less than 1% on their initial evaluation, as demonstrated by one 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 or echocardiography is not recommended 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 or echocardiographic procedure on their initial evaluation because of equivocal or intermediate-risk treadmill results. *(Level of Evidence: C)*
4 Repeat coronary angiography is not recommended 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)*

Future issues

Since publication of these guideline recommendations in 2002, important new evidence has been published. As a result of this new evidence, the next revision of the guidelines, which is currently underway, will likely reflect changes in the following areas:

Special consideration for women

Recent evidence, particularly from the NHLBI-sponsored Women's Ischemic Syndrome Evaluation (WISE) Study [5,6], has suggested that traditional approaches significantly underestimate the presence of obstructive CAD in women, particularly younger women. Moreover, many women without obstructive disease continue to have symptoms and a poor quality of life [7,8]. Many have evidence of microvascular dysfunction [9]. There is growing interest in the development of gender-specific tools for the assessment of ischemic heart disease in women, but the evidence is not yet robust enough to support the widespread use of a new approach.

New information on percutaneous revascularization to be considered for the next chronic stable angina guideline

As listed above, the 2002 guidelines included a Class I recommendation for PCI or CABG in symptomatic or asymptomatic patients with "one- or two-vessel CAD . . . with high risk criteria on noninvasive testing." A randomized trial reported in 2007 has challenged the assumption that revascularization improves patient outcomes in many patients with multi-vessel coronary disease. The COURAGE (Clinical Outcomes Utilizing Revascularization and Aggressive Drug Evaluation) trial – the largest reported randomized clinic trial on coronary artery disease to date – enrolled 2287 patients with significant coronary artery disease and inducible ischemia. In contrast to previous trials, medical therapy in the COURAGE trial focused not only on symptomatic relief, but also risk factor reduction. Medical therapy resulted in very high rates of adherence to the recommendations for blood pressure, lipid levels, exercise, diet, and smoking cessation that are detailed above. When added to such medical therapy, PCI did not provide any advantage for the primary endpoint of death or myocardial infarction. Future revisions of the stable angina clinic practice guideline will consider the results of COURAGE. Although we do not want to prejudge the careful rigorous process of guideline development, it certainly seems likely that the indications for revascularization in asymptomatic patients, and in selected symptomatic patients, are likely to be more cautious than those listed above [10–12].

New therapeutic agents to be considered for the next chronic stable angina guideline

Ranolazine is a novel therapeutic agent recently approved by the FDA for the treatment of refractory angina. It appears to reduce anginal episodes and to increase exercise tolerance without increasing cardiovascular risk despite a potential to increase the QT interval. Varenicline is a partial nicotine receptor agonist that shows great promise to help patients overcome addiction to smoking. Both of these agents will be thoroughly assessed by the next chronic stable angina writing group with a new guideline expected in late 2008 [13–18].

References available online at www.Wiley.com/go/AHAGuidelineHandbook.

During the production of this book this relevant AHA statement and guideline was published: ACCF/ASE/ACEP/AHA/ASNC/SCAI/SCCT/SCMR 2008 Appropriateness Criteria for Stress Echocardiography, http://circ.ahajournals.org/cgi/content/full/117/11/1478.