CLINICAL PRACTICE

Chronic Stable Angina

Jonathan Abrams, M.D.

This Journal *feature begins with a case vignette highlighting a common clinical problem. Evidence supporting various strategies is then presented, followed by a review of formal guidelines, when they exist. The article ends with the author's clinical recommendations.*

A 47-year-old man reports a six-month history of intermittent chest discomfort while playing squash. He describes lower substernal tightness with numbness of the left upper arm only during exertion. He does not smoke. His father died suddenly at the age of 49 years. His blood pressure is 138/84 mm Hg. The level of total cholesterol is 261 mg per deciliter (6.7 mmol per liter), of low-density lipoprotein cholesterol 172 mg per deciliter (4.4 mmol per liter), and of high-density lipoprotein cholesterol 50 mg per deciliter (1.3 mmol per liter), and the triglyceride level is 113 mg per deciliter (2.9 mmol per liter). The result of an exercise test is positive, with pain and 1.5 mm of horizontal ST-segment depression at stage 4 of the Bruce protocol. How should the patient's case be managed?

THE CLINICAL PROBLEM

The diagnosis of chronic stable angina pectoris includes predictable and reproducible left anterior chest discomfort after physical activity, emotional stress, or both; symptoms are typically worse in cold weather or after meals and are relieved by rest or sublingual nitroglycerin. The presence of one or more obstructions in major coronary arteries is likely; the severity of stenosis is usually greater than 70 percent.

From the Department of Internal Medicine, Division of Cardiology, University of New Mexico, Albuquerque. Address reprint requests to Dr. Abrams at the Department of Internal Medicine, Division of Cardiology, University of New Mexico, Albuquerque, NM 87131 or at jabrams@salud.unm.edu.

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PATHOPHYSIOLOGY

Angina occurs when there is regional myocardial ischemia caused by inadequate coronary perfusion and is usually but not always induced by increases in myocardial oxygen requirements. Cardinal features of chronic stable angina include complete reversibility of the symptoms and repetitiveness of the anginal attacks over time, typically months to years. New, prolonged, or recent-onset symptoms are characteristic of unstable angina. Coexisting conditions, such as poorly controlled hypertension, anemia, or thyrotoxicosis, can precipitate or accentuate angina.

As coronary atherosclerosis progresses, there is deposition of plaque external to the lumen of the artery; the plaque may extend eccentrically and outward without compromising the lumen (Fig. 1). Thus, stress testing or angiography may not suggest coronary disease, even in the presence of significant atherosclerosis. As atherosclerosis worsens, encroachment of the plaque mass into the lumen can result in hemodynamic obstruction and angina[1] (Fig. 1). Disordered endothelial vasomotor function of the coronary arteries is common in patients with angina and results in diminished vasodilatation or even vasoconstriction in response to various stimuli, including exercise.[5,6] Occasionally, patients with severe aortic-valve disease or hypertrophic cardiomyopathy have angina-like chest pain in the absence of overt coronary disease.

CLASSIFICATION OF ANGINA PECTORIS

Chest pain is characterized as classic, or typical, angina; as atypical angina, which includes symptoms that have some but not all the features of angina; and as nonanginal

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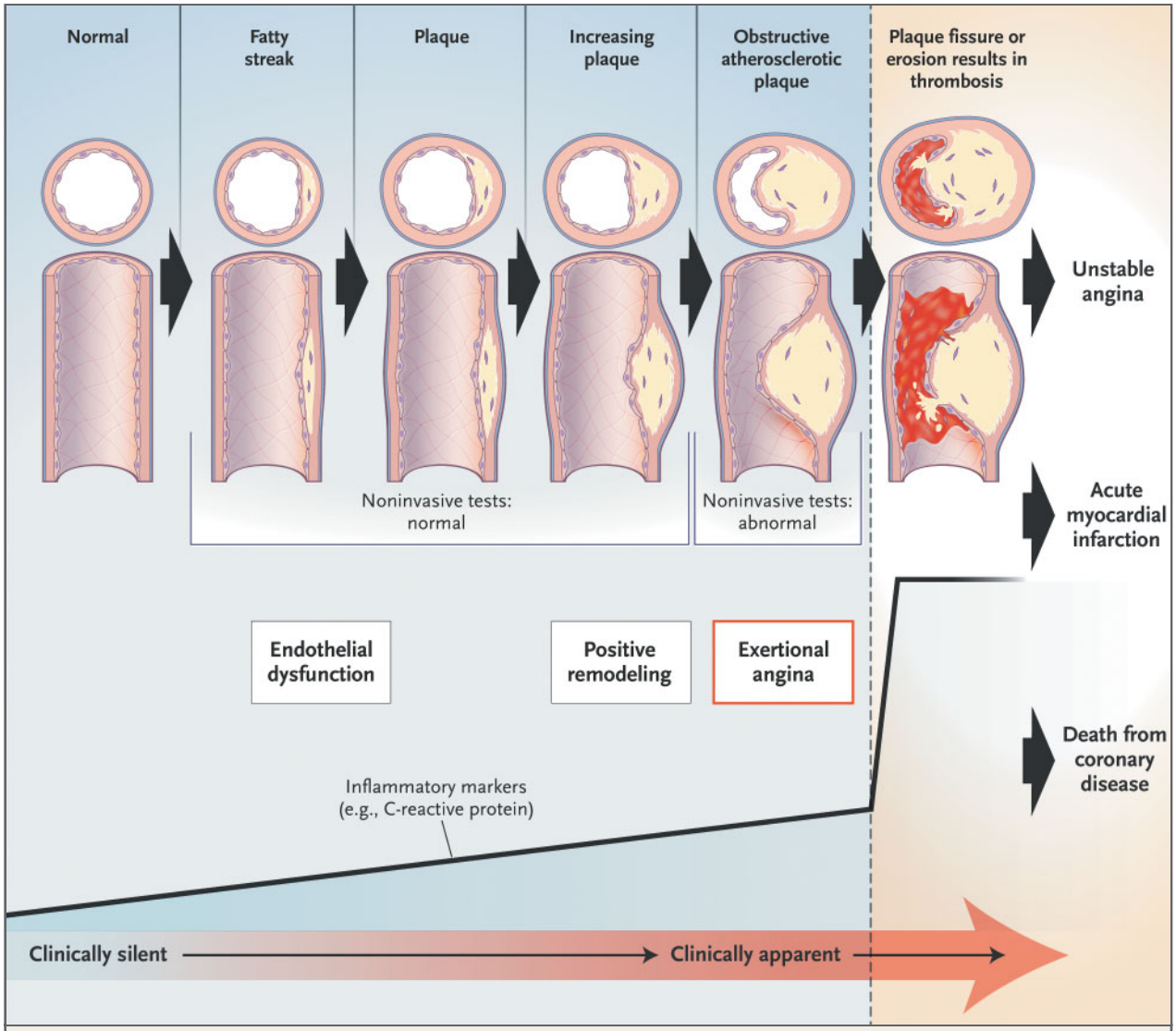

Figure 1. Typical Progression of Coronary Atherosclerosis.

As the plaque burden increases, the atherosclerotic mass tends to stay external to the lumen, which allows the diameter of the lumen to be maintained; this is known as the Glagov effect, or positive remodeling.[1] As plaque encroaches into the lumen, the coronary artery diameter decreases. Myocardial ischemia results from a discordant ratio of coronary blood supply to myocardial oxygen consumption. Luminal narrowing of more than 65 to 75 percent may result in transient ischemia and angina. In acute coronary syndromes, vulnerable plaque is a more important factor than is the degree of stenosis; acute coronary events result from ulceration or erosion of the fibrous cap, with subsequent intraluminal thrombosis.[2,3] Vulnerable plaque within the vessel wall may not be obstructive and thus may remain clinically silent until it causes rupture and associated consequences. (The figure has been modified from Greenland et al.,[4] with permission.)

chest pain, which has none of the features of angina (Table 1).[7] Chest pain that occurs during rest or at night[8] is well described in persons with chronic stable angina, particularly women.[9-11]

Atypical presentations of angina are more common in women than in men. Women with ischemia are more likely than men to report variable pain thresholds, inframammary pain, palpitations, or sharp, stabbing pain.[12,13] Overall, chest pain in women is quite common and usually is not due to coronary artery disease.[9,10,13] Data from the Women's Ischemia Syndrome Evaluation initiative of the National Heart, Lung, and Blood Institute indicate that many women with anginal symptoms have in-

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Table 1. Symptoms of Angina.*

Classic (Typical)	Atypical, Noncardiac
Sensations in chest of squeezing, heaviness, pressure, weight, vise-like aching, burning, tightness	Pain that is pleuritic, sharp, pricking, knife-like, pulsating, lancinating, choking
Radiation to shoulder, neck, jaw, inner arm, epigastrium (can occur without chest component); band-like discomfort	Involves chest wall; is positional, tender to palpation; can be inframammary; radiation patterns highly variable
Relatively predictable	Random onset
Lasts 3–15 min	Lasts seconds, minutes, hours, or all day
Abates when stressor is gone or nitroglycerin is taken	Variable response to nitroglycerin

* Data are from Sangareddi et al.[7]

ducible ischemia and a reduced coronary flow reserve yet no significant obstruction on coronary angiography.[9,10,13] Atypical presentations of angina are also more frequent in older patients (who often have exertional dyspnea, weakness, or sweating) than in younger patients and in patients with diabetes (who often have atypical or even silent ischemic episodes) than in those without diabetes; a high level of suspicion for coronary disease is needed in these groups. The severity of angina should be assessed to aid in management decisions (Table 2). However, there is no direct correlation between the class of angina and the severity of coronary artery disease as determined on angiography.[7]

STRATEGIES AND EVIDENCE

DIAGNOSTIC STRATEGIES

Stress Testing

Various diagnostic tests are available for the evaluation of suspected coronary disease.[14] Previous Clinical Practice articles in the *Journal* have focused on noninvasive testing for coronary artery disease.[15,16] Table 3 summarizes common stress-testing methods. Adults with typical or atypical features of chest pain, especially those with major risk factors for coronary artery disease, should undergo stress testing. False positive and false negative exercise tests occur in up to 20 to 30 percent of persons (more commonly in women); coronary angiography is often necessary to resolve equivocal test results. Noninvasive testing may provide useful additional prognostic information, such as total exercise time, the inducibility of left ventricular dysfunction, blood-pressure and heart-rate responses, and, most important, the degree of myocardial ischemia.[14-16] In general, poor aerobic performance and disordered heart-rate or blood-pressure responses increase the likelihood of subsequent clinical events.

Coronary Angiography

Coronary angiography remains the diagnostic gold standard for obstructive coronary artery disease, but it may miss extraluminal plaque related to coronary remodeling[1] (Fig. 1). Indications for angiography include poorly controlled symptoms; abnormal results on stress testing, particularly with a substantial burden of ischemia (e.g., 1 mm or more of ST-segment depression); ischemia at a low workload (below 5 to 6 metabolic equivalents); large, inducible single or multiple wall-motion abnormalities; and substantial nuclear-perfusion defects. Atypical chest pain or inconclusive or discordant test results occasionally warrant the use of angiography. Intermediate-grade coronary obstructions (e.g., 50 to 70 percent stenosis) may require additional evaluation, such as assessment of coronary flow reserve. Suspected vasospastic or microvascular angina requires additional specialized testing.

Cardiac Biomarkers

Elevated levels of high-sensitivity C-reactive protein[17] and other markers, including brain natriuretic peptide,[18] have prognostic value with respect to cardiovascular events in patients with stable angina or asymptomatic coronary artery disease. However, the clinical utility of such testing remains uncertain.

THERAPY

It is useful to classify therapeutic drugs into two categories: antianginal (anti-ischemic) agents and vasculoprotective agents. Although medications for angina are widely used (Table 4), therapy to slow the progression of coronary artery disease, to induce the

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stabilization of plaque, or to do both is a newer concept (Table 5),[19-21] and these forms of treatment are underprescribed.

Antianginal Agents

All antianginal drugs — nitrates, beta-adrenergic blockers, and calcium-channel blockers — have been shown to prolong the duration of exercise before the onset of angina and ST-segment depression as well as to decrease the frequency of angina.[22-24] Treadmill performance typically increases by 30 to 60 seconds with antianginal drugs as compared with performance with placebo. However, none of these agents have been shown to prevent myocardial infarction or death from coronary disease in patients being treated specifically for chronic stable angina.

Head-to-head comparative trials have not demonstrated that any single class of drugs has greater antianginal efficacy than the others.[22-24] Thus, it is reasonable to begin therapy with agents from any of the three groups.

Beta-blockers work primarily by decreasing myocardial oxygen consumption through reductions in heart rate, blood pressure, and myocardial contractility. Although beta-blockers have not been shown to reduce the rate of coronary events or mortality specifically in patients with chronic stable angina, they are identified as class I drugs (i.e., there is evidence or general agreement that they are useful and effective), according to the 2002 American College of Cardiology–American Heart Association guidelines for the management of stable angina.[24] This classification is based on older trials showing that these agents prolong survival after myocardial infarction and on recent data showing that they have a similar benefit after primary angioplasty for acute non–ST-elevation myocardial infarction.[25] There have been no large trials assessing the effects of beta-blockers on survival or on rates of coronary events in patients with chronic stable angina. The side effects associated with beta-blockers (Table 4) are often overemphasized; these drugs can be used effectively in many patients with chronic obstructive pulmonary disease or peripheral vascular disease.[26]

Calcium antagonists dilate coronary and systemic arteries, increase coronary blood flow, and decrease myocardial oxygen consumption. Although the safety of long-acting calcium-channel blockers has been questioned, data from ALLHAT (the Antihypertensive and Lipid-Lowering Treatment to Prevent Heart Attack Trial)[27] and the results of a recent meta-analysis by the Blood Pressure Lowering Treatment Trialists' Collaboration[28] indicate that the use of these drugs for hypertension does not increase morbidity or mortality.

Table 2. Classification and Severity of Angina.*

Class I	
	No angina with ordinary physical activity (e.g., walking, climbing stairs)
	Angina with strenuous or prolonged exertion
Class II	
	Early-onset limitation of ordinary activity (e.g., walking rapidly or walking >2 blocks; climbing stairs rapidly or climbing >1 flight); angina may be worse after meals, in cold temperatures, or with emotional stress
Class III	
	Marked limitation of ordinary activity
Class IV	
	Inability to carry out any physical activity without chest discomfort
	Angina occurs during rest

* The classification is from Sangareddi et al.[7]

Nitrates dilate systemic and coronary arteries, including some coronary stenoses, and particularly the systemic veins; venous pooling of blood decreases cardiac work and chamber size. Sublingual or oral spray nitroglycerin relieves acute episodes of angina within 5 to 10 minutes; prophylactic use before activity can be helpful in persons with frequent angina. Whereas long-acting nitrates decrease angina and prolong exercise performance, experimental data and data from catheterization laboratories suggest that nitrates increase vascular oxidative stress and may induce paradoxical coronary arterial vasoconstriction.[29] Both appear to contribute to the development of nitrate tolerance.[30,31] Prevention of tolerance requires an intermittent dosing strategy, with a nitrate-free interval of 12 to 14 hours (Table 4). Phosphodiesterase type 5 inhibitors (e.g., sildenafil, vardenafil, and tadalafil) and nitrates should not be used within 24 hours of one another because of the potential for serious hypotension.

Combination Therapy

Underdosing with antianginal agents is common. Even when the dosage is appropriate, physicians should anticipate the need for treatment with two or three agents in many patients.[22,24] Certain drug combinations are recommended, and others should be avoided because of potential hypotension or bradycardia (Table 4). Data from randomized clin-

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Table 3. Common Stress-Testing Procedures for the Evaluation of Chest Pain.*

Test	Protocol	Positive Result	Comments	Estimated Sensitivity (%)	Estimated Specificity (%)
Standard treadmill or bicycle exercise	Patient able to perform adequate amount of physical activity Baseline ECG is normal or near normal (e.g., minimal ST-segment depression) Should not be used if patient has left-bundle-branch block or electronic pacemaker	New horizontal or downsloping ST-segment depression ≥1 mm or ≥2 mm in presence of baseline repolarization abnormality	Blood-pressure response, exercise duration, ventricular arrhythmias, Duke treadmill score, and heart rate recovery should also be assessed Functional capacity and Duke treadmill score have significant prognostic value	65–70	70–75
Exercise stress echocardiography	Patient able to perform physical activity Two-dimensional echocardiogram immediately after exercise	One or more new segmental wall-motion abnormalities (hypokinesis, akinesis, or dyskinesis), left ventricular dilation, or both	Useful for abnormal baseline ECG (should not be used if patient has left-bundle-branch block or electronic pacemaker) Technically high-quality echocardiogram is essential	80–85	80–85
Dobutamine stress echocardiography	For patients unable to exercise adequately with or without abnormal ECG Incremental dobutamine infusion	Inducible segmental left ventricular wall-motion abnormalities, worsening of existing wall-motion abnormalities, or left ventricular dilation	Technically high-quality echocardiogram is essential	80–85	85–90
Exercise myocardial perfusion SPECT, with quantitative analysis	For patients able to perform physical activity Should be used when results of baseline ECG preclude assessment of ischemia (e.g., nonspecific ST-T changes) Can be used in patients with left-bundle-branch block or electronic pacemaker	Inducible single or multiple perfusion abnormalities; left ventricular dilation	Also can provide information on left ventricular function and wall motion	85–90	85–90
Pharmacologic myocardial perfusion SPECT, with quantitative analysis	For patients unable to exercise adequately Intravenous adenosine or dipyridamole Can be used in patients with left-bundle-branch block or electronically paced rhythm	Provides information similar to that provided by exercise SPECT		80–90	80–90
Electron-beam computed tomography	Calcium score closely correlates with extent of coronary atherosclerosis	If score is >100, consider follow-up stress test	Cannot predict coronary obstructions or detect vulnerable plaque or degree of stenosis Poor specificity	—	—

* Estimates of sensitivity and specificity are derived from multiple databases and from the chronic stable angina guidelines of the American College of Cardiology and the American Heart Association.[26] The sensitivity, specificity, and predictive accuracy of all noninvasive stress-testing methods are influenced by age, sex, degree of coronary atherosclerosis, and, most important, the likelihood of coronary artery disease in the patient being tested. ECG denotes electrocardiogram, and SPECT single-photon-emission computed tomography.

ical trials support the efficacy of combined therapy with two drugs but provide less support for the use of three agents together.

Vasculoprotective Therapy

There is considerable evidence that lifestyle changes and pharmacologic therapy may reduce the progression of atherosclerosis, stabilize plaque, or both in chronic stable angina.[19,21,24,32] Aggressive interventions are warranted to control all cardiovascular risk factors, including diabetes and hypertension (a target blood pressure of ≤130/80 mm Hg is appropriate for both conditions) in persons with coronary artery disease.

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Table 4. Recommended Antianginal Drugs.*

Drug Class and Drug	Dosage Range	Adverse Effects	Cautions
Nitrates†		Headache, dizziness, nausea, palpitations Tolerance is a major limiting factor	Contraindicated with medications for erectile dysfunction
Isosorbide dinitrate, short-acting formulations	20–60 mg twice daily		
Isosorbide dinitrate, sustained-release formulations	60–120 mg once daily		
Isosorbide mononitrate, short-acting formulations	20 mg twice daily, 7 hr apart		
Isosorbide mononitrate, sustained-release formulations	60–120 mg once daily		
Nitroglycerin, patch	0.4–0.6 mg, taken for no more than 12–14 hr		
Beta-adrenergic blockers		Fatigue, shortness of breath, wheezing, weakness, dizziness	Should be used with caution in patients with chronic obstructive pulmonary disease, diabetes, depression, severe peripheral vascular disease, coronary vasospasm, sinus or atrioventricular nodal dysfunction, or erectile dysfunction
Propranolol, long-acting formulations	80–240 mg once daily		
Metoprolol, short-acting formulations	50–150 mg twice daily		
Metoprolol, sustained-release formulations	100–300 mg once daily		
Atenolol	25–100 mg once daily		
Calcium-channel blockers		Headache, dizziness, edema Constipation (with verapamil)	Verapamil and diltiazem should be used with caution in patients with low ejection fraction (<30%) or with sinus or atrioventricular nodal dysfunction
Nifedipine, sustained-release formulations	30–90 mg once daily		
Amlodipine	2.5–10 mg once daily		
Verapamil, short-acting formulations	40–120 mg 2–3 times daily		
Verapamil, sustained-release formulations	180–240 mg once or twice daily		
Diltiazem, sustained-release formulations	120–480 mg once daily		

* Recommended combination therapies include a nitrate with a beta-blocker and a dihydropyridine calcium-channel blocker with a beta-blocker. The combination of a dihydropyridine calcium-channel blocker with a nitrate or the combination of a rate-slowing calcium-channel blocker with a beta-blocker is not recommended.
† A nitrate-free interval of 12 to 14 hours daily is necessary.

Lifestyle Changes

Regular exercise reduces the frequency of anginal symptoms, increases functional capacity, and improves endothelial function.[24,33] Patients with chronic stable angina who are receiving medical therapy should exercise regularly, beginning at low levels for 20 to 30 minutes and increasing as symptoms allow. A recent randomized trial that compared the effects of daily exercise with those of angioplasty and stenting among patients with chronic stable angina and single-vessel coronary artery disease demonstrated better outcomes (in terms of major adverse events and improved exercise capacity) at one year in the exercise group than in the revascularization group.[34]

Although dietary modification has not been studied specifically in patients with chronic stable angina, in a trial involving patients with a history of myocardial infarction who had been randomly assigned to follow either a Mediterranean diet or a prudent Western diet, the rate of cardiovascular events was 47 percent lower in the Mediterranean-diet group than in the Western-diet group, and this difference persisted for four years.[35] Trials involving multifactorial risk modification, including exercise, a low-fat diet, and smoking cessation, have demonstrated improvements in the progression of angina and coronary disease.[36]

Vigorous efforts at smoking cessation and weight control are mandatory in patients with chronic stable angina. For patients with diabetes, a multifactorial approach that includes lifestyle changes and medications for glycemic control and coronary risk factors substantially reduces the risk of cardiovascular events.[37]

Pharmacologic Therapy

The use of aspirin at a dose of 81 to 150 mg per day reduces cardiovascular morbidity and mortality by 20 to 25 percent among patients with coronary artery disease. The results of several large, randomized trials indicate that the use of statins reduces the rate of coronary events and mortality in patients with established coronary artery disease and hyperlipidemia by 25 to 35 percent. Furthermore, a 25 to 30 percent reduction in revascularization rates in the large statin trials suggests a decrease in angina during the trials.[38] A recent trial involving patients

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Table 5. The Vasculoprotective Regimen for Stable Angina.*

Agent	Indications	Comment
Aspirin	All patients, except those with aspirin allergy or resistance	Dosage, 81–150 mg daily or 325 mg every other day
Statin	All patients, to achieve target LDL cholesterol level ≤100 mg/dl; goal of 70 mg/dl in very high-risk patients (those with diabetes, multivessel disease, or multiple risk factors for coronary artery disease)	May use C-reactive protein level to guide dosage, with target <2 mg/liter, although this strategy has not been prospectively tested
Beta-blocker	All patients with exertion-related or emotion-related chest pain, previous MI, hypertension, depressed left ventricular function (in absence of contraindication)	
Clopidogrel	All patients after PCI or those with aspirin intolerance or resistance	Duration of therapy, 1 year after PCI, indefinitely if aspirin cannot be used
ACE inhibitor	High-risk patients: those with diabetes, chronic kidney disease, hypertension, previous MI, left ventricular systolic dysfunction, or age ≥55 yr	Uncertain utility in low-risk patients

* LDL denotes low-density lipoprotein, MI myocardial infarction, PCI percutaneous coronary intervention, and ACE angiotensin-converting enzyme. To convert the values for cholesterol to millimoles per liter, multiply by 0.02586.

with stable coronary artery disease demonstrated that treatment with 80 mg of atorvastatin daily slowed the progression of coronary atherosclerosis, as measured by intravascular ultrasound, over a period of 18 months, as compared with treatment with 40 mg of pravastatin daily.[19] In another trial (the PROVE-IT–TIMI 22 [Pravastatin or Atorvastatin Evaluation and Infection Therapy–Thrombolysis in Myocardial Infarction 22 study), the reduction of low-density lipoprotein (LDL) cholesterol levels to a mean of 62 mg per deciliter (1.6 mmol per liter) decreased the number of clinical events further than did a lesser reduction (to 95 mg per deciliter [2.5 mmol per liter]) in subjects with acute coronary ischemia.[20] A recent trial likewise showed a significantly lower rate of cardiovascular events among patients with stable coronary disease who were treated with 80 mg of atorvastatin daily (achieved mean LDL cholesterol, 77 mg per deciliter [2.0 mmol per liter]) than among those treated with 10 mg daily; persistent elevations in aminotransferase levels complicated therapy in 1.2 percent of patients in the high-dose group, as compared with 0.2 percent of those in the low-dose group.[39] The Adult Treatment Panel III of the National Cholesterol Education Program recently recommended target LDL cholesterol levels of 60 to 70 mg per deciliter (1.6 to 1.8 mmol per liter) in high-risk patients with coronary artery disease.[40]

Statins reduce the levels of C-reactive protein, and two recent studies suggest that lowering these levels is as important as decreasing LDL cholesterol levels for the optimal reduction of coronary events.[41,42] Angiotensin-converting–enzyme (ACE) inhibitors have been reported to reduce morbidity and mortality among patients with coronary disease,[21,43] although the recent PEACE Trial (Prevention of Events with Angiotensin Converting Enzyme Inhibition Trial) did not confirm these findings,[44] possibly owing to the relatively low risk among patients in this trial as compared with those in the HOPE trial (Heart Outcomes Prevention Evaluation study) and the EUROPA study (European Trial on Reduction of Cardiac Events with Perindopril in Stable Coronary Artery Disease).[21,43] ACE inhibitors should be prescribed for patients with chronic stable angina who have a history of myocardial infarction, hypertension, left ventricular systolic dysfunction, or diabetes, as well as for patients with impaired renal function who do not have a contraindication to the use of these agents.

REVASCULARIZATION

Revascularization includes either percutaneous coronary intervention (i.e., balloon angioplasty and stenting) or coronary-artery bypass surgery. More than 1 million percutaneous coronary interventions were performed in the United States in 2003, far surpassing the number of surgical revascularizations. More than 80 percent of percutaneous interventions in the United States in 2004 were performed with the use of drug-eluting stents coated with sirolimus or paclitaxel.

Revascularization (performed by any technique) has not been shown to decrease the risk of myocardial infarction or death from coronary artery disease in patients with chronic stable angina and preserved left ventricular function. However, revascularization should be considered for persons with lifestyle-limiting angina who have a good medical regimen or for those with high-risk factors, such as symptomatic multivessel disease, proximal left anterior descending or left main artery disease, left ventricular systolic dysfunction, diabetes, a large ischemic bur-

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den on nuclear or echocardiographic stress testing, early onset of ischemia on stress testing, or ST-segment depression of 2 mm or more.[24,45] Although coronary-artery bypass surgery achieves more complete and durable control of angina than percutaneous coronary intervention (with the use of noncoated stents), subsequent rates of myocardial infarction and death are similar over a five-year period with the two strategies.[46-48] Trials in which the use of noncoated stents were compared with balloon angioplasty have not shown significant differences in the rate of major adverse events, including acute myocardial infarction and death.[49] The long-term effect of drug-eluting stents on outcomes in chronic stable angina is still under evaluation; current data indicate that there have been significant reductions in the rate of restenosis at 6 to 12 months with coated stents, as compared with noncoated stents, resulting in substantial decreases in recurrent angina and the need for revascularization of target lesions. It is not clear how the long-term outcomes compare with those of coronary-artery bypass grafting.[50] Decisions regarding strategies for revascularization should take into account patients' preferences and local experience.[24,45,46,48]

CARDIOPROTECTIVE THERAPY VERSUS PERCUTANEOUS INTERVENTION

Marked regional variability in the use of revascularization procedures suggests excessive use in some geographic areas. Several trials have indicated that treatment with a combination of vasculoprotective agents, along with lifestyle changes — with the option to proceed to percutaneous revascularization if symptoms worsen — results in rates of myocardial infarction and death that are not significantly different from those associated with revascularization in patients with class I or II stable angina whose disease involves one or two vessels.[51-53]

AREAS OF UNCERTAINTY

Some patients who are not candidates for coronary revascularization continue to have severe or limiting angina; almost all have multivessel coronary artery disease and have previously undergone revascularization and have target vessels that are not suitable for the procedure (because they are distal, diffuse, or of small caliber). The optimal approach to management of these cases remains uncertain. One option is the use of enhanced external counterpulsation; results of a sham-controlled, randomized trial, as well as observational data, suggest that this form of therapy decreases the severity and frequency of angina,[24] although objective reductions in ischemia have been variable.[54,55] Another approach is transmyocardial laser revascularization, in which multiple laser channels are made directly into the myocardium.[24,56,57] Both procedures are approved by the Food and Drug Administration (FDA), although the mechanisms by which they relieve angina remain uncertain. The role of promising new agents, including trimetazidine[58] and ranolazine,[59] that alter myocardial metabolism is currently unclear with regard to the treatment of angina; neither drug has received FDA approval.

GUIDELINES

The 1999 guidelines on stable angina, revised in 2002, of the American College of Cardiology, the American Heart Association, and the American College of Physicians,[24,60] represent the most comprehensive available treatise on chronic stable angina. The American College of Cardiology–American Heart Association guidelines on coronary-artery bypass grafting, updated in 2004, are also useful.[45] Recent National Cholesterol Education Program–Adult Treatment Panel III guidelines support aggressive lipid lowering in patients with chronic stable angina.[40] All recommendations in this review are consistent with those guidelines.

SUMMARY AND CONCLUSIONS

The diagnosis of chronic stable angina is made on the basis of anginal symptoms, a noninvasive stress test that is positive for myocardial ischemia, and documentation of coronary atherosclerosis on angiography. Antianginal drugs should be prescribed in effective doses, usually beginning with a beta-blocker; aspirin is mandatory. Management should routinely include lifestyle modifications, including smoking cessation, weight control, and regular exercise, and aggressive control of other cardiovascular risk factors. Drugs to slow the progression of atherosclerosis, including statins and, in many cases, ACE inhibitors, are also indicated. The target LDL cholesterol level in persons with chronic stable angina is below 100 mg per deciliter (2.6 mmol per liter); in high-risk patients, the level is 60 to 70 mg per deciliter. Angiography is generally indi-

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cated if symptoms continue despite treatment with antianginal medications or if high-risk features appear on stress testing. I would recommend this, along with the other interventions described above, in a case such as that described in the vignette. Revascularization should be considered for persons with class II and III symptoms, a high risk as determined by diagnostic tests, or angina that the patient finds unacceptable despite medical management.

Dr. Abrams reports having received consulting honoraria from Pfizer and CV Therapeutics and lecture fees from Pfizer and Merck.

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