ACC/AHA 2002 Guideline Update for the Management of Patients With Chronic Stable Angina—Summary Article

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

The Clinical Efficacy Assessment Subcommittee of the American College of Physicians–American Society of Internal Medicine acknowledges the scientific validity of this product as a background paper and as a review that captures the levels of evidence in the management of patients with chronic stable angina as of November 17, 2002.

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The ACC/AHA Task Force on Practice Guidelines makes every effort to avoid any actual or potential conflicts of interest that might arise as a result of an outside relationship or personal interest of a member of the writing panel. Specifically, all members of the writing panel are asked to provide disclosure statements of all such relationships that might be perceived as real or potential conflicts of interest. These statements are reviewed by the parent task force, reported orally to all members of the writing panel at the first meeting, and updated as changes occur. The conflict of interest information for the writing committee members is posted on the ACC and AHA World Wide Web sites with the full-length version of the update.

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Copies: This document and the full-text guideline are available on the World Wide Web sites of the ACC (www.acc.org) and the AHA (www.americanheart.org). To obtain a single copy of this summary article published in the January 7/14, 2003, issue of *Circulation* and the January 1, 2003, issue of the *Journal of the American College of Cardiology*, call 800-253-4636 (US only) or write the American College of Cardiology, Resource Center, 9111 Old Georgetown Road, Bethesda, MD 20814-1699, and ask for reprint No. 71-0244. To purchase additional reprints: up to 999 copies, call 800-611-6083 (US only) or fax 413-665-2671; 1000 or more copies, call 410-528-4426, fax 410-528-4264, or e-mail klbradle@lww.com.

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I. Introduction

The American College of Cardiology (ACC)/American Heart Association (AHA) Task Force on Practice Guidelines regularly reviews existing guidelines to determine when an update or a full revision is needed. This process gives priority to areas in which major changes in text, and particularly recommendations, are merited on the basis of new understanding or evidence. Minor changes in verbiage and references are discouraged.

The ACC/AHA/American College of Physicians–American Society of Internal Medicine (ACP-ASIM) Guidelines for the Management of Patients With Chronic Stable Angina, which were published in June 1999, have now been updated. The full-text guideline incorporating the updated material is available on the Internet (www.acc.org or www.americanheart.org) in both a track-changes version showing the changes in the 1999 guideline in strike-out (deleted text) and highlighting (new text) and a "clean" version that fully incorporates all the changes.

This summary article describes the 4 most important areas of change reflected in the update in a format that we hope can be read and understood as a stand-alone document. Interested readers are referred to the full-length version on the Internet to completely understand the location of these changes within the full-length guideline, as well as their proper context. The full-length guideline includes some additional changes that are not reflected in this summary article. All new references appear in bold-faced type; all original references appear in normal type.

Although the primary focus of this guideline is on symptomatic patients, asymptomatic patients with known or suspected coronary disease are included in this update and are described in Section V.

The customary ACC/AHA classifications I, IIa, IIb, and III and the corresponding levels of evidence are used throughout the document.

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

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

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

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

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

Level of Evidence A: **Data derived from multiple randomized clinical trials.**
Level of Evidence B: **Data derived from a single randomized trial or nonrandomized studies.**
***Level of Evidence C*: Consensus opinion of experts.**

The ACC/AHA Task Force on Practice Guidelines welcomes feedback on this update process and the format of this article. Please direct your comments to the Task Force in care of Dawn Phoubandith, American College of Cardiology, or via e-mail (dphouban@acc.org).

II. Angiotensin Converting Enzyme Inhibitors

New Recommendations for Angiotensin Converting Enzyme (ACE) Inhibitors

Class I

1. **ACE inhibitor in all patients with coronary artery disease (CAD)* who also have diabetes and/or left ventricular systolic dysfunction. *(Level of Evidence: A)***

Class IIa

1. **ACE inhibitor in patients with CAD* or other vascular disease. *(Level of Evidence: B)***

***Significant CAD by angiography or previous myocardial infarction.**

The results of the Heart Outcomes Prevention Evaluation (HOPE) trial now confirm that use of the ACE inhibitor ramipril (10 mg/d) reduced the incidence of cardiovascular death, myocardial infarction (MI), and stroke in patients who were at high risk for, or had, vascular disease in the absence of heart failure.[1] The primary outcome in HOPE was a composite of cardiovascular death, MI, and stroke. However, the results of HOPE were so definitive that each of the components of the primary outcome by itself also showed statistical significance. Furthermore, only a small part of the benefit could be attributed to a reduction in blood pressure (−2 to −3 mm Hg).

The results of HOPE were extremely impressive when one considers the magnitude of the difference between ramipril and placebo in the primary outcomes of cardiovascular death, MI, and stroke. The HOPE study was unique in that of the 9541 patients in the study, 3577 (37.5%) had diabetes. There was a very significant reduction in diabetic complications, a composite for the development of diabetic nephropathy, need for renal dialysis, and laser therapy for diabetic retinopathy, in those patients receiving ramipril. Even more fascinating was the finding that among the patients who were not designated as diabetic at the beginning of the trial, fewer were diagnosed with diabetes during the 4-year observation period if they were treated with ramipril. Before the HOPE trial, numerous clinical trials suggested that ACE inhibitor treatment may delay or prevent cardiovascular outcomes in patients with diabetes after an MI, in the presence of hypertension, and in the presence of a low ejection fraction or

heart failure. Furthermore, ACE inhibitors may also prevent overt nephropathy and other microvascular outcomes in patients with type 1 or type 2 diabetes.

The Microalbuminuria, Cardiovascular, and Renal Outcomes (MICRO)-HOPE study, a substudy of the HOPE study, has provided new clinical data on the cardiorenal therapeutic benefits of ACE inhibitor intervention in a broad range of middle-aged patients with diabetes mellitus who are at high risk for cardiovascular events. The risk of MI was reduced by 22% ($P=0.01$), stroke by 33% ($P=0.0074$), cardiovascular death by 37% ($P=0.0001$), and the combined primary outcome of these events by 25% ($P=0.0004$). Ramipril also lowered the risk of overt nephropathy by 24% ($P=0.027$).

ACE inhibitors should be used in most cases as routine secondary prevention for patients with known CAD, particularly in diabetics without severe renal disease. There are 2 ongoing clinical trials evaluating the effect of 2 different ACE inhibitors in patient populations that do not include patients with diabetes mellitus. These studies will answer the question whether a vasculoprotective effect can be accomplished in a lower-risk group of patients than those enrolled in the HOPE study.

III. Treatment of Risk Factors

New/Changed Recommendations†

Class IIa

1. **In patients with documented or suspected CAD and low-density lipoprotein (LDL) cholesterol 100 to 129 mg/dL, several therapeutic options are available:** ***(Level of Evidence: B)***
   a. **Lifestyle and/or drug therapies to lower LDL to less than 100 mg/dL.** ***(Level of Evidence: B)***
   b. **Weight reduction and increased physical activity in persons with the metabolic syndrome.** ***(Level of Evidence: B)***
   c. **Institution of treatment of other lipid or nonlipid risk factors; consider use of nicotinic acid or fibric acid for elevated triglycerides or low high-density lipoprotein (HDL) cholesterol.** ***(Level of Evidence: B)***
2. **Therapy to lower non-HDL cholesterol in patients with documented or suspected CAD and triglyceride levels greater than 200 mg/dL, with a target non-HDL cholesterol level of less than 130 mg/dL.** ***(Level of Evidence: B)***
3. **Weight reduction in obese patients in the absence of hypertension, hyperlipidemia, or diabetes mellitus.** ***(Level of Evidence: C)***

Class III

1. **Initiation of hormone replacement therapy (HRT) in postmenopausal women for the purpose of reducing cardiovascular risk.** ***(Level of Evidence: A)***
2. **Vitamin C and E supplementation.** ***(Level of Evidence: A)***
3. **Coenzyme Q.** ***(Level of Evidence: C)***

†The original recommendations, and particularly the 6 Class I recommendations, continue to apply.

Many of the new recommendations reflect the latest recommendations of the National Cholesterol Education Program–Adult Treatment Panel III (ATP-III),[2] which the writing committee strongly endorses.

The results of the largest cholesterol-lowering trial yet performed, the Heart Protection Study (HPS), were published as this update was in the final stages of preparation.[2a] This trial included more than 20 000 men and women age 40 to 80 years with coronary disease, other vascular disease, diabetes, and/or hypertension. Patients were randomized to simvastatin 40 mg or matching placebo and were followed for a mean of five years. The primary end point, total mortality, was reduced by statin treatment by approximately 25% overall and similarly in all important prespecified subgroups, including: women, patients more than 75 years old, diabetics, and individuals with baseline LDL cholesterol of less than 100 mg per dL. Analysis of these data by all appropriate authorities, including the National Cholesterol Education project, will be necessary to clarify their implications for these guidelines.

A. LDL Cholesterol

The clinical trial data indicate that in patients with established coronary disease, including chronic stable angina pectoris, dietary intervention and treatment with lipid-lowering medications should not be limited to those with extreme values. The benefits of lipid-lowering therapy were evident in patients in the lowest baseline quartile of LDL cholesterol (modest elevations) in the Scandinavian Simvastatin Survival Study (4S) and in those with minimal elevation of LDL cholesterol level in the Cholesterol And Recurrent Events (CARE) study. These trials establish the benefits of aggressive lipid-lowering treatment for most patients with coronary disease, even when LDL cholesterol is within a range considered acceptable for patients in a primary prevention setting. For patients with established coronary disease, nonpharmaceutical treatment and drug treatment are warranted in the vast majority of patients. The goal of treatment is an LDL cholesterol level less than 100 mg/dL. When LDL cholesterol is 101 to 129 mg/dL, either at baseline or with LDL-lowering therapy, several therapeutic options are available:

- Initiate or intensify lifestyle and/or drug therapies specifically to lower LDL.
- Emphasize weight reduction and increased physical activity in persons with the metabolic syndrome (see below).
- Delay use or intensification of LDL-lowering therapies and institute treatment of other lipid or nonlipid risk factors; consider use of other lipid-modifying drugs (eg, nicotinic acid or fibric acid) if the patient has elevated triglyceride or low HDL cholesterol levels.

B. Non-HDL Cholesterol

The finding that elevated triglycerides are an independent risk factor for coronary heart disease (CHD) suggests that some triglyceride-rich lipoproteins are atherogenic. The latter are partially degraded very-low-density lipoproteins (VLDL), commonly called “remnant lipoproteins.” In clinical practice, non-HDL cholesterol is the most readily available measure of

the total pool of atherogenic lipoproteins, including remnants. Thus, non-HDL cholesterol can be a target of cholesterol-lowering therapy. Moreover, non-HDL cholesterol is highly correlated with total apolipoprotein B (apoB)[3,4]; apoB is the major apolipoprotein of all atherogenic lipoproteins. Serum total apoB also has been shown to have a strong predictive power for severity of coronary atherosclerosis and CHD events.[5–12] Because of the high correlation between non-HDL cholesterol and apoB levels,[3,4] non-HDL cholesterol represents an acceptable surrogate marker for total apoB; the latter is not widely available for routine measurement in clinical practice. Therefore, ATP III[2] identifies the sum of LDL and VLDL cholesterol (termed "non-HDL cholesterol" [total cholesterol minus HDL cholesterol]) as a secondary target of therapy in persons with high triglycerides (greater than 200 mg/dL). The goal for non-HDL cholesterol (for persons with serum triglycerides greater than or equal to 200) is 130 mg/dL; this is 30 mg/dL higher than the goal for LDL cholesterol, because the normal VLDL cholesterol level is 30 mg/dL.

C. HDL Cholesterol

ATP III has defined a low HDL cholesterol level as less than 40 mg/dL.[2] Patients with established coronary disease and low HDL cholesterol are at high risk for recurrent events and should be targeted for aggressive nonpharmacological treatment (dietary modification, weight loss, and/or physical exercise). ATP III does not specify a goal for HDL raising. Although clinical trial results suggest that raising HDL will reduce risk, the evidence is insufficient to specify a goal of therapy. Furthermore, currently available drugs do not robustly raise HDL cholesterol. A low HDL level should receive clinical attention and management according to the following sequence. In all persons with low HDL cholesterol, the primary target of therapy is LDL cholesterol; ATP III guidelines for diet, exercise, and drug therapy should be followed to achieve the LDL cholesterol goal. Second, after the LDL goal has been reached, emphasis shifts to other issues. When a low HDL cholesterol level is associated with high triglycerides (200 to 499 mg/dL) secondary priority goes to achieving the non-HDL cholesterol goal, as outlined earlier. Also, if triglycerides are less than 200 mg/dL (isolated low HDL cholesterol), drugs to raise HDL (fibrates or nicotinic acid) can be considered. Nicotinic acid and fibrates usually raise HDL levels, as do 3-hydroxy-3-methylglutaryl coenzyme A (HMG-CoA) reductase inhibitors.

D. Triglycerides

Triglyceride levels are predictive of CHD risk in a variety of observational studies and clinical settings.[13] Much of the association of triglycerides with CHD risk is related to other factors, including diabetes, obesity, hypertension, high LDL cholesterol, and low HDL cholesterol.[14] In addition, hypertriglyceridemia is often found in association with abnormalities in hemostatic factors.[15] Recently, however, a borderline (150 to 199 mg/dL) or high (greater than 200 mg/dL) triglyceride level has been established by meta-analyses of prospective studies as an independent risk factor for CHD.[2,16,17]

Nonpharmacological management of high triglycerides consists of weight loss, reduction in alcohol consumption for those in whom this mechanism may be causal, smoking cessation, and physical activity. Drugs that can lower triglycerides include nicotinic acid, fibrate derivatives, and, to a lesser degree, statins. It is not clear whether treatment directed at high triglyceride levels will reduce risk for initial or recurrent CHD events. Also, triglyceride measurements vary considerably for individual patients. Accordingly, the ATP III[2] provides guidance for the management of elevated triglyceride levels by focusing on a combination of therapeutic lifestyle changes and by a secondary lipid target for non-HDL cholesterol.

E. Obesity

Obesity is a common condition associated with increased risk for coronary disease and mortality.[18] Obesity is defined as a body mass index (weight in kilograms divided by the square of height in meters) of 30 kg/m^2, and overweight begins at 25 kg/m^2.[19] Obesity is associated with and contributes to other coronary disease risk factors, including high blood pressure, glucose intolerance, low HDL cholesterol, and elevated triglyceride levels. Hence, much of the increased CAD risk associated with obesity is mediated by these risk factors. Risk is particularly raised in the presence of abdominal obesity, which can be identified by a waist circumference greater than 102 cm (40 inches) in men or 88 cm (35 inches) in women.[19] Because weight reduction in overweight and obese people is a method to reduce multiple other risk factors, it is an important component of secondary prevention of CHD.

F. Metabolic Syndrome

Evidence is accumulating that risk for future CHD events can be reduced beyond that achieved by LDL-lowering therapy by modification of a specific secondary target of therapy—the metabolic syndrome—represented by a constellation of lipid and nonlipid risk factors of metabolic origin. This syndrome is closely linked to a generalized metabolic disorder called insulin resistance in which the normal actions of insulin are impaired. Excess body fat (particularly abdominal obesity) and physical inactivity promote the development of insulin resistance, but some individuals also are genetically predisposed to insulin resistance. In a field that has been confused by nomenclature, ATP III has introduced a standard definition for the diagnosis of the metabolic syndrome, as shown in the Table. The metabolic syndrome is considered to be present when 3 or more of the characteristics are present.

Management of the metabolic syndrome has a 2-fold objective: (1) to reduce underlying causes (ie, obesity and physical inactivity) and (2) to treat associated nonlipid and lipid risk factors. First-line therapies for all lipid and nonlipid risk factors associated with the metabolic syndrome are weight reduction and increased physical activity, as well as appropriate control of LDL cholesterol. In patients with triglycerides greater than 200 mg/dL, a non-HDL cholesterol goal of less than 130 mg/dL is a secondary target (see the Table).

G. Hormone Replacement Therapy

On the basis of epidemiological studies and prospective studies of the effects of estrogen administration on cardiac

Characteristics Used to Define Metabolic Syndrome

Risk Factor	Defining Level
Abdominal obesity	Waist circumference
Men	Greater than 103 cm (40 in)
Women	Greater than 88 cm (35 in)
Triglycerides	Greater than 150 mg/dL
HDL cholesterol	
Men	Less than 40 mg/dL
Women	Less than 50 mg/dL
Blood pressure	Greater than or equal to 130/85 mm Hg
Fasting serum glucose	Greater than or equal to 110 mg/dL

risk factors, postmenopausal estrogen replacement has been advocated for both primary and secondary prevention of CAD in women. However, the first published randomized trial of estrogen plus progestin therapy in postmenopausal women with known CAD did not show any reduction in cardiovascular events over 4 years of follow-up,[20] despite an 11% lower LDL cholesterol level and a 10% higher HDL cholesterol level in those women receiving HRT. In addition, women receiving HRT had higher rates of cardiovascular events during the first 2 years, more thromboembolic events, and more gallbladder disease.[20] A subsequent angiographic study also revealed no benefit from HRT.[21] Another prospective randomized controlled trial with HRT in women with a history of stroke found no benefit in reducing mortality or stroke after 2.8 years.[22] The Women's Health Initiative, a randomized controlled primary prevention trial of estrogen plus progestin, found that the overall health risks of this therapy exceeded its benefits.[23] Thus, current information suggests that HRT in postmenopausal women does not reduce risk for major vascular events or coronary deaths in secondary prevention. Women who are taking HRT and who have vascular disease can continue this therapy if it is being prescribed for other well-established indications and no better alternative therapies are appropriate. However, at the present time, there is no basis for adding or continuing estrogens in postmenopausal women with clinically evident CAD or cerebrovascular disease in an effort to prevent or retard progression of their underlying disease.[24]

If a woman develops an acute CAD event while undergoing HRT, it is prudent to consider discontinuance of the HRT.[24] In women who are immobilized, HRT should be discontinued, or venous thromboembolism prophylaxis should be used.[24]

H. Oxidative Stress

Evidence from clinical trials is negative regarding the effects of supplementation with antioxidant vitamins. Although several small trials and in vitro data from basic research in vascular biology have suggested that vitamin C and/or E might interfere with formation of atherosclerotic lesions, 2 large randomized clinical trials have shown no benefit when vitamin E was given to post-MI patients[25] or in those with vascular disease or diabetics with a high-risk CAD profile.[26–28] Furthermore, a small coronary regression trial, the HDL Atherosclerosis Treatment Study (HATS), suggested an adverse effect of antioxidant vitamins on coronary atherosclerosis, clinical events, and HDL and apoA-1 metabolism.[27,28] The use of vitamin E (administered with vitamin C and beta-carotene) was the subject of a large (more than 20 000 participants) trial of patients at risk for CAD and with CAD.[26] Antioxidant therapy had no effect on the end points of cardiovascular death, cardiovascular events, stroke, or revascularization, considered alone or in combination. Although previous observational and epidemiological studies have suggested a benefit from dietary supplementation with antioxidants or a diet rich in antioxidants, especially vitamin E, there is currently no basis for recommending that patients take vitamin C or E supplements or other antioxidants for the express purpose of preventing or treating CAD.

IV. Alternative Therapies for Chronic Stable Angina in Patients Refractory to Medical Therapy Who Are Not Candidates for Percutaneous Intervention or Revascularization

Recommendations

Class IIa

1. **Surgical laser transmyocardial revascularization (TMR). *(Level of Evidence: A)***

Class IIb

1. **Enhanced external counterpulsation (EECP). *(Level of Evidence: B)***
2. **Spinal cord stimulation (SCS). *(Level of Evidence: B)***

Evidence has emerged regarding the relative efficacy, or lack thereof, of a number of techniques for the management of refractory chronic angina pectoris. These techniques should only be used in patients who cannot be managed adequately by medical therapy and who are not candidates for revascularization (interventional and/or surgical).

A. Spinal Cord Stimulation

Since approximately 1987, SCS has been proposed as a method for providing analgesia for patients with chronic angina pectoris refractory to medical, catheter interventional, or surgical therapy. The efficacy of SCS depends on the accurate placement of the stimulating electrode in the dorsal epidural space, usually at the C7-T1 level. A review of the literature has revealed 2 small randomized clinical trials involving implanted spinal cord stimulators, 1 of which directly tested its efficacy. One report studied the efficacy of SCS in 13 treated patients versus 12 control subjects, both groups with chronic intractable angina pectoris studied for 6 weeks.[29] Another small randomized trial involved 24 patients with refractory angina.[30] Nine other studies, either retrospective[31–33] or prospective[29,34–38] cohort studies, were identified in the literature. Although the results of these studies appear promising, there is still a paucity of data on the intermediate- and long-term benefit of these devices.

B. Enhanced External Counterpulsation

Another nonpharmacological technique that has been described for treatment of patients with chronic stable angina is known as EECP. EECP was evaluated in a randomized, placebo-controlled multicenter trial to determine its safety and efficacy.[39] Patients (n=139) with chronic stable angina, documented CAD, and a positive exercise treadmill test were randomly assigned to receive EECP (35 hours of active counterpulsation) or inactive EECP over a 4- to 7-week period. The authors concluded that EECP decreased angina frequency ($P<0.05$) and improved time to exercise-induced ischemia ($P=0.01$). Two multicenter registry studies that included 978 patients from 43 centers[40] and 2289 patients from more than 100 centers[41] evaluated the safety and effectiveness of EECP in treating chronic stable angina. These studies found the treatment to be generally well tolerated and efficacious; anginal symptoms were improved in approximately 75% to 80% of patients. However, additional clinical trial data are necessary before this technology can be recommended definitively.

C. Laser TMR

Another emerging technique that has been studied for the treatment of more severe chronic stable angina refractory to medical or other therapies is laser TMR. This technique has either been performed in the operating room (with a carbon dioxide or holmium:YAG laser) or by a percutaneous approach with a specialized (holmium:YAG laser) catheter. Eight prospective randomized clinical trials have been performed, 2 with the percutaneous technique and the other 6 with an epicardial surgical technique.[42–48] The goal in both approaches is to create a series of transmural endomyocardial channels to improve myocardial revascularization. Percutaneous TMR technology has not been approved by the Food and Drug Administration and should therefore be considered an experimental therapy.

The surgical TMR technique has generally been associated with improvement in symptoms in patients with chronic stable angina. The mechanism for improvement in anginal symptoms is still controversial. Possible mechanisms for this improvement include increased myocardial perfusion, denervation of the myocardium, stimulation of angiogenesis, or perhaps some other unknown mechanism.[49–51] There are conflicting data regarding improvement in exercise capacity.[43,44,47] Despite the apparent benefit in decreasing anginal symptoms, no definite benefit has been demonstrated in terms of increasing myocardial perfusion.[43,46,47]

There are currently no published studies to document the long-term efficacy of surgical TMR. Nonetheless, this technique appears to provide symptomatic relief for end-stage chronic angina in the short term. Additional follow-up studies are necessary to evaluate procedural efficacy in patients who have undergone surgical laser TMR alone, as well as coronary bypass surgery plus TMR.

V. Asymptomatic Patients With Known or Suspected CAD

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

The full-text guideline includes many subsections on asymptomatic patients, which appear at the end of the appropriate sections for symptomatic patients. They are integrated here into a single summary. The recommendations for noninvasive testing, which follow, appear in multiple different lists of recommendations in the full-length document.

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

Class IIb

1. **Exercise ECG testing without an imaging modality in asymptomatic patients with possible myocardial ischemia on ambulatory ECG (AECG) monitoring or with severe coronary calcification on EBCT in the absence of one of the following ECG abnormalities:**
   a. **Preexcitation (Wolff-Parkinson-White) syndrome *(Level of Evidence: C)***
   b. **Electronically paced ventricular rhythm *(Level of Evidence: C)***
   c. **More than 1 mm of ST depression at rest *(Level of Evidence: C)***
   d. **Complete left bundle-branch block. *(Level of Evidence: C)***
2. **Exercise perfusion imaging or exercise echocardiography in asymptomatic patients with possible myocardial ischemia on AECG monitoring or with severe coronary calcification on EBCT who are able to exercise and have one of the following baseline ECG abnormalities:**
   a. **Preexcitation (Wolff-Parkinson-White) syndrome *(Level of Evidence: C)***
   b. **More than 1 mm of ST depression at rest. *(Level of Evidence: C)***
3. **Adenosine or dipyridamole myocardial perfusion imaging in patients with severe coronary calcification on EBCT but with one of the following baseline ECG abnormalities:**
   a. **Electronically paced ventricular rhythm *(Level of Evidence: C)***
   b. **Left bundle-branch block. *(Level of Evidence: C)***
4. **Adenosine or dipyridamole myocardial perfusion imaging or dobutamine echocardiography in patients with possible myocardial ischemia on AECG monitoring or with coronary calcification on EBCT**

who are unable to exercise. ***(Level of Evidence: C)***

5. **Exercise myocardial perfusion imaging or exercise echocardiography after exercise ECG testing in asymptomatic patients with an intermediate-risk or high-risk Duke treadmill score.** ***(Level of Evidence: C)***
6. **Adenosine or dipyridamole myocardial perfusion imaging or dobutamine echocardiography after exercise ECG testing in asymptomatic patients with an inadequate exercise ECG.** ***(Level of Evidence: C)***

Class III

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

The use of exercise ECG testing in asymptomatic patients as a means of screening for CAD is discussed in detail in the ACC/AHA Guideline Update for Exercise Testing.[52]

In the absence of symptoms, AECG monitoring can reveal transient ST-segment depression suggestive of CAD. However, as indicated in the ACC/AHA Guidelines for Ambulatory Electrocardiography,[53] there is presently no evidence that AECG monitoring provides reliable information concerning ischemia in asymptomatic subjects without known CAD.

In the absence of symptoms, EBCT is sometimes used as a means of screening for CAD. However, as indicated in the ACC/AHA Expert Consensus Document on Electron-Beam Computed Tomography for the Diagnosis and Prognosis of Coronary Artery Disease,[54] available data are insufficient to support recommending EBCT for this purpose to asymptomatic members of the general public.

Physicians are often confronted with concerned asymptomatic patients with abnormal findings on AECG and EBCT. Although the published data on this situation are scant, in the absence of symptoms, such patients probably still have a low pretest probability of significant CAD. A negative exercise test result only confirms the low probability of disease, and a positive test result may not increase the probability of disease enough to make a clinical difference.

Stress imaging procedures (ie, either stress myocardial perfusion imaging or stress echocardiography) are generally not indicated as the initial stress test in most such patients. However, in patients with resting ECG abnormalities that preclude adequate interpretation of the exercise ECG, stress imaging procedures are preferable to the exercise ECG. If the baseline ECG shows preexcitation or more than 1 mm of ST depression, exercise stress imaging procedures are preferred. If the resting ECG shows a ventricularly paced rhythm or left bundle-branch block, vasodilator perfusion imaging is preferred. In patients who are unable to exercise, pharmacological stress imaging is preferable to exercise ECG testing. The preference for stress imaging under these circumstances is based on the available literature in symptomatic patients. There are scant published data on the use of stress imaging procedures in asymptomatic patients in general and in particular on asymptomatic patients with resting ECG abnormalities or asymptomatic patients who are unable to exercise. In asymptomatic patients with an intermediate-risk or high-risk Duke treadmill score on exercise ECG testing, stress imaging procedures are potentially useful as a second diagnostic test. Given the low pretest probability of asymptomatic patients, an abnormal exercise ECG in such a patient is likely a false-positive that will be confirmed by a negative stress image. However, the published data demonstrating the efficacy of stress imaging procedures in these specific circumstances are scant. In the presence of a low-risk Duke treadmill score on exercise ECG testing, stress imaging procedures in asymptomatic patients are usually not justified.

In asymptomatic patients, risk stratification and prognosis are more important considerations than diagnosis. Because the treatment of asymptomatic patients cannot improve their symptoms, the principal goal of evaluation and treatment is the improvement of patient outcome by reducing the rate of death and nonfatal MI. In one large study dominated by asymptomatic patients,[55] the Duke treadmill score predicted subsequent cardiac events. However, the absolute event rate was low, even in patients with high-risk scores, which suggests that the ability to improve outcome with revascularization in such patients is limited.

The prognostic value of stress imaging procedures in asymptomatic patients is not well established. Some of the published series did include asymptomatic patients. However, this subset of patients was generally not analyzed separately. Blumenthal et al[56] reported a small study using exercise thallium testing in siblings of patients with premature coronary atherosclerosis. They demonstrated that the combination of an abnormal exercise ECG and a positive thallium image was prognostically important. However, many of the events included in their analysis were subsequent revascularizations, the performance of which was clearly influenced by the results of the exercise thallium test. Given the generally low event rate in asymptomatic patients, the ability of stress imaging procedures to identify a subset with a substantial absolute risk of subsequent events is problematic, with the possible exception of patients with previous MI.

Recommendations for Coronary Angiography for Risk Stratification in Asymptomatic Patients

Class IIa

1. **Patients with high-risk criteria that suggest ischemia on noninvasive testing.** ***(Level of Evidence: C)***

Class IIb

1. **Patients with inadequate prognostic information after noninvasive testing.** ***(Level of Evidence: C)***

Class III

1. **Patients who prefer to avoid revascularization.** ***(Level of Evidence: C)***

The noninvasive test findings that identify high-risk patients are based on studies in symptomatic patients. These findings are probably also applicable to asymptomatic patients but associated with a lower level of absolute risk in the absence of symptoms. The mere presence of left ventricular dysfunction in an asymptomatic patient probably does not justify coronary angiography. However, other high-risk noninvasive test findings that reflect myocardial ischemia, such as a high-risk Duke treadmill score, a large stress-induced perfusion defect, or an extensive echocardiographic wall-motion abnormality that develops at a low heart rate, are probably appropriate indications for coronary angiography, although there are only limited data to support this approach. The ability to improve outcome in such patients has not been demonstrated.

Recommendations for Pharmacotherapy to Prevent MI and Death in Asymptomatic Patients

Class I

1. **Aspirin in the absence of contraindication in patients with prior MI.** ***(Level of Evidence: A)***
2. **Beta-blockers as initial therapy in the absence of contraindications in patients with prior MI.** ***(Level of Evidence: B)***
3. **Lipid-lowering therapy in patients with documented CAD and LDL cholesterol greater than 130 mg/dL, with a target LDL of less than 100 mg/dL.** ***(Level of Evidence: A)***
4. **ACE inhibitor in patients with CAD* who also have diabetes and/or left ventricular systolic dysfunction.** ***(Level of Evidence: A)***

Class IIa

1. **Aspirin in the absence of contraindications in patients without prior MI.** ***(Level of Evidence: B)***
2. **Beta-blockers as initial therapy in the absence of contraindications in patients without prior MI.** ***(Level of Evidence: C)***
3. **Lipid-lowering therapy in patients with documented CAD and LDL cholesterol 100 to 129 mg/dL, with a target LDL of 100 mg/dL.** ***(Level of Evidence: C)***
4. **ACE inhibitor in all patients with CAD* or other vascular disease.** ***(Level of Evidence: B)***

***Significant CAD by angiography or previous MI.**

Even in asymptomatic patients, aspirin and beta-blockers are recommended in patients with prior MI. The data in support of these recommendations are detailed in the ACC/AHA Guidelines for the Management of Patients With Acute Myocardial Infarction.[57] In the absence of prior MI, patients with documented CAD on the basis of noninvasive testing or coronary angiography probably also benefit from aspirin, although the data on this specific subset of patients are limited.

Several studies have investigated the potential role of β-blockers in patients with asymptomatic ischemia demonstrated on exercise testing and/or ambulatory monitoring. The data generally demonstrate a benefit from β-blocker therapy, but not all trials have been positive.

Lipid-lowering therapy in asymptomatic patients with documented CAD was demonstrated to decrease the rate of adverse ischemic events in 4S,[58] as well as in the CARE study,[59] as mentioned previously.

A. Treatment of Risk Factors

In asymptomatic patients with documented CAD on the basis of noninvasive testing or coronary angiography, the treatment of risk factors outlined above is clearly appropriate. The recommendations for symptomatic patients should be followed as detailed in the 1999 guideline and the update section above.

In the absence of documented CAD, asymptomatic patients should also undergo treatment of risk factors according to primary prevention standards. Therapy should be directed toward hypertension, smoking cessation, diabetes, exercise training, and weight reduction in the presence of other risk factors. Lipid-lowering therapy should be administered according to the primary prevention standards outlined in the 2001 National Cholesterol Education Program guidelines.[2]

B. Revascularization

In asymptomatic patients, revascularization cannot improve symptoms. The only appropriate indication for revascularization with either percutaneous coronary intervention or coronary artery bypass grafting is therefore to improve prognosis. Most of the recommendations for revascularization that were published in 1999 for patients with stable angina also apply to asymptomatic patients, because their underlying rationale is to improve prognosis. The single Class I recommendation for revascularization in patients who have not been successfully treated by medical therapy is an exception and obviously does not apply to asymptomatic patients. However, the level of evidence in support of these recommendations in asymptomatic patients is clearly weaker than in symptomatic patients. Most of the available randomized trial data have focused on symptomatic patients. Their extrapolation to asymptomatic patients appears reasonable but is based on far more limited evidence.

In the Coronary Artery Surgery Study Registry,[60] asymptomatic patients with left main CAD who underwent coronary artery bypass grafting had a better outcome than those patients treated with medical therapy, but this was not a randomized trial. The most compelling randomized trial data on asymptomatic patients comes from the previously mentioned Asymptomatic Cardiac Ischemia Pilot (ACIP) study.[61,62] In patients with CAD who were either free of angina or had well-controlled symptoms, patients randomized to revascularization had a lower cardiac event rate than patients who were randomized to medical management

guided by angina or medical management guided by noninvasive ischemia. The patients entered in this study, who were required to have ischemia during ambulatory monitoring and exercise testing, as well as significant CAD, were more likely to have extensive CAD and prior MI. In the overall study group, 39% of the patients had 3-vessel disease, 40% had prior MI, 22% had prior revascularization, and 59% had angina within the previous 6 weeks. Many of the patients enrolled in this trial presumably came to medical attention because of symptoms or prior MI. The degree to which the results of ACIP can be applied to patients who have never been symptomatic and have less severe asymptomatic CAD is uncertain.

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KEY WORDS: ACC/AHA Guideline Update ■ angina ■ risk factors ■ coronary disease ■ revascularization

ACC/AHA 2002 Guideline Update for the Management of Patients With Chronic Stable Angina—Summary Article: A Report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (Committee on the Management of Patients With Chronic Stable Angina)

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