SJHG Heartbeat

Number 108 **June 2006**

ACC/AHA Update Secondary-Prevention Guidelines

Mounting evidence that scores of heart patients can avoid second heart attacks or strokes with intensive treatment to reduce their risks prompted the nation's top two heart organizations to jointly issue new secondary prevention recommendations. The American Heart Association (AHA) and the American College of Cardiology (ACC) have updated their guidelines for the secondary prevention of coronary and other atherosclerotic vascular diseases to reflect the results of evidence from recent clinical trials.[1]

Published last month, this update is the first since 2001 and begins a new process of monitoring recent clinical trials and results from major cardiology meetings for compelling evidence that would necessitate an update of the guidelines.

Two major developments have made these guidelines even more important in clinical practice. First, the aging of the population continues to expand the number of patients who could benefit from appropriate therapy—13 million estimated with coronary heart disease (CHD) alone. Secondly, many studies conclude that compliance, although improving slowly, is still considerably less than optimal. This *Heartbeat* will highlight the changes and includes tables which will summarize the guidelines. We urge that you provide these therapies to the patients who can benefit from them.

Cholesterol: How Low?

Findings from additional lipid trials involving more than 50,000 patients confirmed the benefits of aggressively lowering cholesterol, which resulted in new optional therapeutic targets. The secondary prevention guidelines echo the NCEP ATP III Lipid Guidelines of July 2004[2] covered in *Heartbeat 91*.[3] They indicate that all patients with coronary artery disease (CAD) and other forms of vascular disease should have LDL cholesterol lowered to under 100 mg/dL (Class 1 indication—proven evidence of benefit).

In addition, this guideline states it is “reasonable" to treat all those with acute and chronic CHD until their LDL is < 70 mg/dL (Class IIa indication—weight of evidence is in favor of efficacy). This is slightly more aggressive than the recent NCEP III guidelines which stated it was reasonable to treat to < 70mg/dL if they had high-risk CHD (CHD + tobacco dependence or diabetes or acute coronary syndrome). But for those with other forms of vascular disease (non-coronary), evidence is still pending to determine if lowering LDL below 70 will be beneficial.

Flu Shots for All

Influenza vaccination is now recommended for all patients with chronic cardiovascular disease (CVD). Recent data has shown a 50% reduction in mortality.

Clarification of Aspirin Dosages

The present update finally recommended lower-dose aspirin (ASA) for chronic maintenance of all CVD patients unless a contraindication exists. The recommended dosage has been reduced to between 75 and 162 mg/day, down from the previous guide of 75 to 325 mg/ day. This reflects the fact that the lower dose of ASA reduces cardiovascular events by the same magnitude as the higher dose but with less bleeding. The lone exception is for patients undergoing CABG where there are no trial data with lower doses of aspirin. Doses between 100 and 325mg appear efficacious. Doses above 162mg can be continued for 1 year and then switched to the lower dosages.

Changes for recommendations for ASA with clopidogrel following percutaneous coronary intervention (PCI) reflect the new PCI guidelines.[4]

- Bare metal stent: Continue ASA 325mg for 1 month.
- Sirolimus-eluting (Cypher) stent: Continue ASA 325mg for 3 months.
- Paclitaxel-eluting (Taxus) stent: Continue ASA 325mg for 6 months.

Clopidogrel 75 mg should be continued in all patients post PCI and acute coronary syndrome out to 12 months. Then ASA 81 to 162mg should be continued indefinitely. The data from the CHARISMA trial presented at the American College of Cardiology meeting in March further supports not continuing the clopidogrel, although this was not actually addressed in these guidelines.[5]

ACE-inhibitor Use Expanded and "Reduced"?

ACE-inhibitor usage was expanded to include heart failure patients with LVEF < 40%. This was just late in coming but a foregone conclusion.

The PEACE trial, involving ACE-inhibitor therapy among patients at relatively low-risk with stable CHD and normal LV function, influenced the recommendations.[6] Now, the use of ACE-inhibitors in patients with stable CHD is considered ***optional***, and the decision to use them should be made on an individual basis. This confusion was caused by the neutral results of PEACE which were in contradistinction to the beneficial results seen with ACE-inhibitors in HOPE[7] and EUROPA[8] in patients with CHD.

Putting PEACE in perspective, as risk decreases, benefit also will decrease.[9] The dosage of ACE-inhibitor was low in PEACE, and these low-risk patients were not followed long enough—an under-powered study. A recent meta-analysis of all the ACE-inhibitor trials led French investigators to suggest that ACE-inhibitors should be used systematically in all patients with CHD.[10] They were pushing for them to be included in the new European Society of Cardiology guidelines for stable CHD to be released shortly. I plan to use ACE-inhibitors in all my patients with CHD.

Aldosterone Blockade Added

The results of additional studies have confirmed the benefits of aldosterone blockade in patients with depressed LV function (LVEF < 40%). This treatment was added to the guideline in patients without hyperkalemia or significant azotemia.[11]

TLC

Regarding TLC (Therapeutic Lifestyle Changes), emphasis was placed on reducing waist circumference to < 40 inches and < 35 inches in men and women respectively. Physical activity is encouraged 30-60 min 7 days / week (minimum 5 days). Cessation of smoking and avoidance of passive smoking are encouraged.

TABLE 1. AHA/ACC Secondary Prevention for Patients With Coronary and Other Vascular Disease*: 2006 Update

	Intervention Recommendations With Class of Recommendation and Level of Evidence
SMOKING: Goal Complete cessation. No exposure to environmental tobacco smoke.	• Ask about tobacco use status at every visit. **I (B)** • Advise every tobacco user to quit. **I (B)** • Assess the tobacco user's willingness to quit. **I (B)** • Assist by counseling and developing a plan for quitting. **I (B)** •Arrange follow-up, referral to special programs, or pharmacotherapy (including nicotine replacement and bupropion). **I (B)** • Urge avoidance of exposure to environmental tobacco smoke at work and home. **I (B)**
BLOOD PRESSURE CONTROL: Goal < 140/90 mm hg or < 130/80 mm Hg if patient has diabetes or chronic kidney disease	**For all patients:** • Initiate or maintain lifestyle modification—weight control; increased physical activity; alcohol moderation; sodium reduction; and emphasis on increased consumption of fresh fruits, vegetables, and low-fat dairy products. **I (B)** **For patients with blood pressure >140/90 mm Hg (or >130/80 mm Hg for individuals with chronic kidney disease or diabetes):** • As tolerated, add blood pressure medication, treating initially with _-blockers and/or ACE inhibitors, with addition of other drugs such as thiazides as needed to achieve goal blood pressure**. I (A)** [For compelling indications for individual drug classes in specific vascular diseases, see Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure (JNC 7).
LIPID MANAGEMENT: Goal LDL-C<100 mg/dL If Triglycerides are ≥ 200mg/dL, non-HDL should be < 130mg/dL. [Non HDL-C = TC – HDL-C]	**For all patients:** • Start dietary therapy. Reduce intake of saturated fats (to < 7% of total calories), *trans*-fatty acids and cholesterol (to < 200mg/d). **(1B)** • Adding plant stanol/sterols (2g/d) and viscous fiber (>10 g/d) will further lower LDL-C. • Promote daily physical activity and weight management. **I (B)** • Encourage increased consumption of omega-3 fatty acids in the form of fish‡ or in capsule form (1 g/d) for risk reduction. For treatment of elevated triglycerides, higher doses are usually necessary for risk reduction. **IIb (B)** **For lipid management:** Assess fasting lipid profile in all patients, and within 24 hours of hospitalization for those with an acute cardiovascular or coronary event. For hospitalized patients, initiate lipid-lowering medication as recommended below before discharge according to the following schedule: • LDL-C should be < 100 mg/dL **I (A)**, **and** • Further reduction of LDL-C to < 70 mg/dL is reasonable. **IIa (A)** • If baseline LDL-C is ≥ 100 mg/dL, initiate LDL-lowering drug therapy.§ **I (A)** • If on-treatment LDL-C is ≥ 100 mg/dL, intensify LDL-lowering drug therapy (may require LDL-lowering drug combination //). **I (A)** • If baseline LDL-C is 70 to 100 mg/dL, it is reasonable to treat to LDL-C <70 mg/dL. **IIa (B)** • If triglycerides are 200 to 499 mg/dL, non-HDL-C should be < 130 mg/dL. **I (B)**, **and** • Further reduction of non-HDL-C to < 100 mg/dL is reasonable. **IIa (B)** • Therapeutic options to reduce non-HDL-C are: (1) More intense LDL-C–lowering therapy **I (B)**, or (2) Niacin (after LDL-C–lowering therapy) **IIa (B)**, or (3) Fibrate therapy# (after LDL-C–lowering therapy) **IIa (B)** • If triglycerides are > 500 mg/dL#, therapeutic options to prevent pancreatitis are fibrate¶ or niacin¶ before LDL-lowering therapy; and treat LDL-C to goal after triglyceride-lowering therapy. Achieve non-HDL-C < 130 mg/dL if possible. **I (C)**
PHYSICAL ACTIVITY: Goal 30 minutes, 7 days per week (minimum 5 days per week)	• For all patients, assess risk with a physical activity history and/or an exercise test, to guide prescription. **I (B)** • For all patients, encourage 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 lifestyle activities (eg, walking breaks at work, gardening, household work). **I (B)** • Encourage resistance training 2 days per week. **IIb (C)** • Advise medically supervised programs for high-risk patients (eg, recent acute coronary syndrome or revascularization, heart failure). **I (B)**
WEIGHT MANAGEMENT: Goal Body mass index: 18.5 to 24.9 kg/m^2 Waist circumference: men < 40 inches, women < 35inches	• Assess body mass index and/or waist circumference on each visit and consistently encourage weight maintenance/reduction through an appropriate balance of physical activity, caloric intake,and formal behavioral programs when indicated to maintain/achieve a body mass index between 18.5 and 24.9 Kg/m2. **1 (B)** • If waist circumference (measured horizontally at the iliac crest) is ≥ 35 inches in women and ≥ 40 inches in men, initiate lifestyle changes and consider tx strategies for MetS as indicated. **I (B)** • The initial goal of weight loss therapy should be to reduce body weight by approximately 10% from baseline. With success, further weight loss can be attempted if indicated through further assessment. **I (B)**

TABLE 1. Continued

	Intervention Recommendations With Class of Recommendations and Level of Evidence
DIABETES MANAGEMENT: Goal HgA1c < 7%	• Initiate lifestyle and pharmacotherapy to achieve near-normal HgA1c. **1(B)** • Begin vigorous modification of other risk factors (eg, physical activity, weight management, blood pressure control, and cholesterol management as recommended above). **I (B)** • Coordinate diabetic care with patient's primary care physician or endocrinologist. **I (C)**
ANTIPLATELET AGENTS/ ANTICOAGULANTS:	• Start aspirin 75 to 162 mg/d and continue indefinitely in all patients unless contraindicated. **I (A)** - For patients undergoing coronary artery bypass grafting, aspirin should be started within 48 hours after surgery to reduce saphenous vein graft closure. Dosing regimens ranging from 100 to 325 mg/d appear to be efficacious. Doses higher than 162 mg/d can be continued for up to 1 year. **I (B)** • Start and continue clopidogrel 75 mg/d in combination with aspirin for up to 12 months in patients after acute coronary syndrome or percutaneous coronary intervention with stent placement (≥ 1 month for bare metal stent, ≥ 3 months for sirolimus-eluting stent, and ≥ 6 months for paclitaxel-eluting stent). **I (B)** - Patients who have undergone percutaneous coronary intervention with stent placement should initially receive higher-dose aspirin at 325 mg/d for 1 month for bare metal stent, 3 months for sirolimus-eluting stent, and 6 months for paclitaxel-eluting stent. **I (B)** • Manage warfarin to international normalized ratio_2.0 to 3.0 for paroxysmal or chronic atrial fibrillation or flutter, and in post–myocardial infarction patients when clinically indicated (eg, atrial fibrillation, left ventricular thrombus). **I (A)** • Use of warfarin in conjunction with aspirin and/or clopidogrel is associated with increased risk of bleeding and should be monitored closely. **I (B)**
RENIN-ANGIOTENSIN-ALDOSTERONE SYSTEM BLOCKERS:	**ACE inhibitors:** • Start and continue indefinitely in all patients with left ventricular ejection fraction < 40% and in those with hypertension, diabetes, or chronic kidney disease, unless contraindicated. **I (A)** • Consider for all other patients. **I (B)** • Among lower-risk patients with normal left ventricular ejection fraction in whom cardiovascular risk factors are well controlled and revascularization has been performed, use of ACE inhibitors may be considered optional. **IIa (B)** **Angiotensin receptor blockers:** • Use in patients who are intolerant of ACE inhibitors and have heart failure or have had a myocardial infarction with left ventricular ejection fraction < 40%. **I (A)** • Consider in other patients who are ACE inhibitor intolerant. **I (B)** • Consider use in combination with ACE inhibitors in systolic-dysfunction heart failure. **IIb (B)** **Aldosterone blockade:** • Use in post–myocardial infarction patients, without significant renal dysfunction** or hyperkalemia††, who are already receiving therapeutic doses of an ACE inhibitor and β blocker, have a left ventricular ejection fraction < 40%, and have either diabetes or heart failure. **I (A)**
B-BLOCKERS:	• Start and continue indefinitely in all patients who have had myocardial infarction, acute coronary syndrome, or left ventricular dysfunction with or without heart failure symptoms, unless contraindicated. **I (A)** Consider chronic therapy for all other patients with coronary or other vascular disease or diabetes unless contraindicated. **IIa (C)**
INFLUENZA VACCINATION:	Patients with cardiovascular disease should have an influenza vaccination. **I (B)**

* Patients covered by these guidelines include those with established coronary and other atherosclerotic vascular disease, including peripheral arterial disease, atherosclerotic aortic disease, and carotid artery disease. Treatment of patients whose only manifestation of cardiovascular risk is diabetes will be the topic of a separate AHA scientific statement. ACE indicates angiotensin-converting enzyme.

‡ Pregnant and lactating women should limit their intake of fish to minimize exposure to methylmercury.

§ When LDL-lowering medications are used, obtain at least a 30% to 40% reduction in LDL-C levels. If LDL-C < 70 mg/dL is the chosen target, consider drug titration to achieve this level to minimize side effects and cost. When LDL-C < 70 mg/dL is not achievable because of high baseline LDL-C levels, it generally is possible to achieve reductions of > 50% in LDL-C levels by either statins or LDL-C–lowering drug combinations.

// Standard dose of statin with ezetimibe, bile acid sequestrant, or niacin.

¶ The combination of high-dose statin fibrate can increase risk for severe myopathy. Statin doses should be kept relatively low with this combination. Dietary supplement niacin must not be used as a substitute for prescription niacin.

Patients with very high triglycerides should not consume alcohol. The use of bile acid sequestrant is relatively contraindicated when triglycerides are > 200 mg/dL.

** Creatinine should be < 2.5 mg/dL in men and < 2.0 mg/dL in women.

††Potassium should be < 5.0 mEq/L.

TABLE 2. Classification of Recommendations and Level of Evidence*

Classification of Recommendations

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

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

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

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

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

Level of Evidence

Level of Evidence A: Data derived from multiple randomized clinical trials or meta-analyses.

Level of Evidence B: Data derived from a single randomized trial or nonrandomized studies.

Level of Evidence C: Only consensus opinion of experts, case studies, or standard-of-care.

Mario L Maiese DO, FACC, FACOI
Clinical Associate Professor of Medicine, UMDNJSOM Email: maiese1@comcast.net
Heartbeats online: www.sjhg.org

***Heartbeat* is a South Jersey Heart Group publication.**

---

[1] Smith C S et al. AHA/ACC Guidelines for secondary prevention for patients with coronary and other atherosclerotic vascular disease: 2006 Update: Endorsed by the National Heart, Lung and Blood Institute. *J Am Coll Cardiol* May 16 2006; 47: 2130-39.

[2] Grundy SM et al. Implications of recent clinical trials for the National Cholesterol Education Program Adult Treatment Panel III guidelines. *Circulation* July 13 2004; 110: 227-239.

[3] Maiese M L. Aggressive LDL-C Lowering. *Heartbeat* August 2004; # 91.

[4] Lansky A J et al. Percutaneous Coronary Intervention and adjunctive pharmacotherapies in women. A statement for healthcare professionals from the American Heart Association. Endorsed by the American College of Cardiology foundation. *Circulation* February 2005; 111: 940-53.

[5] Maiese M L. CHARISMA sparks risk and debate. *Heartbeat* March 2006; # 107.

[6] PEACE Trial Investigators. Angiotensin-converting-enzyme inhibitor in stable CAD. *N Engl J Med* 2004; 351; 2058-2068.

[7] The Heart Outcomes Prevention Evaluation (HOPE) Study Investigators. Effects of an angiotensin converting enzyme inhibitor, ramipril, on cardiovascular events in high-risk patients. *N Engl J Med* January 2000; 342: 145-153.

[8] The European Trial On reduction of cardiac events with Perindopril in stable coronary Artery disease Investigators. Efficacy of perindopril in reduction of cardiovascular events among patients with stable coronary artery disease: randomized, double-blind, placebo-controlled, multi-center trial (the EUROPA study). *Lancet* Sept 6 2003; 326:782-788.

[9] Maiese M L. MetS/T2DM/HBP ACEI vs ARB. *Heartbeat* March 2005; # 97: 2-3.

[10] Danchin N et al. Angiotensin-converting enzyme inhibitors in patients with coronary artery disease and absence of heart failure or left ventricular dysfunction. An overview of long-term randomized trials. *Arch Intern Med* April 2006; 166: 787-96.

[11] Maiese M L. Role of aldosterone blockade. *Heartbeat* April 2005; # 98.