Editorial

Summary of the American Heart Association's Evidence-Based Guidelines for Cardiovascular Disease Prevention in Women

Lori Mosca for the Expert Panel/Writing Group

Cardiovascular disease (CVD) is the largest killer of women in the United States.[1] More than 500 000 women die of CVD annually, more than the number of CVD-related deaths in men or related to the next 7 causes of death in women combined.[1] Despite these statistics, a national survey in 2003 by the American Heart Association (AHA) showed that less than half of all women know that CVD is their leading cause of death.[2] In an effort to raise awareness and educate health care providers and the public about methods to prevent incident and recurrent CVD events, an expert panel was convened to establish evidence-based guidelines for the prevention of CVD in women. The panel consisted of representatives from 11 AHA Scientific Councils and 11 federal and other professional organizations. There were an additional 22 endorsers. Details of the process and the complete guidelines have been published.[3]

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Briefly, candidate recommendations for CVD risk-reducing interventions were discussed, prioritized, and then selected for a systematic literature search. Randomized, clinical trials and large, prospective, cohort studies evaluating cardiovascular risk-reducing interventions with a focus on major clinical endpoints (death, myocardial infarction [MI], stroke, revascularization procedure, congestive heart failure, or a composite CVD endpoint), whether or not there were female participants, were included. Nearly 7000 abstracts were identified in the initial search; 1279 were included for full-text screening and 399 studies were included in the summary evidence tables for each recommendation, with sex-specific information if available. The evidence tables are published online at http://atvb.ahajournals.org. The expert panel used an evidence rating system based on methods used in previous AHA/American College of Cardiology (ACC) guidelines and is outlined in Table 1.[4] In addition, a generalizability index was used to rate the likelihood that results generated from studies conducted in men would be applicable to women.

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Risk Assessment and Stratification

The Expert Panel recommended stratifying women into 3 risk groups (high, intermediate, and lower risk) based on the absolute 10-year probability of a coronary event (using the Framingham Risk Score for women) and based on clinical diagnoses. Women at high risk have a calculated 10-year CHD risk >20% and/or established CHD, other vascular disease, diabetes, or chronic kidney disease. Women at intermediate risk have a 10-year risk of 10% to 20% and may have subclinical CVD (ie, coronary calcification), metabolic syndrome, multiple risk factors, markedly elevated levels of 1 risk factor or a first-degree relative with early CVD. Women at lower risk have a 10-year risk <10% and may have metabolic syndrome or variable numbers of risk factors. Additionally, an optimal risk group was defined as women who have desirable levels of risk factors and who have a heart-healthy lifestyle.

Clinical Recommendations

Clinical recommendations are grouped by lifestyle interventions, major risk factor interventions, preventive drug interventions, atrial fibrillation/stroke prevention, and a class III category, which outlines interventions that are not recommended for CVD prevention in women. Clinical recommendations are prioritized based on strength of the recommendation and the level of evidence. A summary of priorities for CVD prevention in women based on risk classification is presented in Table 2. The complete list of recommendations is available online at http://atvb.ahajournals.org.

Lifestyle Interventions

All women should be encouraged not to smoke and to avoid environmental smoke, and to get at least 30 minutes of moderate exercise (ie, brisk walking) on most and preferably all days or, in women with a recent coronary event, to participate in a rehabilitation program. A heart-healthy diet is recommended; for women without hyperlipidemia, that incorporates a variety of fruits, vegetables, grains, low-fat or non-fat dairy products, fish, legumes, and sources of protein that are low in saturated fat (limit saturated fat to <10% of calories and cholesterol to <300 mg/d). In addition, for women who also need lipid-lowering, saturated fat should be limited to <7% of calories, and cholesterol should be limited to <200 mg/d. Weight control should be encouraged to achieve a body mass index (BMI) between 18.5 and 24.9 kg/m^2 and a waist circumference <35 inches.

These lifestyle interventions received class I recommendations (useful and effective), although supporting evidence was classified as B (limited to single randomized trial and/or

TABLE 1. Recommendation Classifications and Levels of Evidence

Classification
Class I: Intervention is useful and effective
Class IIa: Weight of evidence/opinion is in favor of usefulness/efficacy
Class IIb: Usefulness/efficacy less well-established by evidence/opinion
Class III: Intervention is not useful/effective and may be harmful
Level of Evidence
A: Sufficient evidence from multiple randomized trials
B: Limited evidence from single, randomized trial or other nonrandomized studies
C: Based on expert opinion, case studies, or standard of care

Adapted with permission from Gibbons et al.[4]

several non-randomized studies). This reflects the strength of the observational data and ethical issues that prevent controlled trials of certain interventions (ie, smoking cessation). Furthermore, a "heart-healthy lifestyle" can prevent the development of major risk factors for CVD. Other lifestyle interventions that may be considered in women at high risk include the use of omega-3 fatty acids and folic acid (both class IIb, level B), as well as referral/treatment for depression (class IIa, level B). Regardless of risk group, lifestyle interventions are a top priority for CVD prevention in women.

Major Risk Factor Interventions

Major risk factor interventions target hypertension, dyslipidemia, and diabetes. Previously published guidelines, including the National Cholesterol Education Program—Adult Treatment Panel III,[5] the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure,[6] and the American Diabetes Association,[7] can be referred to for specific management strategies. In addition, previous AHA prevention guidelines[8–10] were used as a resource to develop and update sex-specific recommendations for women.

Clinical recommendations include maintenance of an optimal blood pressure <120/80 mm Hg through lifestyle approaches, including the dietary approaches to stop hypertension (DASH) eating plan (class I, level B).[6] Pharmacotherapy is indicated at levels ≥140/90 mm Hg or even lower in the setting of blood pressure-related target organ damage or diabetes. Thiazide diuretics are recommended as part of the antihypertensive regimen, unless contraindicated (class I, level A).

Optimal levels of lipids and lipoproteins for women were defined as low-density lipoprotein cholesterol (LDL-C) <100 mg/dL, triglycerides <150 mg/dL, non-high-density lipoprotein cholesterol (HDL-C) <130 mg/dL, and HDL-C >50 mg/dL. For women at high risk, LDL-C–lowering therapy (statins preferred) was recommended to be initiated in conjunction with lifestyle therapy if LDL-C ≥100 mg/dL (class I, level A). Statin therapy was also recommended in high-risk women with LDL-C <100 mg/dL unless contraindicated (class I, level B). Niacin or a fibrate was recommended for treatment of low HDL-C or elevated non-HDL-C (class I, level B) among high-risk women. For women at intermediate risk, LDL-C–lowering with statins was recommended if levels were ≥130 mg/dL with lifestyle therapy (class I, level A). For women at lower risk, LDL-C–lowering was recommended if levels were ≥190 mg/dL or ≥160 mg/dL in the presence of multiple risk factors (class IIa, level B). Niacin or a fibrate was recommended for treatment of low HDL-C or

TABLE 2. Priorities for Prevention in Practice Based on Risk Classification

Women at High Risk (>20% Risk)
Class I Recommendations
Smoking cessation/environmental smoke avoidance
Physical activity/cardiac rehabilitation
Diet therapy
Weight maintenance/reduction
Blood pressure control
Lipid control with LDL-C–lowering agents, niacin, fibrates
Statin therapy in women with LDL-C <100 mg/dL
Aspirin therapy (75–162 mg)
Beta-blocker therapy unless contraindicated
ACE inhibitor therapy (ARBs if contraindicated)
Glycemic control in diabetics
Class IIa Recommendation:
Evaluation/referral for depression
Class IIb Recommendations:
Omega 3 fatty-acid supplementation
Folic acid supplementation
Women at Intermediate Risk (10%–20% Risk)
Class I Recommendations:
Smoking cessation/environmental smoke avoidance
Physical activity
Heart-healthy diet or lipid-lowering diet
Weight maintenance/reduction
Blood pressure control
Lipid control
Class IIa Recommendation:
Aspirin therapy (75–162 mg)
Women at Lower Risk (<10% Risk)
Class I Recommendations
Smoking cessation/environmental smoke avoidance
Physical activity
Heart-healthy diet or lipid-lowering diet
Weight maintenance/reduction
Treat individual CVD risk factors as indicated
Stroke Prevention Among Women With Atrial Fibrillation
Class I Recommendations:
High–intermediate risk of stroke
Warfarin therapy
Low risk of stroke (<1%/year) or contraindication to warfarin
Aspirin 325 mg therapy
Class III (Not Recommended for CVD Prevention):
Hormone therapy in postmenopausal women
Antioxidant supplements
Aspirin therapy in low risk women

Adapted with permission from Mosca et al.[3]

elevated non-HDL-C once the LDL-C goal was reached for both intermediate-risk (class I, level B) and lower-risk (class IIa, level B) groups. Among diabetic women, diet and pharmacotherapy were recommended to achieve an Hb_{A1C} <7% (class I, level B).

Preventive Drug Interventions

Several pharmacologic interventions were recommended for women at high cardiovascular risk. ACE inhibitors are indicated in all high-risk women (class I, level A); if contraindicated, then angiotensin receptor blockers (ARBs) should be used in those with clinical evidence of heart failure or a left ventricular ejection faction <40% (class I, level B). Beta-blockers are recommended in all women after MI or with chronic ischemic syndromes (class I, level A). Aspirin (75 to 162 mg/d), or clopidogrel for intolerance, is a class I, level A recommendation for high-risk women unless contraindicated. Aspirin is a class IIa, level B recommendation in those at intermediate risk if blood pressure is controlled and the benefits outweigh the risks of adverse gastrointestinal effects. In women with atrial fibrillation, warfarin is recommended (class I, level A) unless the patient has a contraindication or the risk for stroke is low (<1%/year), in which cases aspirin (325 mg/d) is recommended (class I, level A).

Class III Recommendations

A unique aspect of these guidelines is the designation of class III interventions that should not be used for CVD prevention. Aspirin in lower-risk women, hormone therapy in postmenopausal women, and antioxidant vitamin supplements in all women were rated as class III, because of the unproven benefits and possible harm associated with their use, pending results of ongoing and future trials.

Conclusions

The expert panel concluded that high-quality observational and clinical trial evidence supports the use of risk-modifying interventions that may have a substantial impact on reducing CVD in women if more uniformly implemented. As part of the AHA "Go Red for Women" national campaign to raise awareness about CVD in women, these guidelines will be disseminated to health care providers as well as other partners and will be incorporated into continuing medical education programs. Because a recent national survey documented that less than half of all women recognize that CVD is their leading killer, these guidelines can be used as an educational tool to help women understand their risk and take appropriate action.[2] The report highlighted the persistent gap in knowledge related to racial/ethnic minorities and elderly women. The panel also emphasized that the guidelines are never a substitute for good clinical practice.

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