Risk Factor Control in Women

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BERRA: ***Risk Factor Control in Women.*** *The World Heart Federation estimates that one third of all deaths in women is caused by cardiovascular disease (CVD). By 2010, CVD death rates in women are predicted to rise by 120% compared to 1990. Women in developing countries suffer from higher death rates from CVD compared to women in industrialized countries. The landmark INTERHEART Study found that 90% of the population attributable risk for acute myocardial infarction worldwide is related to well recognized and treatable "risk factors "such as smoking, abnormal lipids, hypertension, and diabetes. Poverty, social isolation, low levels of illiteracy, and lack of access to health care are also associated with a higher risk of CVD and stroke in women. It is critical to continue our focus on the unique needs of women in order to reduce morbidity and mortality from CVD and stroke. (J HK Coll Cardiol 2010;18(Suppl 1:25-30)*

Guidelines, Heart disease, Prevention, Women

Introduction

Women comprise approximately 50% of the world's population.[1] The World Heart Federation estimates that one third of all deaths in women is caused by cardiovascular disease (CVD).[2] By 2010, CVD death rates in women are predicted to rise by 120% compared to 1990.[2,3] It has also been shown that women in developing countries suffer from higher death rates from CVD compared to women in industrialized countries.[4] These staggering statistics demand an increased emphasis on awareness, treatment, and research to prevent CVD in women.

Yusef et al, in the INTERHEART Study, found that 90% of the population attributable risk for acute myocardial infarction worldwide is related to well recognized and treatable "risk factors." This holds true for women as well as for men.[5] These risk factors include age, family history, abnormal lipids, physical inactivity, overweight/obesity, hypertension, smoking, diabetes, depression, increased waist circumference, a diet low in fiber, fruits, vegetables, fish, mono/polyunsaturated fats and high in saturated fats. Poverty, social isolation, illiteracy, and lack of access to health care are also associated with a higher risk of CVD and stroke in women.[6,7]

Stroke rates in women also continue to rise. Stroke results in significant hospitalizations, disability, diminished quality of life, and the need for expensive long term care.[8] Worldwide, 15 million persons suffer an acute stroke each year.[9] Stroke is the second leading cause of death in persons over 60 years of age and ranks as the third most common cause of death in developed countries.[10] Many of the risk factors for CVD and stroke overlap. Thus, all efforts directed at CVD prevention in women will also result in a reduction of death and disability from stroke.

Worldwide, CVD risk factors are similar.[5] However, important differences exist in the prevalence of heart disease risk based on ethnicity within the female population. In the Unites States, the estimated prevalence of CVD in Mexican-American, Black, and White women is 32.5%, 45.9%, and 33.3% respectively.[8] Associated with the increased prevalence is found

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significant differences in Body Mass Index (>30) and a physician diagnosis of Type 2 Diabetes. For Mexican-American, Black, and White women the prevalence for BMI > 30 is 41.9%, 52.9% and 32.7%. Associated with this is a prevalence of physician diagnosed Type 2 Diabetes of 14.2%, 13.1%, and 6.1%. These differences clearly define important areas of research to improve the identification and prompt treatment for specific ethnic populations know to be at increased risk for heart attack and stroke.[8] Other important factors that influence CVD and stroke risk in women include older age and the presence of co-morbidities.[11]

Around the world, women are the primary caregivers for their families. As part of this role, women influence family lifestyles including patterns of physical activity and nutrition. This influence also has the potential to affect the lifestyles of friends and social communities. Steinberger et al evaluated metabolic syndrome (MS) in children and adolescents. They found that childhood/adolescent weight was correlated to the amount of daily Television (TV) viewing plus the presence of overweight in one or two parents. TV viewing and parental overweight resulted in a 15 or 32% greater risk of being overweight compared to children of normal weight. Metabolic syndrome in children/adolescents is due to a combination of shared genetic and environmental risk factors such as physical inactivity and weight. Children with parents who have MS and CVD risk factors are at very high risk of developing MS. In addition, children in families with early onset of atherosclerotic heart disease tended to be heavier, had elevated lipids, were more likely to have high blood pressure, elevated glucose, impaired endothelial function, and had evidence of carotid intimal medial thickness.[12] Addressing ways to prevent CVD and stroke in women has great potential to reduce their risk but and that of their family, friends, and community.[13-17]

Risk Reduction in Women

The management of risk factors in women includes the identification of risk factors through biological and physiological measures, education and counseling, use of self-monitoring and self care skills, regular follow up to titrate medical therapies and intensify lifestyle interventions. Setting goals based on *level of risk* is the first step in achieving effective CVD risk factor reduction.

In 2007, the American Heart Association published updated guidelines for CVD risk reduction in women.[18] The updated guidelines include measures of "lifetime risk" and short term (10 year risk) in order to emphasize that prevention is important for all women throughout their lifespan (See Table 1). Adding family history of CVD, evidence of sub-clinical heart disease, and poor functional capacity to the *Classification of CVD Risk* in women helps identify those at higher lifetime risk at much lower ages compared to the Framingham Risk Score alone.[18] Understanding the influence of risk factors at a young age and the correlation of these risk factors with the future development of CAD, guides our education, counseling and treatment interventions. Tables 2 and 3 define the specific risk factors with recommended clinical and lifestyle interventions. Interventions found not to be useful, effective or potentially harmful are listed in Table 4. Evaluation of risk and implementation of lifestyle risk reduction is the *Gold Standard* of care around the world. Women identified at the highest risk, should be offered intensive lifestyle plus medical therapies that have been shown to reduce both morbidity and mortality. Providing optimal medical therapies includes control of hypertension, dyslipidemia, diabetes, and smoking cessation as the most critical. For women with a recent cardiovascular event, referral to cardiac rehabilitation program or a home based exercise program must be included as part of their overall treatment plan.[18,19] For women at intermediate or low risk, lifestyle counseling is always important with medical therapies provided as indicated by guidelines.

For women, for their families, and for the health of generations to come, CVD risk reduction holds the promise to reduce death and disability and improve quality of life.

He who takes medicine and neglects to diet wastes the skill of his doctors.
~ Chinese Proverb ~

Table 1. Classification of CVD risk in women

Risk status	Criteria
High risk	Established coronary heart disease Cerebrovascular disease Peripheral arterial disease Abdominal aortic aneurysm End-stage or chronic renal disease Diabetes mellitus 10-year Framingham global risk >20%*
At risk	≥1 major risk factors for CVD, including: Cigarette smoking Poor diet Physical inactivity Obesity, especially central adiposity Family history of premature CVD (CVD at <55 years of age in male relative and <65 years of age in female relative) Hypertension Dyslipidemia Evidence of subclinical vascular disease (eg, coronary calcification) Metabolic syndrome Poor exercise capacity on treadmill test and/or abnormal heart rate recovery after stopping exercise
Optimal risk	Framingham global risk <10% and a healthy lifestyle, with no risk factors

CVD indicates cardiovascular disease.

*Or at high risk on the basis of another population-adapted tool used to assess global risk.

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Table 2. Guidelines for prevention of CVD in women: clinical recommendations

Lifestyle interventions

Cigarette smoking

Women should not smoke and should avoid environmental tobacco smoke. Provide counseling, nicotine replacement, and other pharmacotherapy as indicated in conjunction with a behavioral program or formal smoking cessation program *(Class I, Level B)*.

Physical activity

Women should accumulate a minimum of 30 minutes of moderate-intensity physical activity (eg, brisk walking) on most, and preferably all, days of the week *(Class I, Level B)*.

Women who need to lose weight or sustain weight loss should accumulate a minimum of 60 to 90 minutes of moderate-intensity physical activity (eg, brisk walking) on most, and preferably all, days of the week *(Class I, Level C)*.

Rehabilitation

A comprehensive risk-reduction regimen, such as cardiovascular or stroke rehabilitation or a physician-guided home- or community-based exercise training program, should be recommended to women with a recent acute coronary syndrome or coronary intervention, new-onset or chronic angina, recent cerebrovascular event, preripheral arterial disease *(Class I, Level A)*, or current/prior symptoms of heart failure and an LVEF <40% *(Class I, Level B)*.

Dietary intake

Women should consume a diet rich in fruits and vegetables; choose whole-grain, high-fiber foods; consume fish, especially oily fish,* at least twice a week; limit intake of saturated fat to <10% of energy, and if possible to <7%, cholesterol to <300 mg/d, alcohol intake to no more than 1 drink per day,† and sodium intake to <2.3 g/d (approximately 1 tsp salt). Consumption of trans-fatty acids should be as low as possible (eg, <1% of energy) *(Class I, Level B)*.

Weight maintenance/reduction

Women should maintain or lose weight through an appropriate balance of physical activity, caloric intake, and formal behavioral programs when indicated to maintain/achieve a BMI between 18.5 and 24.9 kg/m^2 and a waist circumference ≤35 in *(Class I, Level B)*.

Omega-3 fatty acids

As an adjunct to diet, omega-3 fatty acids in capsule form (approximately 850 to 1000 mg of EPA and DHA) may be considered in women with CHD, and higher doses (2 to 4 g) may be used for treatment of women with high triglyceride levels *(Class IIb, Level B)*.

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Table 2. Guidelines for prevention of CVD in women: clinical recommendations (cont'd)

Depression
Consider screening women with CHD for depression and refer/treat when indicated *(Class IIa, Level B)*.

Major risk factor interventions

Blood pressure – optimal level and lifestyle
Encourage an optimal blood pressure of <120/80 mm Hg through lifestyle approaches such as weight control, increased physical activity, alcohol moderation, sodium restriction, and increased consumption of fresh fruits, vegetables, and low-fat dairy products *(Class I, Level B)*.

Blood pressure – pharmacotherapy
Pharmacotherapy is indicated when blood pressure is ≥140/90 mm Hg or at an even lower blood pressure in the setting of chronic kidney disease or diabetes (≥130/80 mm Hg). Thiazide diuretics should be part of the drug regimen for most patients unless contraindicated or if there are compelling indications for other agents in specific vascular diseases. Initial treatment of high-risk women[‡] should be with β-blockers and/or ACE inhibitors/ARBs, with addition of other drugs such as thiazides as needed to achieve goal blood pressure *(Class I, Level A)*.

Lipid and lipoprotein levels – optimal levels and lifestyle
The following levels of lipids and lipoproteins in women should be encouraged through lifestyle approaches: LDL-C <100 mg/dL, HDL-C >50 mg/dL, triglycerides <150 mg/dL, and non-HDL-C (total cholesterol minus HDL cholesterol) <130 mg/dL *(Class I, Level B)*. If a woman is at high risk[‡] or has hypercholesterolemia, intake of saturated fat should be <70% and cholesterol intake <200 mg/d) *(Class I, Level B)*.

Lipids – pharmacotherapy for LDL lowering, high-risk women
Utilize LDL-C – lowering drug therapy simultaneously with lifestyle therapy in women with CHD to achieve an LDL-C <100 mg/dL *(Class I, Level A)* and similarly in women with other atherosclerotic CVD or diabetes mellitus or 10-year absolute risk >20% *(Class I, Level B)*.
A reduction to <70 mg/dL is reasonable in very-high-risk women[§] with CHD and may require an LDL-lowering drug combination *(Class IIa, Level B)*.

Lipids – pharmacotherapy for LDL lowering, other at-risk women
Utilize LDL-C – lowering therapy if LDL-C level is ≥130 mg/dL with lifestyle therapy and there are multiple risk factors and 10-year absolute risk 10% to 20% *(Class I, Level B)*.
Utilize LDL-C – lowering therapy if LDL-C level is ≥160 mg/dL with lifestyle therapy and multiple risk factors even if 10-year absolute risk is <10% *(Class I, Level B)*.
Utilize LDL-C – lowering therapy if LDL ≥190 mg/dL regardless of the presence or absence of other risk factors or CVD on lifestyle therapy *(Class I, Level B)*.

Lipids – pharmacotherapy for low HDL or elevated non-HDL, high-risk women
Utilize niacin[¶] or fibrate therapy when HDL-C is low or non-HDL-C is elevated in high-risk women[¶] after LDL-C goal is reached *(Class IIa, Level B)*.

Lipids – pharmacotherapy for low HDL or elevated non-HDL, other at-risk women
Consider niacin[¶] or fibrate therapy when HDL-C is low or non-HDL-C is elevated after LDL-C goal is reached in women with multiple risk factors and a 10-year absolute risk 10% to 20% *(Class IIb, Level B)*.

Diabetes mellitus
Lifestyle and pharmacotherapy should be used as indicated in women with diabetes *(Class I, Level B)* to achieve an HbA_{1c} <7% if this can be accomplished without significant hypoglycemia *(Class I, Level C)*.

ACE, angiotensin-converting enzyme; ARB, angiotensin receptor blocker; BMI, body mass index; EPA, eicosapentaenoic acid; CHD, coronary heart disease; CVD, cardiovascular disease; DHA, docosahexaenoic acid; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; and LVEF indicates left ventricular ejection fraction.

[*]Pregnant and lactating women should avoid eating fish potentially high in methylmercury (eg, shark, swordfish, king mackerel, or tile fish) and should eat up to 12 oz/wk of a variety of fish and shellfish low in mercury and check the Environmental Protection Agency and the US Food and Drug Administration's Web sites for updates and local advisories about safety of local catch.

[†]A drink equivalent is equal to a 12-oz bottle of beer, a 5-oz glass of wine, or a 1.5-oz shot of 80-proof spirit.

[‡]Criteria for high risk include established CHD, cerebrovascular disease, peripheral arterial disease, abdominal aortic aneurysm, end-stage or chronic renal disease, diabetes mellitus, and 10-year Framingham risk >20%.

[§]Criteria for very high risk include established CVD plus any of the following: multiple major risk factors, severe and poorly controlled risk factors, diabetes mellitus.[20]

[¶]Dietary supplement niacin should not be used as a substitute for prescription niacin.

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Table 3. Preventive drug interventions

Preventive drug interventions

Aspirin, high risk

Aspirin therapy (75 to 325 mg/d)* should be used in high-risk† women unless contraindicated *(Class I, Level A)*.
If a high-risk† women is intolerant of aspirin therapy, clopidogrel should be substituted *(Class I, Level B)*.

Aspirin – other at-risk or healthy women

In women ≥65 Years of age, consider aspirin therapy (81 mg daily or 100 mg every other day) if blood pressure is controlled and benefit for ischemic stroke and MI prevention is likely to outweigh risk of gastrointestinal bleeding and hemorrhagic stroke *(Class IIa, Level B)* and in women <65 years of age when benefit for ischemic stroke prevention is likely to outweigh adverse effects of therapy *(Class IIb, Level B)*.

β-Blockers

β-Blockers should be used indefinitely in all women after MI, acute coronary syndrome, or left ventricular dysfunction with or without heart failure symptoms, unless contraindicated *(Class I, Level A)*.

ACE inhibitors/ARBs

ACE inhibitors should be used (unless contraindicated) in women after MI and in those with clinical evidence of heart failure or an LVEF ≤40% or with diabetes mellitus *(Class I, Level A)*. In women after MI and in those with clinical evidence of heart failure or an LVEF ≤40% or with diabetes mellitus who are intolerant of ACE inhibitors, ARBs should be used instead *(Class I, Level B)*.

Aldosterone blockade

Use aldosterone blockade after MI in women who do not have significant renal dysfunction or hyperkalemia who are already receiving therapeutic doses of an ACE inhibitor and β-blocker, and have LVEF ≤40% with symptomatic heart failure *(Class I, Level B)*.

ACE, angiotensin-converting enzyme; ARB, angiotensin receptor blocker; LVEF indicates left ventricular ejection fraction; and MI, myocardial infarction.

*After percutaneous intervention with stent placement or coronary artery bypass grafting within previous year and in women with noncoronary forms of CVD, use current guidelines for aspirin and clopidogrel.[21]

†Criteria for high risk include established CHD, cerebrovascular disease, peripheral arterial disease, abdominal aortic aneurysm, end-stage or chronic renal disease, diabetes mellitus, and 10-year Framingham risk >20%.

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Table 4. Not useful/effective and may be harmful for CVD or MI prevention in women

Menopausal therapy

Hormone therapy and selective estrogen-receptor modulators (SERMs) should not be used for the primary or secondary prevention of CVD *(Class III, Level A)*.

Antioxidant supplements

Antioxidant vitamin supplements (eg, vitamin E, C, and beta carotene) should not be used for the primary or secondary prevention of CVD *(Class III, Level A)*.

Folic acid*

Folic acid, with or without B6 and B12 supplementation, should not be used for the primary or secondary prevention of CVD *(Class III, Level A)*.

Aspirin for MI in women <65 years of age†

Routine use of aspirin in healthy women <65 years of age is not recommended to prevent MI *(Class III, Level B)*.

CVD indicates cardiovascular disease; MI, myocardial infarction.

*Folic acid supplementation should be used in the childbearing years to prevent neural tube defects.

†For recommendation to prevent CVD in women ≥65 years of age or stroke in women <65 years of age, please see Table 3.

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