New information about hormone therapy and cardiovascular disease prevention in women

Whether information from new studies is used for our patients or for us is equally important. As the oral-systemic link becomes more established, dental hygienists and dentists should be aware of general health guidelines. This article will review new research in the area of hormones, cardiovascular disease (CVD), and CVD in women.

A new analysis of combined data from two parts of the Women's Health Initiative directed by the National Heart, Lung and Blood Institute has found that women in their 50 s do not have a higher risk of heart attack if they take hormones (1). Also, women in their 60 and 70 s who continue to have menopausal symptoms were at increased risk for heart attacks independent of whether they were taking hormones. The timing of initiation of hormone therapy may influence its effect on CVD.

The two studies involved 27 347 women from the ages of 50–79 who were randomly assigned to receive hormones or not. One study involved women who had not had hysterectomies and took Prempro™ (Wyeth Pharmaceuticals Inc., Philadelphia, PA, USA), which is a combination of estrogen and progestins. The other group involved women who underwent a hysterectomy and who took just took estrogen alone. The studies were combined to assess the specific health risk of women in their 50, 60 and 70 s. Their new analysis of the combined studies concluded that women in their 50 s who take Prempro™ or estrogen alone had a slightly increased risk of strokes and breast cancer, but there was no increase in the risk of heart attacks.

Researchers believe that the implications of their analysis are that if women in their 50 s want to take hormone therapy to relieve menopause symptoms, their blood pressure should be monitored and controlled and they should have regular mammograms. This would mean that there is a small opportunity for women to use hormone therapy safely as early as menopause first starts. Further, women should also be aware that they may not be able to continue taking hormones safely into their 60 and 70 s.

New guidelines

Cardiovascular disease is the most common cause of mortality among women, and it accounts for one third of all deaths. More women than men die each year from CVD in the United States. The public health impact of CVD on women is not solely related to mortality because advances in medicine have helped many women survive the disease. However, with the continued increase in the average life expectancy, the burden of CVD on women will also continue to rise. CVD causes 8.6 million deaths among women annually. It is the largest single cause of mortality among women, accounting for a third of all deaths in women *worldwide* (http://www.worldheart.org/awareness-women.php).

Cardiovascular disease is often preventable in women, and even modest control could have a large impact. By reducing the rate of death from chronic diseases by 2% over one decade, it is estimated that 36 million lives could be saved.

Although some exceptions do exist, the guidelines presented by the American Heart Association (AHA) to prevent CVD in women do not differ for men. However, health care professionals should be aware that some of these recommendations are contraindicated in women who are pregnant or who want to become pregnant. This update represents the most current clinical recommendations for the prevention of CVD in women 20 years and older. (2) The last guidelines were in 2004 (3).

Risk factors

Women who have one or more risk factors for heart disease, evidence of subclinical disease with or without risk factors, poor exercise capacity, or unhealthy lifestyles may be at risk of CVD. Factors such as medical and lifestyle history, Framingham risk score, and family history of CVD and other genetic conditions (e.g. familial hypercholesterolaemia) should be considered when determining a patient's risk of CVD (3).

Clinical recommendations

Recommendations for the prevention of CVD in women are based on the level of evidence to support a clinical recommendation as well as other factors, such as their practical application in randomized controlled trials with women. They are divided

into the following categories: lifestyle interventions, major risk-factor interventions, and preventive drug interventions (3).

Lifestyle interventions – modifiable risk reduction

Cigarette smoking

Counseling women against tobacco use and smoking is recommended, as is nicotine replacement or another indicated pharmacotherapy combined with participation in a behavioral or formal smoking cessation programme. Women should also try to avoid secondhand smoke. In addition to CVD risk, a study published in the *Journal of Periodontology* found that subjects with periodontitis who were exposed to secondhand smoke were more likely to develop bone loss, the number one cause of tooth loss (4).

Physical activity

Women at risk of CVD should have a minimum of 30 min of moderate exercise (e.g. brisk walking) on most, and preferably all, days of the week and 60–90 min of daily moderate exercise for those who need to lose weight or sustain weight loss.

Weight maintenance

To maintain or lose weight, it is recommended that women find an appropriate balance of physical activity and caloric intake. Body mass index should be between 18.5 and 24.9 kg m^{-2}, and waist circumference should not exceed 35 inches.

Dietary intake

A high intake of fruits and vegetables is recommended for women at risk. Selecting whole-grain, high-fiber foods and consuming oily fish at least twice a week is recommended. Dietary cholesterol should be <300 mg day^{-1}, and saturated fat should make up no more than 7–10% of the diet; women at risk of hypercholesterolaemia should have diets with <7% saturated fat and <200 mg of cholesterol each day.

In conjunction with diet, omega-3 fatty acids in capsule form may be considered for women with coronary heart disease (CHD).

Rehabilitation

Women who have had a recent cerebrovascular event; acute coronary syndrome or coronary intervention; peripheral arterial disease; new-onset or chronic angina; or symptoms of heart failure should be offered a comprehensive risk-reduction regimen (e.g. physician-guided community- or home-based exercise training programme, cardiovascular or stroke rehabilitation).

Depression

Screening for depression in women with CHD should be considered.

Major risk-factor interventions

Blood pressure

Optimal blood pressure is <120/80 mmHg (3). Physicians should encourage patients to achieve optimal blood pressure through weight control; sodium restriction; increased physical activity; and consumption of low-fat dairy products, fruits, and vegetables. Dental hygienists should be aware of patient's blood pressure in the office. See the *Guidelines for Management of Dental Patients with Elevated Blood Pressure* (http://www.db.uth.tmc.edu/clinic-pat/Documents/bpguidelines-2004.pdf).

If blood pressure is 140/90 mmHg or more, or if the patient has chronic kidney disease or diabetes with blood pressure of 130/80 mmHg or more, pharmacotherapy is recommended. Unless contraindicated or other agents are indicated for specific vascular diseases, thiazide diuretics should be considered as part of the drug regimen. Beta blockers used alone or in conjunction with angiotensin-converting enzyme (ACE) inhibitors or angiotensin receptor blockers (ARBs), with the addition of thiazides as needed to control blood pressure, are recommended for the initial treatment of women at high risk of CVD.

Lipids

Lifestyle changes are recommended to achieve an optimal low-density lipoprotein (LDL) cholesterol level of <100 mg dL^{-1} (2.60 mmol L^{-1}), high-density lipoprotein (HDL) cholesterol level greater than 50 mg dL^{-1} (1.30 mmol L^{-1}), triglycerides <150 mg dL^{-1} (3.90 mmol L^{-1}), and non-HDL levels <130 mg dL^{-1} (3.35 mmol L^{-1}).

For women with CHD or another atherosclerotic CVD, with diabetes, or with a 10-year absolute risk of more than 20%, LDL-cholesterol-lowering drug therapy in conjunction with lifestyle therapy is recommended to achieve an LDL cholesterol level of <100 mg dL^{-1}. A reduction to <70 mg dL^{-1}

(1.80 mmol L^{-1}) is considered reasonable for women with CHD who are already at very high risk (e.g. women with diabetes mellitus and CHD).

Low-density lipoprotein-cholesterol-lowering therapy is recommended for moderate-risk women (multiple risk factors, and who had a 10-year absolute risk of 10–20%) if the LDL cholesterol level is 130 mg dL^{-1} or more despite lifestyle therapy. For low-risk women whose 10-year absolute risk is <10%, LDL-cholesterol-lowering therapy is recommended if the patient's LDL cholesterol level is 160 mg dL^{-1} (4.15 mmol L^{-1}) or more despite lifestyle therapy. Regardless of the absence or presence of other risk factors or CVD, LDL-cholesterol-lowering therapy is recommended if the patient's LDL is 190 mg dL^{-1} (4.90 mmol L^{-1}) or more despite lifestyle therapy.

For women at high risk and women with multiple risk factors and a 10-year absolute risk of 10–20%, consider the use of fibrate therapy or niacin (Niacor: Upsher Smith Laboratories, Minneapolis, MN, USA) when HDL cholesterol is low or when non-HDL cholesterol is elevated after an appropriate LDL cholesterol level is reached.

Diabetes

If an A1C level of <7% can be accomplished without significant hypoglycaemia, lifestyle therapy and pharmacotherapy should be used as indicated in women with diabetes. See references for *Basic Guidelines for Diabetes Care* (http://www.hpsm.org/Documents/Providers/2005-06BasicGuidelinesandExplanatoryNotes.pdf). For *Diabetes and Oral Health*, see the special American Dental Association supplement (http://www.ada.org/prof/resources/pubs/jada/reports/diabetes.asp).

Preventive drug interventions

Aspirin

Unless contraindicated, 75–325 mg day^{-1} of aspirin is recommended for women with CHD or another atherosclerotic CVD, diabetes, or with a 10-year absolute risk of more than 20% (3). For patients at high risk who are intolerant of aspirin, clopidogrel (Plavix: Sanofi-synthelabo Inc., Bridgewater, NJ, USA) may be substituted.

For women 65 years and older, aspirin in a dosage of 81 mg daily or 100 mg every other day is recommended if blood pressure is controlled and the benefit for the prevention of myocardial infarction and ischemic stroke is likely to outweigh the risk of haemorrhagic stroke and gastrointestinal bleeding. The same recommendations apply to women younger than 65 years when the benefit for prevention of ischemic stroke will likely outweigh the adverse effects of aspirin therapy.

Beta blockers

Unless contraindicated, beta blockers should be used indefinitely in all women with acute coronary syndrome; left ventricular dysfunction, with or without heart failure symptoms; and after myocardial infarction.

ACE inhibitors/ARBs

For women with diabetes or who have had a myocardial infarction, or if clinical evidence suggests heart failure or a left ventricular ejection fraction of 40% or less, ACE inhibitors should be considered. ARBs should be used instead if the patient is intolerant to ACE inhibitors.

Aldosterone blockade

Aldosterone blockade is recommended after a myocardial infarction in women who also have diabetes or heart failure or are already receiving therapeutic doses of an ACE inhibitor and beta blocker, but who do not have a significant renal dysfunction or hyperkalaemia.

Clinical limitations

Variations in therapy adherence and patient characteristics exist, so the effectiveness of therapies prescribed in an office or hospital setting may vary widely from the efficacy and safety profiles shown in clinical trials (3). Therefore, the development of guideline recommendations has limitations that vary from one population to another. Many of the studies used to formulate the AHA guidelines did not include older women, especially to those older than 80 years in whom CVD and other comorbidities are common. Health care professionals should use clinical judgment about the aggressiveness of preventive therapy provided to all women, especially those who are older (see Table 1).

Take home message

As oral health care professionals, *Evidence-Based Medicine* (EBM) should be our mantra. The most scientifically credible EBM is based on evidence from double-blind, randomized-controlled clinical trials. However, this form of EBM does not always reflect real-world practice. Some would rather rely on

Table 1. **Classification and levels of evidence for the strength of the evidence for the new guidelines**

	Strength of recommendation
Classification	
Class I	Intervention is useful and effective
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	Intervention is not useful/effective and may be harmful
Level of evidence	
B	Limited evidence from single randomized trial or other nonrandomized studies
C	Based on expert opinion, case studies, or standard of care
Generalizability index	
1	Very likely that results generalize to women
2	Somewhat likely that results generalize to women
3	Unlikely that results generalize to women
0	Unable to project whether results generalize to women

Adapted from Evidence-based guidelines for cardiovascular disease prevention in women (3, 4).

Eminence-based medicine (EBM), usually distributed in practice guidelines, and is respected because it reflects recommendations of a number of experts, usually prominent clinical researchers with a critical approach to data (5). However, many practice guideline algorithms are based on educated opinions and extrapolations from narrow evidence-based data that are extended to various manifestations of a specific disorder. *Experience-based medicine* (EBM), which combines evidence-based principles combined with personal clinical observations in a varied patient population over time, is a prevalent source of information for clinical practitioners (5). Research traditionalists often discount this form of EBM as too subjective, or because they believe employing this method of EBM can lead to dangerous conclusions about how to use a particular therapy. A common criticism of experience-based medicine is that a placebo response may masquerade as a positive outcome.

Careful choices and rationale for products, procedures, and guidelines are imperative, unless you prefer litigation-based medicine or providence-based medicine, where a 'higher power' decides! Or perhaps your favorite is eminence-based medicine, which Dr Isaacs and Dr Fitzgerald define as 'making the same mistakes with increasing confidence over an impressive number of years' (6).

References

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