

Menopause, Cholesterol, and Cardiovascular Disease

a report by

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Cardiovascular disease (CVD) is the leading cause of death in both men and women, yet the extent of the problem in women is frequently underestimated and, compared with men, women are less likely to be offered interventions, are less likely to be represented in clinical trials, and have a worse prognosis. This article aims to examine the extent of the problem of CVD in women, summarize the physiology and effects of menopause, explore the link between menopause and CVD risk factors, and offer suggestions to reduce the risk for CVD in menopausal women.

Cardiovascular Disease in Women—How Big a Problem?

CVD is the leading cause of death in women after the menopause and in fact more women die from heart disease and stroke than from the next five causes of death combined, including breast cancer (see *Figure 1*).^{1,2} Although many women perceive that one of the leading risks to their health is breast cancer, globally women are nine times more likely to die of CVD than of breast cancer.³ CVD is traditionally thought of as being a problem of middle-aged men, but in fact CVD affects just as many women as men—if not more—albeit on average a decade later (see *Figure 2*).⁴ This delay is thought to be due to the protective effects of estrogen that occur in the years before the menopause. As estrogen levels drop, often from the mid-40s onwards, the protective effect is lost and changes occur that lead to an increased risk for heart disease in the ensuing years. Figures from 2005 show that in Europe 55% of women died from CVD as opposed to 43% of men.⁵ Sadly and surprisingly, awareness of this major health risk to women appears to be very low, with a recent survey showing that only 31% of healthcare professionals and 38% of women were aware that menopausal women are at an equal or greater risk for CVD than men, and that only 31% of women associate menopause with heart disease. The health risks that women were most concerned about at menopause were physical menopausal symptoms, osteoporosis, and breast cancer.⁶

The Role of Menopause

Menopause affects all women and occurs when the ovaries either naturally stop producing estrogen due to the decline and cessation of oocyte

development and ovulation, which is essential for the production of both estrogen and progesterone, or when the ovaries are removed or damaged by other therapies. The average age at natural menopause varies between countries and is affected by factors such as genetics, nutrition, smoking, and age of menarche; in Europe it is around 51 years. As oocyte quality and number decline gradually, changes related to lowering levels of estrogen may commence a number of years beforehand. Estrogen deficiency can lead to early, intermediate, and long-term health problems. There is widespread awareness of the common early menopausal symptoms such as hot flashes, night sweats, insomnia, and mood changes. Intermediate symptoms of vaginal dryness, irritation, discomfort, and bladder changes are very common and, although discussed less often than hot flashes, are gradually being reported and treated a little more often than in the past. The long-term effect of menopause on the bones, with the lack of estrogen leading to loss of bone strength (and eventually osteoporosis) with an increased risk for fracture, is fairly well known and frequently addressed. However, there is incredibly poor appreciation of the important long-term effects of the menopause on the cardiovascular system.

The Effect of Menopause on Risk for Cardiovascular Disease

Weight

Being overweight is a significant risk factor for CVD and is an increasing problem in the western world. Obesity is more common in men than in women before 45 years of age, but after this point the trend reverses. During the menopause, and in fact starting within the first year of the menopause, there is a shift in fat distribution and storage in women from the hips to the waist, more resembling that of the abdominal visceral fat storage in men. These are often referred to as 'pear' and 'apple' shapes, the apple shape being associated with an increased risk for CVD. Waist circumference reflects this risk: women with a waist circumference >80cm have an increased risk for CVD, with even greater risk for those whose waist circumference is ≥88cm.⁵ The exact mechanism by which estrogen deficiency leads to weight gain and change in fat distribution is not clear, but is thought to be related to a relative excess of androgens (post-menopausal ovaries still produce some androgens) together with changes in leptin and thyroid function.

Blood Pressure

Hypertension is also a major risk factor for CVD, and after 45 years of age more women than men develop hypertension.⁴

Cholesterol

There is no doubt that raised cholesterol is a significant risk factor for CVD. Menopause is associated with a progressive increase in total cholesterol, with,



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in particular, an increase in low-density lipoprotein (LDL), lipoprotein- α , and triglycerides and a decrease in high-density lipoprotein (HDL).⁷⁻⁹ Therefore, menopausal women are exposed to a more atherogenic lipid profile than pre-menopausal women. Total cholesterol levels peak in women at 55–65 years of age—about 10 years later than the peak in men (see Figure 3).

Agents that lower cholesterol levels reduce heart disease risk in both men and women, but it is thought that a larger proportion of women than men are at high risk and are not being effectively treated. It was shown in a recent survey that only one in four women associates menopause with high cholesterol, leading to a lack of awareness of the need to consider having cholesterol level checked around the time of the menopause.⁵

Smoking

Tobacco use is one of the most important risk factors for CVD in both men and women, although the risks associated with smoking are consistently higher in women than in men. Although in general more men than women smoke, the important and encouraging decline in tobacco use among men is worryingly less apparent in women, while there is a disturbing rising trend in younger women.

Diabetes

Diabetes is becoming increasingly common in both men and women, and changes in insulin secretion and insulin sensitivity after the menopause contribute to this increase in women. The risk for death from CVD associated with diabetes is higher in women than in men: in the 20-year Framingham study, women with diabetes were 3.3 times more likely to die from CVD than women without diabetes, whereas the risk for diabetic men was only 1.7 times that of non-diabetic men.¹⁰

The increase in these risk factors leads to a four-fold increased risk in CVD in women in the 10 years after the menopause.¹¹ The belief that this increase is menopause- or estrogen-deficiency-related rather than purely age-related is confirmed by the findings that for post-menopausal women at any age there is an increased risk for CVD (see Figure 4).

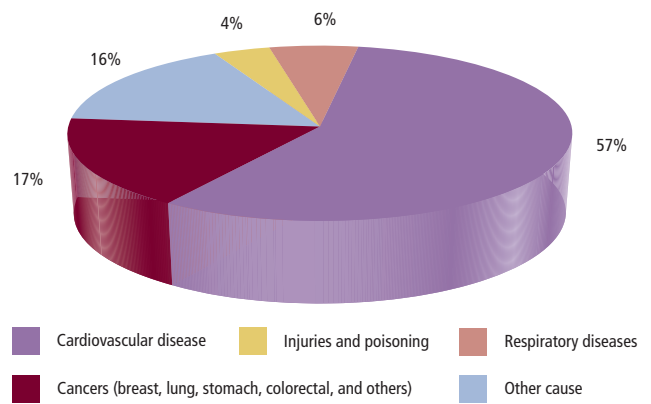
Other Problems

Symptoms of heart disease manifest themselves differently in women and in men, with women being less likely to present with classic, well recognized cardiovascular symptoms.⁷ Angina can be mistaken for indigestion or heartburn, and symptoms of myocardial infarction (MI) can include overwhelming fatigue, shortness of breath, nausea, or indigestion. Women therefore tend to present late in the disease process, by which time they may also have other medical conditions that may affect the prognosis. Furthermore, it is recognized that women are less likely to be offered intervention, and traditionally have been poorly represented in clinical trials. Not surprisingly, then, women have a worse prognosis following an MI than men: in US patients diagnosed with acute MI, 38% of women but only 25% of men die within a year. Within six years of a first MI, 35% of women but only 18% of men will have another MI.¹²

Management of Cardiovascular Disease Risk at Menopause

With the onset of menopausal symptoms, women and their doctors and nurses should not only discuss the symptoms, but also think long-term and consider risk factors for both bone health and heart health. It has been estimated by the World Health Organization (WHO) that 80% of CVD can

Figure 1: Causes of Death in European Women



Source: World Health Organization, 2004.²

Figure 2: Percentage of Population Affected by Cardiovascular Disease with Increasing Age

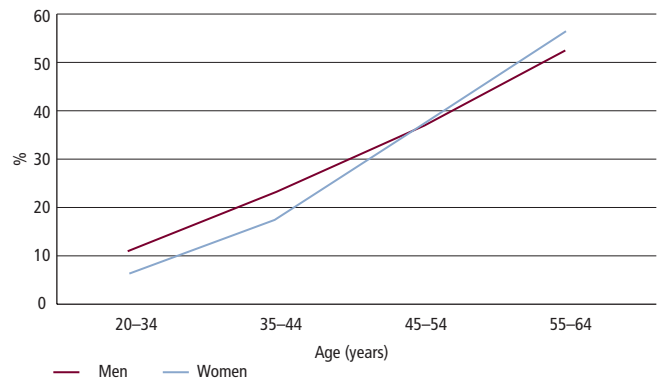
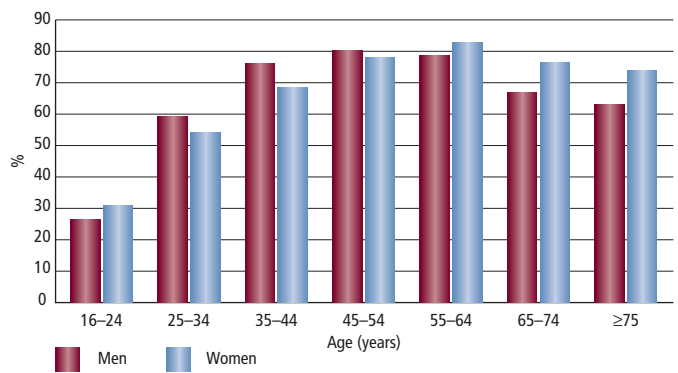


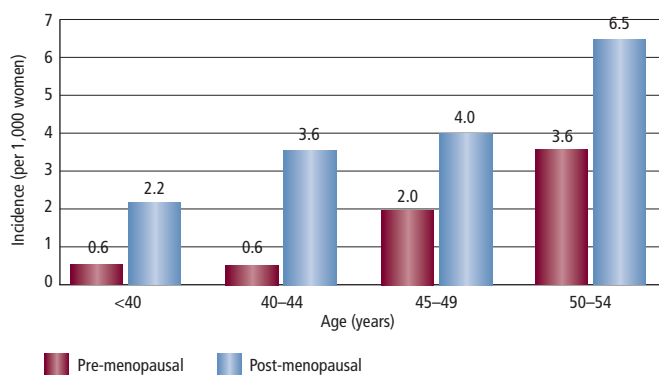
Figure 3: High Cholesterol Levels for Men and Women in England, 2003



Percentage of adults with blood cholesterol levels $\geq 5.0\text{mmol/l}$ in England, 2003.

be prevented by diet and lifestyle changes and, indeed, a recent European survey showed that 73% of respondents said that they would prefer to deal with menopausal symptoms by having the right diet and lifestyle.^{6,13} However, for women who are having troublesome menopausal symptoms, control of the symptoms may be needed first before attention can be given to important diet and lifestyle changes; discussion should still take place early and, indeed, some changes such as reducing weight, stopping smoking, and

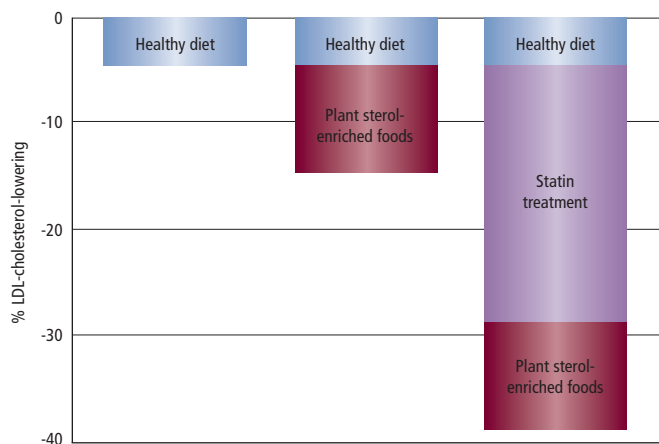
Figure 4: Incidence of Cardiovascular Disease—Relation to Menopause Status (the Framingham Study)



n=2,873.

Source: Kannel WB, et al., *Ann Intern Med*, 1976;85:447-52.

Figure 5: Cholesterol-lowering Effects of Diet and Drug Therapy



LDL = low-density lipoprotein.

increasing exercise can in fact help to reduce symptoms as well as benefiting long-term health. Women should be encouraged to maintain a healthy weight by means of a healthy diet (with five portions of fruit and vegetables per day, using wholegrain, high-fibre foods, cutting down on saturated fats, increasing mono- and polyunsaturated fats and cutting down on salt) and by increasing exercise, aiming for 30 minutes of moderate exercise (brisk walking provides the same benefit as vigorous exercise) at least five days per week. Stopping smoking can improve not only heart health but also bone

health and should be a major consideration in menopausal women. Blood pressure is usually checked as part of a menopause assessment, and subsequently as part of the review for women who take hormone replacement therapy. Increasing exercise and weight loss can help to reduce blood pressure, but often drug therapy is needed. Since cholesterol levels increase with the changes that occur at menopause, checking the cholesterol level should also be considered as part of the menopause assessment. It has been shown that a 10% reduction in LDL cholesterol can lead to a reduction in risk for CVD of up to 20%.¹⁴

Specific Cholesterol-lowering Dietary Methods

Some interest has been shown in specific dietary methods of reducing cholesterol level, with a variety of foods containing active ingredients that have been shown to have LDL-cholesterol-lowering properties. Active ingredients include plant sterols/stanols (added to foods such as margarine, milk products, and yogurts), beta-glucan (a soluble fibre found in oats), and soy protein (found in soy-based products). In the case of beta-glucan, the ingredient in oats-based cereals, the evidence supports cholesterol lowering in the range of 2–5% when 3–5g beta-glucan is consumed daily. Eating 25g per day of soya protein as part of a low-fat diet has also been shown to lower cholesterol by 3–5%.

However, one of the most effective ways to lower LDL cholesterol through dietary changes is by the inclusion of plant sterols or stanols. Plant sterols and stanols lower LDL cholesterol levels by blocking the absorption of cholesterol from food during digestion, and also by blocking the re-absorption of cholesterol from the liver. Taking 2–2.5g of plant sterols per day is thought to lower LDL cholesterol by an average of 10% within two to three weeks. When combined with a healthy diet and lifestyle, LDL cholesterol can be further reduced by 5%.¹⁵ Plant sterols and stanols have no effect on HDL cholesterol or triglycerides. For some women, drugs such as statins may be required and plant sterols and stanols can be used in conjunction with lipid-lowering medications. The 10% cholesterol lowering of plant sterols is additive to that of a healthy cholesterol-lowering diet and cholesterol-lowering medications such as statins and fibrates (see Figure 5).^{15,16}

Conclusion

CVD is by far the biggest cause of death in women after the menopause and yet there is still a low level of awareness among both women and health professionals. Because the changes that occur at menopause lead to an increased risk for CVD, menopause discussion should include assessment of risk factors for long-term health problems, in particular osteoporosis and CVD; consideration should also be given to the measurement of cholesterol level as routine, along with blood pressure and body mass index. When indicated, emphasis on diet and lifestyle advice should be first-line management. ■

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