Editorial

Menopause and Cardiovascular Disease

The risk of cardiovascular disease (CVD) greatly increases after the menopause when estrogen levels decline. Typically, women are around 10 years older than men at the first presentation of atherosclerotic coronary heart disease, and this can be related to decline in ovarian hormone concentrations during the menopausal transition and beyond.[1]

Estrogens can modulate vascular function by targeting estrogen receptors in the endothelial cells and also in the vascular smooth muscle cells. Estrogens can also lead to the release of nitric oxide and prostacyclin, which are both vasodilators. In addition, they can lead to a reduction in the production of endothelin and angiotensin II, which are vasoconstrictors. Estrogens not only can reduce inflammation but also can reduce the secretion of pro-atherogenic cytokines, such as tumor necrosis factor-α, while they can increase prostaglandin I_2, which reduces oxidative stress and also platelet activation.

Women of any age with vasomotor symptoms have a worse cardiovascular risk profile compared with women without vasomotor symptoms. Women experiencing vasomotor symptom have significantly higher systolic and diastolic blood pressures, higher circulating total cholesterol levels, and higher body mass index than their counterparts with no symptoms.[2]

The benefits and risks of hormone therapy (HT) vary by dosage, route of administration, and timing of initiation. Estrogen in HT can have a protective effective in early atherogenesis compared to a potentially harmful effect in established atherosclerosis.[3] In early atherogenesis, estrogen has beneficial effects by improving plasma lipids, maintaining endothelial cell integrity, and promoting nitric oxide production. Conversely, in established atherosclerosis, estrogen can increase matrix metalloproteinase (MMP) expression which can lead to instability of the fibrous cap and rupture of the atheromatous plaque. This means that the cardioprotective effect of estrogen replacement therapy is seen in postmenopausal women in a time-dependent manner.[4]

Estrogen can increase the release of MMPs in a dose-dependent manner. Low-dose estrogen may lead to increase in MMPs, which can normalize vascular remodeling, whereas high-dose estrogen may produce large increases in MMPs and lead to excessive remodeling. This means the starting dose of estrogen in women with established atheroma should be as low as possible to improve symptoms.


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The CVD benefit of taking HT is greatest if the woman starts HT at the earliest with respect to her perimenopause or menopause. A Finnish study has shown that using HT for at least 10 years is associated with 19 fewer Coronary Heart Disease (CHD) deaths and seven fewer stroke deaths per 1000 women.[5] This concept is often referred to as the "timing hypothesis" as the cardiovascular effects of HT strongly depend on individual vascular health and the time since their menopause before starting HT.

The National Institute of Health and Care Excellence states that women should be informed that the presence of cardiovascular risk factors is not a contraindication to Harmonal therapy (HRT) and also that it is essential to optimally manage any underlying cardiovascular risk factor (e.g., hypertension, high cholesterol) before the start of HT.[6] This means that having raised blood pressure is neither a contraindication to taking HT nor a reason to stop prescribing HT.

To sum it up, women with premature ovarian insufficiency, women with early menopause, and women within 10 years of their menopause can potentially gain significant improvements in their cardiovascular health, as well as their general health, by being offered HT in selected cases.

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