NAMS Practice Pearl

The Menopause Transition: A Critical Stage for Cardiovascular Disease Risk Acceleration in Women

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The menopause transition is a critical period for cardiovascular health. During this stage, women experience adverse changes in multiple components that are key for optimal cardiovascular health. Additionally, women struggle to maintain ideal health behaviors, which if adopted collectively, have been shown in observational studies to prevent more than 70% of coronary heart disease cases. Significant efforts should be directed toward increasing awareness among women and healthcare professionals about the menopause transition as a stage of cardiovascular disease risk acceleration that is amenable to reduction with positive lifestyle measures.

Cardiovascular disease (CVD) remains the leading cause of death in women.[1] Yet, the awareness and management of CVD in women are inadequate. In 2019, US women were 74% less likely to identify CVD as their top killer than in 2009. Notably, approximately 70% of postgraduate medical trainees reported none to minimal training on sex-specific medical concepts, and only 22% of primary care physicians and 42% of cardiologists felt well prepared to assess CVD risk in women.

Over time, research has shown that some CVD risk factors are woman-specific.[2] The menopause transition (MT) represents a period of accelerated CVD risk, with timing, mechanism, and symptoms of menopause, as well as their treatment, all associated with this risk.[3] Cardiovascular disease prevention guidelines now acknowledge early menopause as a woman-specific risk-enhancing factor.[4]

The American Heart Association (AHA)'s *Life's Simple 7,* based on seven health behaviors and risk factors, has been used as a measure of cardiovascular health (CVH) since 2010. In 2022, the AHA expanded *Life's Simple 7* to *Life's Essential 8*, with diet, physical activity, nicotine exposure, and sleep health (new addition) as the behavioral components, and body mass index (BMI), lipids, blood pressure (BP) and glucose as the risk factor components.[5] During the MT, women experience adverse changes directly related to all risk components of *Life's Essential 8*. Moreover, women struggle to maintain optimal health behaviors. For example, only 7.2% of midlife women report a physical activity level that meets recommendations, and less than 20% consistently maintain a healthy diet.[3] As such, the MT has been identified as a critical period for CVH.[3]

Cardiovascular health components adversely altered during the menopause transition

Body mass index, fat distribution, and body composition. Women gain weight during the MT—mostly driven by the aging process. Women also experience a redistribution of fat toward the abdomen and visceral organs (eg, heart) that has been directly linked to the MT.[3] Roughly 2 years before the final menstrual period (FMP), significant accumulation of abdominal visceral fat occurs,[2] and body composition adversely changes (eg, the rate of fat gain doubles and lean mass declines). The MT-associated increase in visceral fat is associated with greater carotid atherosclerosis.[3]

Lipids. Within 1 year of the FMP, women experience a steep acceleration in total and low-density lipoprotein cholesterol and apolipoprotein B. Moreover, both the quality and functional capacity of high-density lipoprotein (HDL) change over the MT. High levels of HDL-cholesterol in women traversing menopause are associated with a greater risk of carotid atherosclerosis after menopause.[3] Moreover, the ability of large HDL particles to promote the first step in reverse cholesterol transport becomes weaker postmenopause.[3]

Vascular function and structure and blood pressure. During the MT, women experience steeper increases in their carotid intima-media thickness, an early marker of atherosclerosis and arterial stiffness, independent of aging.[3]

Blood pressure increases with age in both sexes, but the rise in women exceeds that in men after midlife.[6] Women experience different patterns of change in BP during midlife, with almost 35% having low systolic blood pressure (SBP) premenopause (mean, 105±8.5 mm Hg), followed by a sharp increase right after the FMP.[7] Increased risk of CVD manifests at much lower SBP thresholds in women compared with men (as low as 100 mm Hg vs 120 mm Hg, respectively), an effect that is more pronounced in younger women (age <52 y).[6] Thus, the menopause-related increase in SBP could place women at a greater CVD risk even if it is deemed to be below the recommended treatment threshold.

Insulin, glucose metabolism, and risk of the metabolic syndrome. Although the MT is not independently linked to increases in insulin or glucose beyond the age-related risk, the prevalence of the metabolic syndrome appears to sharply increase with menopause beyond the risk imposed by chronologic aging. The progression and increase in severity of the metabolic syndrome are greatest during the perimenopause years compared with the postmenopause years.[3]

Menopause characteristics that put women at a greater risk for cardiovascular disease

Early age at menopause. Increased risk of CVD is most evident in women with early menopause (age at menopause <45 y) or premature menopause (age at menopause <40 y).[8] Premature menopause is an independent risk factor for coronary heart disease (CHD). Moreover, women with premature menopause are three times more likely to develop multimorbidity in their sixties compared with those aged 50 to 51 years at menopause. Additionally, women with early menopause have a higher risk of hyperlipidemia compared with those aged 50 to 51 years at the time of menopause.

Frequent reporting of vasomotor symptoms. Women with vasomotor symptoms (VMS; hot flashes and night sweats) during midlife show unfavorable risk profiles for lipids, hemostatic

markers, and insulin resistance. They are also more likely to develop hypertension than women without VMS.[3] Early, as well as persistent, reporting of VMS during midlife is associated with a greater risk of CVD events.[9] Thus, VMS seem to be more than just troublesome symptoms and might be associated with long-term CVD risk.

Pattern of estradiol levels and cycle length over time. Compared with women with low estradiol levels before and after their FMP, women with higher estradiol levels before their FMP, but lower estradiol levels thereafter appear to be less likely to develop carotid plaque after menopause.[3] Additionally, women with a late increase (2 y before FMP) in their cycle length have lower levels of postmenopausal carotid intima-media thickness and brachial-ankle pulse wave velocity than those with no changes over the MT.[2]

Hormone therapy and cardiovascular disease risk

Hormone therapy (HT) is contraindicated in women at high CVD risk and not recommended for the sole purpose of primary or secondary CHD prevention.[10] The time of initiation of HT use relative to menopause is critical, with initiation before the age of 60 years or within 10 years of menopause appearing to be associated with minimal CVD risk, with evidence of more harmful effects when HT is initiated at older ages or after a longer time since menopause.[2,3,10] Hormone therapy also is recommended for women with premature menopause until they reach the average age of natural menopause.[3,10] The decision to pursue HT should take into consideration a woman's individual CVD risk with shared decision-making.

Risk assessment and promoting a healthy lifestyle during the menopause transition

Guidelines recommend considering risk-enhancing factors, including premature menopause, in the clinician-patient primary CVD prevention risk discussion.[1,4] As such, menopause-specific risk factors could be critical for women who are already at borderline and intermediate risk for CVD. During perimenopause, clinicians should begin with a quantitative risk assessment that includes screening for dyslipidemia, insulin resistance, and hypertension.[1] This should be followed by an assessment of individualized risk, with a particular focus on woman-specific factors linked to higher risks of CVD. Vasomotor symptom experience and changes in cycle length and body fat distribution should be considered because they could help to identify women at greater CVD risk.

Pearls. Adopting a heart-healthy lifestyle should be widely promoted. More than 70% of CHD cases could be prevented with lifestyle changes alone. This requires massive awareness campaigns that target women of different backgrounds and at different stages of life emphasizing CVD as the leading cause of death and the great benefit women can gain from optimizing measures of CVH.

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Disclosures

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