

Editorial

Estradiol/Testosterone Ratio as a Predictor of Coronary Artery Disease in Postmenopausal Women: A Useful Tool!

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Menopause is a universal aspect of women's reproduction physiology and is associated with dramatic increase in risk of coronary artery disease (CAD). It has been widely accepted that decline of endogenous estrogen at menopause and higher androgens are largely responsible for increased cardiovascular disease (CVD) risk. However, there is conflicting evidence from studies examining the associations between sex hormone levels and CVD in postmenopausal women. Observational studies done by Rexrode et al and Barret-Connor et al demonstrated that estradiol levels in postmenopausal women were not associated with CVD, while Benn et al showed inverse association with CV event. Similarly, both high and low androgen levels have been associated with increased risk of CVD.^{1,2}

The article entitled "Association between serum sex hormones and coronary artery disease in postmenopausal women" evaluated association between serum sex hormones and angiographically proven CAD in Indian patients. Fasting serum levels of estradiol (E2), testosterone (T), sex hormone-binding globulin (SHBG), dehydroepiandrosterone sulphate (DHEA), and insulin were measured. A ratio of estradiol/testosterone (E2:T) was calculated, and this ratio was found to be significantly lowered in postmenopausal women with CAD. This association persisted after adjusting traditional CV risk factors, suggesting an independent role of sex hormones on CV events. Authors proposed that E2/T ratio may be used as a predictor of CAD in postmenopausal women.

In a substudy of multiethnic study of atherosclerosis (MESA), Zhao et al evaluated association of sex hormones and CVD events in 2834 postmenopausal women. The study concluded that among postmenopausal women, a E2:T ratio was associated with an elevated risk of CVD and heart failure (HF) events, higher levels of testosterone associated with increased CVD events, whereas higher estradiol levels were

associated with a lower CVD risk. Sex hormone levels, especially higher total testosterone and lower estrogen after menopause, may contribute to women's increased CVD risk in postmenopausal life.²

In another single center study from China, Dai et al concluded similar results in 124 postmenopausal women with CAD and showed a strong association of imbalanced E2:T ratio with cardiovascular risk factors. In the above study, higher E2/T ratio was associated with favorable lipid profile ($p < 0.0001$).³

After years of conflicting data on estradiol and androgen on CVD effects in women, recent studies suggests that it is the balance between both which could be the most important factor in deciding the CVD risk in postmenopausal women. A higher ratio is usually present in postmenopausal women without CAD, while lower levels are seen in women with CAD. In previous studies, higher ratio of E2/T was also shown to be affecting favorable lipid profile; however, in the current study, it is lacking significant association.⁴

Another important aspect is the manner in which to process this information of favorable association of estradiol in postmenopausal women, in order to reduce CVD risk. Major studies which includes both secondary prevention trial like heart and estrogen/progestin replacement study (HERS) and primary prevention study such as women's health initiative (WHI) suggested that long-term use of hormonal therapy for CVD prevention is not recommended. The American College of Obstetrics and Gynecology statement published in 2013 and 2018 endorsed the same.⁵

CVD is the leading causing of mortality and morbidity in women worldwide. Menopause accelerates the risk of CVD in women and could be alarming. The current study reemphasizes the importance of adequate understanding of

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postmenopausal physiology and association with CVD. Even without hormonal therapy, women with higher E2/T ratio could be screened at earlier age, with more focus on lifestyle and modifiable CV risk factors' management to decrease CV event in this very special population.

Conflict of Interest

None declared.

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