How does HT in recent and 10+ years past menopause affect atherosclerosis progression?

Secondary analysis of ELITE trial data among 596 women in early (<6 years) and late (≥10 years) postmenopause indicates that **estradiol (E2) plasma levels** resulting from oral E2 administration were **inversely associated with atherosclerosis progression in the women in early menopause, but positively associated with atherosclerosis progression in those in late menopause**

FAST TRACK

While E2 administration was inversely associated with atherosclerosis progression in women in early menopause, it was positively associated with atherosclerosis progression in women in late menopause

EXPERT COMMENTARY
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Sriprasert I, Hodis HN, Karim R, et al. Differential effect of plasma estradiol on subclinical atherosclerosis progression in early versus late postmenopause. J Clin Endocrinol Metab. 2019;104:293-300. doi:10.1210/jc.2018-01600.

In 2016, the primary findings of the Early versus Late Intervention Trial with Estradiol (ELITE) demonstrated that oral E2 administered to women who were less than 6 years postmenopause slowed progression of subclinical atherosclerosis as assessed by carotid artery intima-media thickness (CIMT), while it had no effect in women who were at least 10 years postmenopause.[1]

That trial included 643 healthy women without cardiovascular disease who at enrollment had a median age of 55.4 years in the early postmenopause group (median 3.5 years since menopause) and 63.6 years in the late postmenopause group (median 14.3 years since menopause). The study medications were oral estradiol 1 mg daily plus progesterone vaginal gel for women with a uterus or placebo and placebo gel for a median of 5 years.

The investigators found also that, in contrast with CIMT, cardiac computed tomography (CT) measures of atherosclerosis did not differ significantly between the estradiol and placebo groups, regardless of age.[1]

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Posttrial data analysis revealed a new finding

In a secondary analysis of data from the ELITE trial, Sriprasert and colleagues dug deeper to assess the impact of plasma E2 levels on progression of subclinical atherosclerosis.[2]

Among 596 women (69.6% white non-Hispanic, 8.7% black, 13.3% Hispanic, and 8.4% Asian/Pacific Islander), E2 levels were available in 248 women in early postmenopause (mean age, 54.7 years) and

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348 women in late postmenopause (median age, 63.6 years).

For women in the estradiol-treated group, mean E2 levels during the trial as well as change of E2 levels from baseline were significantly higher in the early postmenopause group than in the late postmenopause group, even though both groups had similar adherence based on pill count. For those in the placebo group, mean E2 levels and change of E2 levels from baseline were equivalent in early and late menopause.

In the E2-treated group and the placebo group combined, the mixed effects analysis of the CIMT progression rate (based on the mean E2 level during the trial) demonstrated that a higher level of E2 was inversely associated with the CIMT progression rate in early postmenopausal women (beta coefficient = -0.04 [95% confidence interval (CI), -0.09 to -0.001] µm CIMT per year per 1 pg/mL estradiol; P = .04). However, a higher level of E2 was positively associated (beta coefficient = 0.063 [95% CI, 0.018 to 0.107] µm CIMT per year per 1 pg/mL estradiol; P = .006) with CIMT progression rate in the late postmenopausal women.

Bottom line. E2 levels resulting from administration of oral estradiol were inversely associated with atherosclerosis progression in women in early menopause, but they were positively associated with progression in late postmenopause participants. ●

WHAT THIS EVIDENCE MEANS FOR PRACTICE

These new findings from a posttrial analysis of ELITE data provide yet further support for the hormone therapy (HT) "timing hypothesis," which postulates that HT slows atherosclerosis progression in recently menopausal women but has neutral or adverse effects in women who are at least a decade past menopause onset. As the authors suggest, the favorable vascular effects of E2 appear limited to those women (most often in early menopause) who have not yet developed atherosclerosis. Whether or not HT should be considered for cardioprotection remains unresolved (and controversial). By contrast, these data, along with findings from the Women's Health Initiative,[3] provide reassurance regarding the cardiovascular safety of HT when prescribed for recently menopausal women with bothersome vasomotor symptoms.

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References

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