Randomized Controlled Trial Evidence That Estrogen Replacement Therapy Reduces the Progression of Subclinical Atherosclerosis in Healthy Postmenopausal Women Without Preexisting Cardiovascular Disease

To the Editor:

Two articles have appeared in Circulation1,2 that have cited the Estrogen in the Prevention of Atherosclerosis Trial (EPAT)3 as supportive evidence that hormone replacement therapy (HRT) has no benefit on atherosclerosis in women with established cardiovascular disease (CVD). Citation of EPAT as supportive evidence for such a statement is incorrect on two major grounds, as follows: (1) EPAT was a randomized, double-blind, placebo-controlled, 2-year, serial arterial imaging trial conducted in healthy postmenopausal women without preexisting CVD, and (2) the overall primary trial outcome of EPAT demonstrated a positive beneficial effect of unopposed estrogen replacement therapy (ERT) on the progression of subclinical atherosclerosis. In the placebo-treated group, the average rate of progression of subclinical atherosclerosis measured by carotid artery intima-media thickness was +0.0017 mm/year, whereas in the unopposed ERT group, subclinical atherosclerosis regressed at a rate of −0.0006 mm/year (P=0.046 for difference between treatment groups). Among the women who did not use lipid-lowering medication, the placebo-unopposed ERT difference (benefit) in the average rates of atherosclerosis progression was even greater (P=0.002). EPAT supports the growing body of data that indicate that the preexisting state of health of the vasculature and the timing (relative to menopause) of initiation of ERT determine whether atherosclerosis will respond beneficially to hormone therapy. Many important and complex questions generated by the recent body of data remain to be addressed in the area of cardiovascular health and HRT. As pointed out by Mendelsohn and Karas, misinterpretation of data in the field of CVD and HRT only complicates an already complex and confusing area of immense public health importance for women. It is vitally important to clarify that EPAT was a positive outcome trial of unopposed ERT in relatively young postmenopausal women who did not have preexisting CVD.

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Response

We apologize for any confusion created by a regrettable editing error concerning the citation of the Estrogen in the Prevention of Atherosclerosis Trial (EPAT) study in the 2 aforementioned papers. The reference to the EPAT trial was mistakenly included in a list of other randomized trials of hormone replacement therapy (HRT), giving the impression that EPAT found no evidence of benefit of HRT on atherosclerosis in women with established cardiovascular disease. We have accurately cited the EPAT study in a recent review of HRT clinical trials. An erratum will be published in a future issue of Circulation.

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