More analysis from the women's health initiative on hormones, breast cancer

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Analysis of the longer-term influence of menopausal hormone therapy on breast cancer incidence in two Women's Health Initiative (WHI) clinical trials suggests a pattern of changing influences over time on breast cancer, according to an article published online by *JAMA Oncology*.

Use of menopausal hormone therapy decreased dramatically after reports of increased breast cancer risk with estrogen plus progestin from the WHI randomized clinical trial followed by the Million Women Study observational analysis. Following the initial WHI reports, decreases in both combined estrogen plus progestin use as well as estrogen alone use were seen. However, in the WHI randomized trials, while estrogen plus progestin increased breast cancer incidence and breast cancer deaths, estrogen alone in women with prior hysterectomy significantly reduced breast cancer incidence and breast cancer deaths. Those results raised questions about the short- and long-term postintervention effects of these two regimens on breast cancer.

Rowan T. Chlebowski, M.D., Ph.D., of the Los Angeles Biomedical Research Institute at Harbor-UCLA Medical Center, Torrance, Calif., and coauthors examined early and late postintervention effects on breast cancer in the two WHI hormone therapy trials with a current median follow-up of 13 years.

A total of 16,608 women with a uterus were assigned to receive oral conjugated equine estrogens (0.625 mg/d [estrogen]) plus medroxyprogesterone acetate (2.5 mg/d [progestin]) or placebo with a median intervention of 5.6 years, and 10,739 women with prior hysterectomy were assigned to receive the estrogen alone or placebo with a median intervention of 7.2 years.

In the estrogen plus progestin trial, the increasing breast cancer risk seen during the intervention while women were receiving the combined hormones was followed by a substantial drop in risk in the early postintervention period (within 2.75 years from intervention) when hormone therapy was discontinued but a sustained higher breast cancer risk remained during the late postintervention period years after the therapy was stopped, according to the results.

In the estrogen alone trial, the reduced breast cancer risk seen during the intervention when women were receiving the estrogen lasted through the early postintervention phase but was lost during the late postintervention follow-up, the results show.

"The ongoing influences on breast cancer after stopping hormone therapy in the WHI trials require recalibration of breast cancer risk and benefit calculation for both regimens, with greater adverse influence for estrogen and progestin use and somewhat greater benefit for use of estrogen alone," the article concludes.

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