Hormone Replacement Therapy Increases Breast Cancer Recurrence

Hormone replacement therapy (HRT) for peri- and postmenopausal symptoms increases disease recurrence in breast cancer survivors, according to an article published online March 25 in the *Journal of the National Cancer Institute*.

Previous studies have shown that HRT increases breast cancer incidence in healthy women, but its impact on breast cancer survivors has remained obscure. Observational studies and one small randomized trial had suggested that HRT had no effect or even might reduce recurrence. However, two-year follow-up data from the randomized HABITS (Hormonal Replacement After Breast Cancer — Is It Safe?) trial indicated that survivors who took HRT were more likely to suffer disease recurrence than those who did not take HRT.

In the current analysis, Lars Holmberg, M.D., Ph.D., currently at King’s College London and his mostly Scandinavian colleagues examined the breast cancer rates for women in the HABITS trial after a median follow-up of four years.

At the time of this analysis, 39 (17.6 percent) of the 221 women in the HRT treatment arm had developed breast cancer recurrence or a new breast cancer malignancy, compared with 17 (7.7 percent) of 221 women in the control arm. The estimated 5-year cumulative rate for disease recurrence was 22.2 percent for the HRT arm and 9.5 percent in the control arm, for an absolute increase in risk of 14.2 percent.

“The results of the HABITS trial indicate a substantial risk for a new breast cancer event among breast cancer survivors using [HRT]. The risk elevation is in line with the evidence from observational studies and randomized trials that [HRT] increases the risk of breast cancer in healthy women,” the authors write.

In an accompanying editorial, Kathy I. Pritchard, M.D., of the Sunnybrook Odette Cancer Center in Toronto discusses the results of the HABITS trial and the Women’s Health Initiative trial (which showed increased breast cancer risk among healthy women) in the context of the much less worrisome findings from observational studies. Observational studies, she writes, can be misleading because they have inherent biases, such as the types of patients selected for participation in the study. Although a randomized study from Stockholm found no increased risk of breast cancer recurrence among breast cancer survivors taking HRT, there may be key differences between this trial and the HABITS study, including the dosing schedule, the duration of treatment, and the type of hormones used—synthetic versus natural compounds. Those differences leave open several questions.

Despite these issues, the data are clear. “Although randomized data concerning use of HRT for symptomatic intervention in breast cancer survivors are still sparse, it seems that the harmful side effects of HRT have finally been clearly demonstrated,” Pritchard writes.

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