Is new-onset breast tenderness after the start of hormone therapy a sign of elevated cancer risk?

Yes. According to this analysis of data from the Women’s Health Initiative (WHI), women who experienced new-onset breast tenderness, as assessed 12 months after the initiation of conjugated equine estrogen (CEE) plus medroxyprogesterone acetate (MPA), had a significantly higher risk of breast cancer than did women taking CEE plus MPA who did not report such tenderness (hazard ratio [HR], 1.48; 95% confidence interval [CI], 1.08–2.03; \( P = .02 \)).


**WHAT THIS EVIDENCE MEANS FOR PRACTICE**

Counsel women who are considering or continuing estrogen–progestin hormone therapy (HT) about its risks (including a modestly increased risk of breast cancer) and benefits. Also counsel them that breast tenderness commonly occurs after initiation of HT.

During follow-up visits, any woman reporting breast tenderness should be advised that this side effect suggests that her risk of breast cancer may be higher than that of women who use HT but do not experience breast tenderness. This information may factor into decisions about HT continuation and dosage, as well as strategies for breast-cancer surveillance.

**FAST TRACK**

Women who had new-onset breast tenderness after initiating CEE plus MPA had a higher risk of breast cancer than those who did not experience such tenderness after starting CEE plus MPA.

- More than 75% of women who reported new breast tenderness (most often rated as mild) had been assigned to HT.
- Women taking HT who reported new breast tenderness had a risk of breast cancer 48% higher than those who did not report this complaint (\( P = .02 \)).
- New-onset breast tenderness in women assigned to the placebo group was not associated with an elevated risk of breast cancer.

Does breast tenderness reflect an increase in cell proliferation? Earlier studies have linked breast tenderness in women taking CEE plus MPA to high mammographic density, an independent risk factor for breast cancer. They have also established a link between estrogen–progestin therapy and breast cell proliferation. Therefore, as Crandall and colleagues observe, "breast discomfort..."
may be a clinical manifestation of increased proliferation that is manifest radiographically as increased breast density."

Keep in mind that the original WHI estrogen-progestin trial demonstrated that CEE plus MPA is associated with eight additional cases of breast cancer per 10,000 woman-years—a modest increase in risk. Although the study by Crandall and colleagues suggests that new-onset breast tenderness further increases the risk of breast cancer among users of estrogen-progestin therapy, the absolute magnitude of this increased risk is modest.

New-onset breast tenderness has a sensitivity and specificity similar to those of the Gail model for predicting the risk of invasive breast cancer. In this study, based on a mean follow-up of 5.6 years, the sensitivity and specificity of new-onset breast tenderness were 41% and 64%, respectively, and the positive predictive value was 2.7%. In comparison, using a threshold risk of breast cancer of 1.67% over 5 years, the Gail model has sensitivity, specificity, and a positive predictive value of 44%, 66%, and 6.6%, respectively.

LEARNING OBJECTIVES
After reviewing this material, clinicians should be better able to:

• Describe the practical implications of recent reports in the medical literature concerning the safety of hormone therapy
• Discuss issues that should be considered in terms of agent selection
• Review strategies to prescribe the most appropriate agent for the individual patient
• Assess the relevant medical literature that supports the course of treatment

How to appropriately counsel and manage a recently menopausal woman worried about the safety of hormone therapy (PART 1 OF 3)
http://www.obgmanagement.com/pages.asp?id=7656

How to resolve progestogen-related side effects that affect quality of life (PART 2 OF 3)
http://www.obgmanagement.com/pages.asp?id=7718

Long-term use of hormone therapy, quality of life, and statins (PART 3 OF 3)
http://www.obgmanagement.com/pages.asp?id=7896

Click on supplements at www.obgmanagement.com

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