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Breast tenderness in women getting combo hormone therapy associated with increase in breast density

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Post-menopausal women who experience new onset breast tenderness after starting combination hormone therapy may have an increased risk of breast cancer compared to women who don't experience breast tenderness, a study by researchers at UCLA's Jonsson Comprehensive Cancer Center has shown. One reason for this may be that their breasts are becoming more dense.

The new onset tenderness was much more pronounced after initiation of estrogen and progestin therapy than in women getting estrogen therapy alone. The association between new onset breast tenderness and changes in breast density also was more pronounced in the women getting the combination hormone therapy, said study first author Dr. Carolyn Crandall, a professor of general internal medicine and a scientist with UCLA's Jonsson Comprehensive Cancer Center.

Multiple population studies have shown that higher breast density is associated with a higher risk of breast cancer. In women with extremely dense breasts, the cancer risk can be four to six times higher than for women whose breasts are not dense, Crandall said.

Although the present study design did not permit Crandall to directly test whether combined hormone therapy–induced breast tenderness represents increased breast cell proliferation, mammographic density is felt to be an indirect measure of breast tissue growth.

The study appears this week in the early online edition of the peer-reviewed journal *Breast Cancer Research and Treatment.*

For this prospective study, Crandall and her team examined the association between new onset breast tenderness and change in mammographic density after initiation of hormone therapy in 695 women enrolled in the Women's Health Initiative (WHI). Launched in 1991, the WHI consisted of a set of clinical trials and an observational study involving161,808 generally healthy, postmenopausal women.

Crandall looked at women on the combination therapy as well as women taking only estrogen. They analyzed the development of breast tenderness - the absence of baseline breast tenderness and the presence of tenderness at year one follow-up. They also examined change from baseline density in mammograms, measuring the percent of tissue that was dense, and density percentages from year one and two of the WHI.

"New breast tenderness that begins after a woman initiates therapy with routine doses of estrogen is common and almost double that of women taking a placebo," Crandall said. "It's even higher in women who also are taking a progestin, about three times higher than women given placebos."

Among women assigned to the combination therapy, mean increase in mammographic density was greater among participants reporting new onset of breast tenderness (11.3 percent at year 1) than among participants without new onset breast tenderness (3.9 percent at year one). However, in women who took estrogen alone, breast density was not any different between those who experienced new onset breast tenderness and those who did not, Crandall said.

This is important, Crandall said, because estrogens can increase the risk of uterine cancer and often are paired with progestin to prevent the malignancy in those who have not had a hysterectomy. So while the

combination protects women from uterine cancer, it is increasing their risk of developing a breast cancer.

"These findings parallel what is known about breast cancer risk from the WHI. Breast cancer risk was elevated by combination estrogen and progestin therapy, but not by estrogen alone," Crandall said. "Now we know that new onset breast tenderness after combination therapy, but not estrogen alone, is associated with greater increases in breast density."

Using the WHI data, Crandall's team had previously shown in 2009 that women who experienced new onset breast tenderness after initiating combination hormone therapy had a 48% higher risk of subsequent breast cancer than women who did not experience new onset breast tenderness.

These new findings shed light on the biology that might partly explain the link between new onset breast tenderness and increased breast cancer risk during combination therapy, Crandall said. Understanding factors associated with mammographic density changes during therapy with estrogen and progestin may help give biological insights into hormone therapy-associated breast cancer risk.

"These findings emphasize the complexity inherent in the use of surrogate risk markers to assess menopausal hormone therapy-associated breast cancer risk," the study concludes.

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