

# Combined HRT increases risk of lobular breast cancer fourfold after just 3 years of use

**Postmenopausal women who take combined estrogen/progestin hormone-replacement therapy for three years or more face a fourfold increased risk of developing various forms of lobular breast cancer, according to new findings by researchers at Fred Hutchinson Cancer Research Center.**

“Previous research indicated that five or more years of combined hormone-therapy use was necessary to increase overall breast-cancer risk,” said Christopher I. Li, M.D., Ph.D., the lead author of the report, published in the January issue of *Cancer Epidemiology, Biomarkers and Prevention*. “Our study, the first specifically designed to evaluate the relationship between combined HRT and lobular breast cancers, suggests that a significantly shorter length of exposure to such hormones may confer an increased risk.”

The study, which confirms previous reports of the association between combined hormone-therapy use and increased risk of lobular breast cancers, is the largest study of combined HRT and lobular cancer risk in the United States. It is also the first such study to take into account the recency and duration of hormone use and the first to include a centralized pathological review of tumor specimens to confirm their histological type: ductal, lobular or mixed ductal-lobular.

Lobular cancer involves the lobules, or chambers, in the breast that contain milk-producing glands. While lobular carcinoma accounts for only about 15 percent of all invasive breast cancers, it is hormonally sensitive and therefore more treatable than the more common ductal variety, which arises in the ducts that carry milk from the lobules to the nipple. However, lobular breast tumors also present a clinical challenge because they are more difficult to detect both by clinical examination and by mammography than ductal cancers, which account for about 70 percent of invasive breast cancers in the United States.

The study assessed hormone-replacement status in more than 1,500 postmenopausal women in western Washington – 1,044 breast-cancer cases (324 lobular, 196 mixed ductal-lobular and 524 ductal) and 469 controls. The researchers also confirmed tumor status through centralized examination of breast tissue.

The researchers found that current users of combined HRT had a 2.7-fold and 3.3-fold elevated risk of lobular and ductal-lobular cancer, respectively, regardless of tumor stage, size or number of lymph nodes involved. Only women who used combined HRT for three or more years faced an increased risk of lobular cancer. Among mixed ductal-lobular cases, hormone therapy increased the risk of tumors that were predominantly lobular but not tumors that had predominantly ductal characteristics.

The incidence of invasive lobular and ductal-lobular breast cancers has risen rapidly in the United States, increasing 52 percent and 96 percent, respectively, between 1987 and 1999, whereas rates of ductal cancer have increased only 3 percent during this time.

“Our research suggests that the use of postmenopausal hormone-replacement therapy, specifically the use of combined estrogen-plus-progestin preparations, may be contributing to this increase,” said Li, an associate member of the Hutchinson Center’s Public Health Sciences Division.

While the number of postmenopausal women taking combined HRT long-term has dropped by about half in recent years due to Women’s Health Initiative reports of health risks associated with such therapy, such as an increase in heart-disease and breast-cancer risk, a substantial number of women are still taking HRT to manage the symptoms of menopause.

“These findings are still of considerable public-health importance considering the estimated 57 million prescriptions for menopausal hormone therapy that continue to be filled in the United States,” Li said.

Source: Fred Hutchinson Cancer Research Center

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