

# Lobular Involution May Protect Against Breast Ca

BY BRUCE JANCIN  
Denver Bureau

SAN ANTONIO — Young women with a benign breast biopsy showing complete lobular involution are at below-average risk of future breast cancer, according to a large prospective Mayo Clinic study.

This finding—that lobular involution constitutes a novel protective factor against breast cancer in young women with benign breast disease—is an important advance in the effort to better stratify breast cancer risk in the 1 million American women per year who undergo a biopsy showing benign breast disease, Dr. Karthik Ghosh said at the San Antonio Breast Cancer Symposium.

Moreover, the lobular involution findings open the door to new breast cancer chemoprevention strategies. Lobular involution may prove to be a factor that can be modified in order to reduce risk, noted Dr. Ghosh of the Mayo Clinic, Rochester, Minn.

She reported on 4,460 women aged 18-49 years in the Mayo Benign Breast Disease Cohort who underwent excisional breast biopsy for a palpable or mammographic abnormality that proved to be benign breast disease. These young women (average age at biopsy, 39 years) have subsequently been followed for a median of 20 years, during which 7% developed invasive breast cancer.

The initial benign biopsy showed complete lobular involution (defined as a 75% or greater reduction in the number and size of breast duct lobules) in 5% of the 4,460 young women. A total of 34% had no lobular involution at all, whereas 61% had partial lobular involution, in the range of 1%-74%.

In a multivariate analysis, the women with complete lobular involution had a 32% reduction in breast cancer rate compared with the general population, which for purposes of this study came from Iowa SEER (Surveillance, Epidemiology, and End Results) registry data of a population demographically similar to that of the Mayo Clinic.

Women with partial lobular involution had a 43% greater than expected breast cancer rate during 20 years of follow-up, whereas those with no involution had a 72% increased rate ( $P = .001$ ).

Lobular involution is a normal physiological process that happens with aging. Pathologists have long been aware of the phenomenon, but it entered the clinical arena only several years ago when investigators reported that lobular involution was associated with reduced risk of breast cancer in 8,736 participants in the Mayo Benign Breast Disease Cohort (J. Natl. Cancer Inst. 2006;98:1600-7).

Dr. Ghosh focused her new study on cohort members who were younger than age 50 when they were diagnosed with benign breast disease because breast cancer is the leading cause of cancer death in women aged 18-49 years. Moreover, breast cancer in this age group is associated with a higher recurrence rate and greater all-

cause mortality than it is in older patients. The study also examined the impact of conventional histologic categories of benign breast disease and family history.

The initial benign breast biopsy showed atypical hyperplasia in 2% of patients, nonproliferative breast disease in 72%, and proliferative changes without atypia in 26%. The subsequent risk of breast cancer was 6.9-fold greater in the young women with atypical hyperplasia

than in the comparison population, 2-fold greater in those with proliferative disease without atypia, and 1.2-fold greater in those with nonproliferative disease.

A consistent finding was that coexistent complete lobular involution reduced the risks associated with all three types of histology, Dr. Ghosh said.

Strong family history (defined in this study as at least one family member with breast cancer before age 50, or at least

one affected first-degree relative and one other relative with breast cancer) essentially doubled the risks associated with proliferative disease without atypia and with nonproliferative disease. Women with nonproliferative disease and no family history of breast cancer were not at increased risk of the malignancy.

The Mayo Clinic's prospective studies of benign breast disease are funded by the Department of Defense. ■

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\*Whether these observed differences represent true differences in the effects of Levemir®, NPH insulin, and insulin glargine is not known, since these trials were not blinded and the protocols (eg, diet and exercise instructions and monitoring) were not specifically directed at exploring hypotheses related to weight effects of the treatments compared. The clinical significance of the observed differences in weight has not been established.

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