Figure Family Structure Into BRCA Screening

BY BRUCE JANCIN
Denver Bureau

SAN ANTONIO — Consider lowering the threshold for BRCA mutation testing in patients with early-onset breast cancer who have fewer than two first- or second-degree female relatives older than age 45, Dr. Jeffrey N. Weitzel advised at a breast cancer symposium sponsored by the Cancer Therapy and Research Center.

Patients with this sort of family situation, which he terms a "limited family structure," were 3.5-fold more likely to carry a deleterious BRCA mutation than were early-onset breast cancer patients with an adequate family structure, in his observational study.

Current guidelines agree that testing is not appropriate for women without breast cancer in the general population. But the guidelines are less clear regarding what to do about women who develop breast cancer at a young age in the absence of a family history of breast or ovarian cancer. Consideration of family structure provides a quick, useful aid in this decision making, according to Dr. Weitzel, director of the department of clinical cancer genetics and the cancer screening and prevention program at City of Hope National Medical Center, Duarte, Calif.

He reported on 1,097 women who underwent BRCA mutation testing in the center's clinic for genetic cancer risk assessment. Of these women, 210 had breast cancer prior to age 50 and no family history of breast or ovarian cancer in first- or second-degree relatives. Half of these 210 women had a limited family structure.

A BRCA mutation was found in 17.3% of the women with early-onset breast cancer and a limited family structure, and in 5.7% of those with early-onset disease and an adequate family structure.

Family structure as a predictive factor for BRCA mutation had a sensitivity of 75% and a specificity of 54%. Family structure's positive predictive value of 18% and negative predictive value of 91% were superior to the commonly used models for estimating the probability that a woman has a BRCA mutation, Dr. Weitzel said. ■

Breast Cancer Prognosis Tied Tightly to Genes

SAN ANTONIO — Breast cancer prognosis appears to have a strong and previously unrecognized inherited component, Dr. Mikael Hartman said at a breast cancer symposium sponsored by the Cancer Therapy and Research Center.

His study of 2,787 mother-daughter and 831 sister pairs with breast cancer showed that 5-year breast cancer–specific mortality was 60%-80% greater among first-degree relatives of a woman who died of the disease within 5 years of diagnosis than in those whose affected mother or sister had a good prognosis.

"Information about the outcome of breast cancer among affected first-degree relatives may be relevant for optimal clinical management of women with newly diagnosed breast cancer," said Dr. Hartman of the Karolinska Institute, Stockholm.

Among the 831 pairs of sisters, each with breast cancer, 5-year breast cancer–specific survival was 88% if the older affected sister was alive within 5 years of diagnosis, but only 70% if she was not.

After adjusting for potential confounders, including age at cancer diagnosis, treatment era, nulliparity or age at first live birth, and socioeconomic status, the risk of dying because of breast cancer within 5 years after diagnosis was 80% greater in women whose sister died of breast cancer less than 5 years following her diagnosis than in those whose sister had a good-prognosis form of the disease as defined in a multivariate model.

Similarly, the adjusted risk of breast cancer–specific mortality was 60% higher in the daughters of mothers with a poor-prognosis form of breast cancer, compared with mothers with a good prognosis, he continued. Concordance with regard to prognosis was strongest among mother-daughter pairs in whom the mother was diagnosed before age 40.

The determinants of this newly recognized inherited component of breast cancer prognosis are likely to turn out to be genetic, Dr. Hartman said.

—Bruce Jancin