Older women with breast cancer may benefit from genetic testing, study suggests

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About 1 in 40 postmenopausal women diagnosed with breast cancer before age 65 have cancer-associated mutations in their BRCA1 or BRCA2 genes, according to a Stanford-led study of more than 4,500 participants in the long-running Women's Health Initiative.

The prevalence of the mutations in this group is similar to that of Ashkenazi Jewish women, whom the U.S. Preventive Service Task Force suggests should discuss their cancer risk with their physicians to determine if genetic testing is warranted. Currently, most guidelines don't address testing postmenopausal women with breast cancer in the absence of other risk factors.

The finding is the first to suggest that postmenopausal women who have been newly diagnosed with breast cancer but who don't have any hereditary risk factors, such as close family members diagnosed with breast cancer before age 50, may still benefit from genetic testing for inherited cancer-associated mutations.

Identifying women with inherited cancer-associated mutations, particularly in the BRCA1 and BRCA2 genes, is important because some of the mutations also substantially increase the risk of other cancers, including ovarian cancer. Because these mutations are passed through families, knowing that a woman carries one of these mutations may encourage her healthy relatives to discuss their own risk factors with their doctors.

"There's been a lot of controversy in the field as to whether every woman with breast cancer should receive genetic testing," said Allison Kurian, MD, MSc, associate professor of medicine and of epidemiology

and population health at Stanford, "in part because we didn't know how prevalent cancer-associated mutations are in this largest subgroup of newly diagnosed people—that is, women who develop breast cancer after menopause without the presence of any known hereditary risk factors."

Kurian is the lead author of the study, which will be published March 10 in *JAMA*. Marcia Stefanick, Ph.D., professor of medicine and of obstetrics and gynecology at Stanford, is the senior author of the study.

Cancer-associated variants

Unlike mutations that accumulate over time, specifically in cancer cells, germline mutations are inherited and are found in every cell of the body.

Physicians primarily consider a woman's age at diagnosis and her family's cancer history when determining whether to recommend genetic testing. A woman diagnosed with breast cancer before age 50, for example, or a healthy woman with several close family members who have had breast or ovarian cancer, is more likely to be referred for genetic testing than a postmenopausal woman with breast cancer and no other risk factors.

For the study, Kurian and Stefanick and their colleagues set out to compare the prevalence of cancer-associated mutations in 10 breast-cancer risk genes, including BRCA1 and BRCA2. They compared 2,195 women who were diagnosed with breast cancer at an average age of 73 with 2,322 women without breast cancer.

The data for the study came from the Women's Health Initiative, which enrolled more than 160,000 women ages 50 to 79 throughout the United States between 1993 to 1998 to conduct the largest study of postmenopausal health in the country. Stefanick served as chair of the

initiative's steering committee for most of the project.

The researchers found that about 3.5% of the women with breast cancer had a cancer-associated mutation in at least one of the 10 genes, compared with about 1.3% of women without cancer. When they narrowed their focus to just the BRCA1 and BRCA2 genes in women diagnosed before age 65, they found that about 2.2% of women with breast cancers had cancer-associated mutations, versus about 1.1% of those without breast cancer.

Only about 31% of those women with cancer and 20% of those without cancer, both with BRCA1 or BRCA2 mutations, were likely to have been recommended for testing under the current guidelines of the National Comprehensive Cancer Network.

"Now we know that the prevalence of cancer-associated BRCA1 and BRCA2 mutations in women diagnosed with breast cancer after menopause rivals that in women of Ashkenazi Jewish descent—a population that is currently encouraged to discuss genetic testing with their doctors," Kurian said. "We finally have a read on the likely benefit of testing this most common subgroup of breast cancer patients."

Provided by Stanford University Medical Center

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