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First large study details cognitive outcomes among older breast cancer patients

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The first large U.S. study of cognition in older breast cancer patients found that within the first two years after diagnosis and treatment, most women do not experience cancer-related cognitive problems.

Researchers also observed a troubling trend that needs further exploration—the small sub-set of women who experienced cognitive decline were unique in having the APOE4 gene, and this effect was most pronounced after chemotherapy. This gene has been found to substantially increase risk of developing Alzheimer's disease.

Results of this study, comparing hundreds of breast cancer patients ages 60 to 98 before and after treatment to a matched group of cancer-free older women "are good news for the majority of breast cancer patients who worry about potential long-lasting cognitive effects of treatment,"says the study's lead researcher and geriatrician Jeanne Mandelblatt, MD, MPH, professor of oncology at Georgetown Lombardi Comprehensive Cancer Center. The study is published in the *Journal of Clinical Oncology*.

"Our study suggests that for most older breast cancer patients, chemotherapy and hormonal treatments do not have major adverse effects on cognitive function, at least as measured by our current tests," she says.

Mandelblatt explains that cognitive function is a concern for older individuals who face multiple forces that can lead to problems with

memory and other cognitive abilities. Some patients report difficulties remembering things, or taking longer to do daily tasks after their cancer and its treatments, even after considering other factors, she says.

"But this phenomenon has not been well studied in older women who have been treated for breast cancer, a group that may be more vulnerable to cognitive problems based on multiple chronic diseases and aging processes," she adds.

"In this study, patients who were more likely to have cognitive issues were a small group who have one or two copies of the APOE4 gene, but the data are inconclusive and we are examining this more thoroughly," Mandelblatt says.

Researchers found that these patients tended to show a steady decline in cognitive function test scores after chemotherapy compared to APOE4-negative patients, and non-cancer participants.

"It is not that the chemotherapy causes Alzheimer's disease, but that these patients may be at risk for both cancer-related cognitive problems and Alzheimer's—perhaps through a process of accelerated aging or other shared disease processes," Mandelblatt says.

She adds that the apparent interaction of APOE4 and breast cancer chemotherapy will be of interest to the many scientists who research the basis of neurodegeneration. Still, Mandelblatt stresses that this early finding was suggestive and needs to be verified in additional studies that include more breast cancer patients with the APOE4 gene who are exposed to chemotherapy. Only 20-25 percent of individuals in the population are APOE4-positive, and fewer than 30% of older breast cancer patients routinely receive chemotherapy.

If the findings are replicated and extended, then genotyping could be

useful when breast cancer patients discuss treatment options with their oncologists, Mandelblatt says. "In any case, all patients should discuss any concerns about cognitive issues during and after treatment with their care team."

The research being reported is part of the ongoing Thinking and Living with Cancer (TLC) study, the largest prospective, controlled study of cognitive function among older breast cancer patients.

This particular report included 344 newly diagnosed women with non-metastatic breast cancer and 347 non-cancer controls. As a way to tease out effects of treatment on cognitive function, the groups were matched in terms of age, general health status, race, education, lifestyle, and other factors. No one had any cognitive problems or dementia at the start of the study.

Both groups of participants were given a battery of 13 cognitive tests at the beginning of the study (before patients were treated with chemo- or hormonal therapy), and 12 and 24 months later. About 95% of participants in each group provided biospecimens for APOE4 testing. The neuropsychological tests measured attention, processing speed, executive function, and learning and memory. Participants also filled out self-assessments of their cognitive function.

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