MedicalXpress

Beyond BRCA: Links between breast, second primary cancer and inherited mutations

May 31 2018

Rates of inherited mutations in genes other than BRCA1/2 are twice as high in breast cancer patients who have had a second primary cancer—including, in some cases, different types of breast cancer—compared to patients who have only had a single breast cancer. But the rates of these mutations were still found to be low overall, meaning it's difficult to assess whether and how these individual mutations may drive the development of cancer. The study from the Basser Center for BRCA in the Abramson Cancer Center of the University of Pennsylvania also investigated the use of polygenic risk scores—which have recently been added to some commercial clinical multiplex genetic testing panels. Kara N. Maxwell, MD, Ph.D., an instructor of Hematology-Oncology and the study's lead author, will present the findings at the 2018 American Society of Clinical Oncology Annual Meeting in Chicago (Abstract #1503).

Genetic testing can help identify patients have a genetic predisposition that puts them at risk for developing cancer. Recently, new therapies called PARP inhibitors have been FDA approved to specifically target cancers caused by certain mutations—such as BRCA1/2, which carry a lifetime breast cancer risk of as much as 85 percent and 50 percent for ovarian cancer, as well as higher risks of pancreatic, prostate and other cancers.

"We need to gain a better understanding of why patients who have multiple cancers may be susceptible to them, and that work needs to go beyond the common genes we're already been looking at," Maxwell said.

The team—led by Susan M. Domchek, MD, executive director of the Basser Center for BRCA, and Katherine L. Nathanson, MD, deputy director of the Abramson Cancer Center, specifically looked at patients who did not have a BRCA1/2 mutation and tested them for a panel of 15 different genetic mutations. They evaluated 891 patients who had a second primary cancer—breast or otherwise—after initial breast cancer and compared them to 1,928 who only had a single breast cancer. About eight percent of patients who had second primary cancers had mutations, compared to just four percent of patients from the single cancer cohort. The current threshold for whether or not genetic testing is recommended is five percent.

"Our data show that patients who have had multiple primary cancers should undergo genetic testing, and likely this holds true for a number of other types of second cancer," Maxwell said. "However, the overall numbers are still low, which shows the level of uncertainty that still exists and highlights the need for further research."

The research also evaluated polygenic risk scores, a somewhat controversial metric recently added to some commercial clinical multiplex genetic testing panels. Polygenic risk scores are determined by how many single nucleotide polymorphisms (SNPs) a person has. SNPs are common variants with smaller effect sizes, and if a patient has multiple of certain SNPs, they may be at a similar increased for cancer a as patients with a single rare mutation.

"Our study does not provide strong evidence of higher polygenic risk scores in patients with more than one breast cancer," but many more patients will need to be studied to confirm this," Maxwell said.

More information: Maxwell will present the findings as an oral abstract in the Cancer Prevention, Hereditary Genetics, and Epidemiology session on Sunday, June 3rd, at McCormick Place in

Room S404 at 9:00 AM Central.

Provided by Perelman School of Medicine at the University of Pennsylvania