

A Polygenic Risk Score May Predict Future Breast Cancer in Patients With Early-Stage Diagnoses

Patients diagnosed with abnormal breast cells were more likely to receive a later diagnosis of breast cancer if their 313-SNP breast cancer polygenic risk score was high.

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In a retrospective study, the 313-SNP breast cancer polygenic risk score (PRS₃₁₃) blood test could predict future incidents of breast cancer in women diagnosed with ductal carcinoma in situ (DCIS) or lobular carcinoma in situ (LCIS), according to a paper published in [Cancer Epidemiology, Biomarkers & Prevention](#), a journal of the American Association for Cancer Research (AACR).

Breast cancer is the most common form of cancer in women and contributes to [more than 15% of all new cancer cases](#) in the United States. Abnormal cells in the breast ducts (DCIS) and breast lobules (LCIS) can develop into breast cancer, but scientists cannot currently predict which DCIS and LCIS cases will go on to become breast cancer, said [Elinor J. Sawyer, PhD](#), the study's senior author and professor of clinical oncology at King's College London in the United Kingdom. "It is therefore very important that we find ways to predict which women with DCIS and LCIS are most likely to develop invasive breast cancer in the future so they can be given the most appropriate treatment and avoid unnecessary treatment," she said.

The study's lead author, Clinical Information Analyst [Jasmine Timbres](#) at King's College London, wanted to test whether PRS₃₁₃ could be a useful tool in filling this gap in risk assessment and guiding treatment. PRS₃₁₃ is a test that estimates a patient's breast cancer risk by quantifying which of 313 breast cancer-associated gene abnormalities called SNPs they have. Because PRS₃₁₃ has been [previously validated](#) as a genetic test that can predict the risk of breast cancer in women with no cancer history, Timbres hypothesized that it could be used as a prediction factor for the risk of breast cancer in patients with DCIS or LCIS.

To test the predictive power of PRS₃₁₃ in DCIS and LCIS patients, the researchers analyzed the datasets from the U.K. [ICICLE](#) and [GLACIER](#) studies. The team assessed the PRS₃₁₃ scores and follow-up data from 2,169 DCIS cases and 185 LCIS cases. For patients with DCIS, the researchers stratified the PRS₃₁₃ scores into quartiles and compared them with outcomes. For patients with LCIS, they measured associations between increasing PRS₃₁₃ scores and outcomes.

The study found that, among patients with DCIS, those with PRS₃₁₃ scores in the highest quartile were 2.03 times as likely to develop cancer in the breast opposite the original breast (i.e., the contralateral breast) compared with patients in the lowest PRS₃₁₃ quartile. However, the association between a higher PRS₃₁₃ and future same-breast (ipsilateral) cancer in patients with DCIS was not significant.

In patients with LCIS, an increasing PRS₃₁₃ score was associated with an increased risk of ipsilateral breast cancer, being 2.16 times more likely to develop ipsilateral disease per increase in PRS₃₁₃.

Family cancer history also appeared to play a role. The researchers found that, in patients with a family history of breast cancer, increases in PRS₃₁₃ were associated with a more than threefold increase in the risk of ipsilateral disease after LCIS, and the risk increased to fourfold if patients who had received mastectomy and radiotherapy for their cancer were excluded.

“LCIS is not always surgically removed or treated with hormone therapies, as it is considered lower risk than DCIS. However, these results indicate that those with a family history may benefit from such additional treatments, which could reduce their risk of further cancer,” Timbres said.

“The associations found in this study could be useful in helping women decide their treatment options after a diagnosis of DCIS or LCIS,” she added. “By looking at the full picture, rather than just how cells look under a microscope, we can give women more accurate information about their personal risk of recurrence. This could help them make more informed choices about their treatment options and what’s right for them.”

Sawyer noted, “Although more work still needs to be done to confirm the results of this study in other groups of patients or assess additional genetic changes, the results are very promising and have the potential to influence treatment decisions.”

The study’s limitations include PRS₃₁₃’s design as a risk score for invasive disease specifically, and the study therefore may not have tested for important but as-yet-unknown genetic changes associated with in situ breast disease. Another limitation is that the number of women with LCIS in the study’s cohorts was quite small, which may have led to the researchers not detecting statistically significant associations.

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