Risk of a second breast cancer can be better quantified in women carrying a BRCA mutation

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The risk of a second breast cancer in patients with high-risk BRCA gene mutations can be more precisely predicted by testing for several other genetic variants, each of which are known to have a small impact on breast cancer risk.

Breast cancer patients who are diagnosed at a very young age, or who have a strong family history of the disease are regularly found to carry a mutation in either the BRCA1 or BRCA2 gene. They are also at high risk of developing a second cancer in their other breast and may opt for a double mastectomy to reduce their risk.

Technology already exists to test for these genetic 'low risk variants' that each play a small role in breast cancer risk. The new research, presented at the 11th European Breast Cancer Conference, shows that this technology can also be used for BRCA mutation carriers who have already had one cancer to better predict their risk of developing a tumour in the other breast.

The research was presented by Dr Alexandra van den Broek from the Netherlands Cancer Institute in Amsterdam. She explained: "Women with a BRCA mutation are more likely to develop breast cancer when they are young and, unfortunately, some will be unlucky and go on to suffer a second breast cancer later in life. We know these women are at a higher risk, but it has also been shown that individual risks may vary

widely, so we wanted to see if there was any way to better identify patients at lower and higher risks."

The researchers studied a group of around 6,000 breast cancer patients who had a mutation in the BRCA1 gene and around 4,000 who had a mutation in BRCA2. The women were from countries around the world including The Netherlands, Spain, the UK, USA, Australia and Canada.

They used existing technology to examine the low risk variants that each woman carried. The effects of all these variants can be put together to give each person a combined estimate called a polygenic risk score.

The results showed that these polygenic risk scores can predict the risk of a second breast cancer in BRCA breast cancer survivors. The difference in the risk of a second breast cancer between different polygenic risk scores can be up to ten per cent in the ten years following a first diagnosis.

Dr van den Broek added: "These polygenic risk scores were originally developed to try to better predict the risk of developing a first breast cancer. Our research suggests that they can also be used to help patients who have survived their first breast cancer to better understand their level of risk for a second breast cancer. We hope these findings will add to the existing knowledge about predicting risk for a second breast cancer in these survivors."

The researchers will continue to study the significance of these low risk variants and how they interact with other known risk factors, such as age. They acknowledge that their findings could be influenced by the fact that women with a second breast cancer are more likely to be tested for a BRCA mutation, which may mean they are over-represented in this study, and they would like to adjust for that in the future. They also say that validating the results in an independent cohort would strengthen

their findings.

Professor Isabel Rubio is co-chair of the 11th European Breast Cancer Conference and Director of the Breast Surgical Unit at Clinica Universidad de Navarra, in Madrid, Spain, and was not involved in the research. She said: "Facing a diagnosis of breast cancer and carrying a BRCA mutation is overwhelming for many women. New information on the individual risks of developing a contralateral breast cancer in this population will help in the decision-making process on preventive surgery or intensive follow up. Research like this brings new information to help with these difficult decisions."

More information: Abstract no: 7, "The association between Polygenic Risk Scores and contralateral breast cancer risk in BRCA1 and BRCA2 mutation carriers: analyses in the CIMBA consortium" Wednesday 21 March, "Clinical Science Symposium: Risk Modelling" session

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