Global study reports assisted reproduction treatments are safe in young breast cancer survivors with high-risk genes

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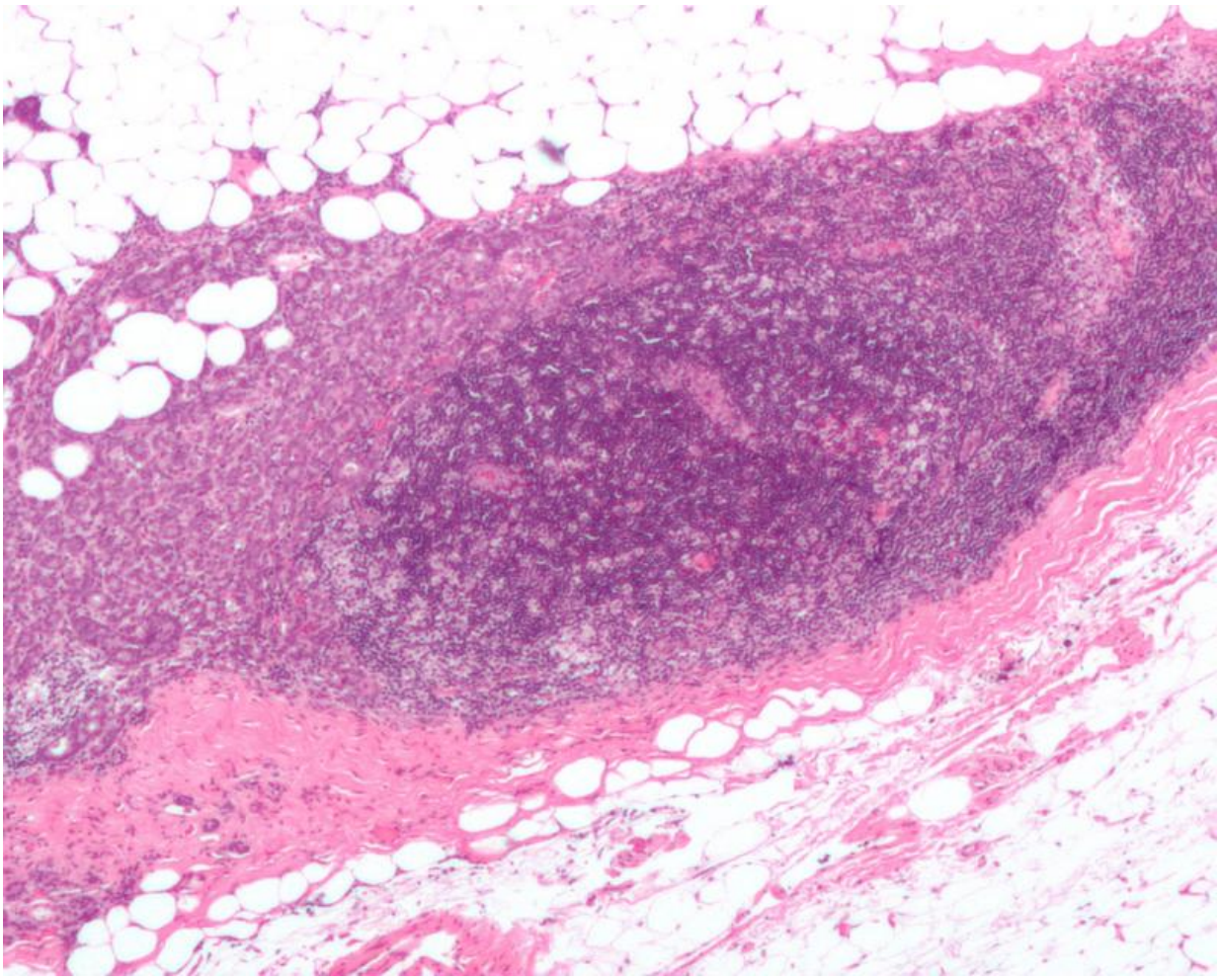

Micrograph showing a lymph node invaded by ductal breast carcinoma, with extension of the tumor beyond the lymph node. Credit: Nephron/Wikipedia

Assisted reproductive techniques (ART) in young women with high-risk genes who have survived breast cancer do not increase the risk of cancer recurrence or adversely affect the resulting pregnancies and babies, show results from a global study reported at ESMO Breast Cancer 2024. The research is published in the journal *Annals of Oncology*.

"This study provides the first evidence that use of fertility procedures is safe in young women with germline pathogenic/likely pathogenic variants in the BRCA1 or BRCA2 genes, which are known to increase the risks of developing breast and other cancers," said Matteo Lambertini, Associate Professor and Consultant in Medical Oncology at the University of Genova, and IRCCS Policlinico San Martino Hospital, Genova, Italy, who will present the study.

"The results provide reassuring evidence for these women and their doctors to consider when discussing the risks and benefits of using ART to preserve their chances of having a baby following completion of anticancer therapies," he suggests.

Fertility is a major concern for women developing breast cancer at a young age before they have had children, because treatment can stop the ovaries from working and trigger the menopause. One way a woman can preserve her fertility is to freeze oocytes (eggs) or embryos before starting breast cancer treatment. These techniques generally involve use of fertility drugs to stimulate the ovaries to produce eggs, but this increases levels of the hormone estrogen.

"We have previously been concerned that increasing hormone levels for fertility preservation techniques before starting breast cancer treatment may increase the risk of cancer recurrence in the future. There has been even more concern in women with pathogenic variants in the BRCA genes because of their increased risk of breast cancer and other cancers. And so strategies to preserve fertility were often not even discussed with these patients," explained Lambertini.

"This was the main rationale for our study: to provide the evidence on whether fertility treatments are safe in patients with breast cancer and, specifically in those with pathogenic variants in the BRCA genes, or not.

"In light of these results, now when we counsel a young woman with breast cancer who has such variants, we can safely discuss the use of fertility preservation before starting treatment, without major concern," Lambertini added, proposing that these findings will have immediate implications for clinical practice.

The new study analyzed data for nearly 5000 women with BRCA1/2 pathogenic variants who were diagnosed with breast cancer aged 40 years or younger at 78 cancer centers across the world between 2000 and 2020. Researchers compared the risk of breast cancer recurrence in 107 of these women who had a pregnancy using ART with 436 who conceived naturally.

Results showed no significant difference in breast cancer recurrence in women undergoing ART compared to those having a baby without ART after following them up for an average of just over five years after conception. The study also showed no statically significant differences in pregnancy complications, although women conceiving with ART had more miscarriages and less induced abortions than those conceiving naturally, or on the babies born to these women.

"The main take-home message from this study is that there is no increased risk of breast cancer recurrence with assisted reproductive techniques in young women with BRCA pathogenic variants having a pregnancy after breast cancer. We also found that these procedures are safe for the baby: having a pregnancy with the use of fertility procedures does not increase the risk of complications," said Lambertini.

He acknowledged that the numbers of women in the study groups may appear small, but he pointed out that only 5–6% of all cases of breast cancer occur in young women under 40 and, of these, around one in six have BRCA pathogenic variants. "We put together centers from all over the world to collect data on this unique group of patients," he explained.

"These findings add really reassuring information for this subgroup of young breast cancer patients," agreed Ann Partridge, Professor of Medicine at Harvard Medical School and Vice-Chair of Medical Oncology at Dana-Farber Cancer Institute and Brigham and Women's Hospital, Boston, U.S., a co-author of the study.

She added, "We always worry a little more about the patients with BRCA pathogenic variants, because not only do they have a risk of recurrence like all breast cancer patients, but they also have a higher risk of a new cancer not related to the original breast cancer."

Dr. Partridge considered the study provides very useful information for doctors to discuss with young women with early breast cancer and a BRCA1/2 variants to help them make decisions about fertility treatments. "These new data provide reassuring evidence that pursuing fertility preservation before undergoing breast cancer treatment or using the products of fertility preservation (eggs or embryos) or undergoing fertility preservation after surviving breast cancer, all appear to be safe from a cancer standpoint and in terms of the baby's outcome," she said.

Dr. Partridge added that there is an additional reason why young women with BRCA1/2 breast cancer may want to use ART, in addition to overcoming infertility. She said, "These women might want to use ART for pre-implantation genetic diagnosis to select embryos that do not carry the same risky genes to avoid passing on a potential risk of hereditary breast cancer to the next generation."

More information: M. Lambertini et al, Fertility preservation and post-treatment pregnancies in post-pubertal cancer patients: ESMO Clinical Practice Guidelines†, *Annals of Oncology* (2020). DOI: 10.1016/j.annonc.2020.09.006

Ellen R Copson et al, Germline BRCA mutation and outcome in young-onset breast cancer (POSH): a prospective cohort study, *The Lancet Oncology* (2018). DOI: 10.1016/S1470-2045(17)30891-4

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