



RESEARCH NEWS

Young women with BRCA mutation can safely postpone radical surgery

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Young women with breast cancer and a BRCA mutation do not need to rush to have a double mastectomy, after a large prospective study found that breast conservation with radiotherapy was a safe option in the first decade after diagnosis. Experts said that young women with a BRCA mutation should take time to discuss whether radical breast surgery was the right choice for them.

The study, published in the *Lancet Oncology*, found that survival after treatment of women with a BRCA mutation was similar to overall survival in women without the mutation—at least for the first 10 years.¹

The POSH study included 2733 women recruited between 2000 and 2008 from 127 hospitals in the UK. The women were all aged 40 years or younger when they were first given a diagnosis of invasive breast cancer. Genotyping detected a BRCA mutation in 12% of the women: 201 patients with the BRCA1 gene and 137 with the BRCA2. Treatment was carried out according to local protocols, with 89% of the women undergoing chemotherapy, 49% having breast conserving surgery, half having a mastectomy, and less than 1% having no breast surgery.

After a median follow-up period of 8.2 years there were 678 deaths, including 651 from breast cancer, 18 from other cancers, and nine from other causes. The study found that overall survival at two years was 97.0% among BRCA mutation carriers and 96.6% among non-carriers (hazard ratio 0.96 (95% confidence interval 0.76 to 1.22)). Survival at five years was 83.8% among women with a BRCA mutation and 85% among non-carriers, and at 10 years the figures were 73.4% and 70.1%.

However, in patients with triple negative breast cancer, BRCA mutation carriers might have a small survival advantage over non-carriers in the first few years after diagnosis, the study concluded. In a subgroup analysis of 558 patients with triple negative breast cancer, it found that women who had a BRCA mutation had better overall survival than non-carriers at two years (95% v 91%; hazard ratio 0.59 (0.35 to 0.99), P=0.047), although the results showed no differences between the groups at five years or 10 years. The researchers said that the survival benefit was not caused by these women having early risk-reducing surgery and said that the reasons for it remained unclear and that the result needed confirmation.

In the cohort, double mastectomy was not associated with better survival, although its use was fairly low. Of the 338 women with a BRCA mutation 107 had a double mastectomy. The

researchers said that this probably reflected the low level of clinical testing for the mutation at the time of the study.

One limitation of the study was that treatment of women with BRCA mutations has changed substantially since the beginning of the trial in 2000. The researchers also noted that the study results might not translate to older women with a BRCA mutation. And the study did not look at women with a BRCA mutation who did not have a cancer diagnosis and who had undergone preventive double mastectomy.

The study's leader, Diana Eccles, from the University of Southampton and University Hospital Southampton NHS Foundation Trust, said, "Women diagnosed with early breast cancer who carry a BRCA mutation are often offered double mastectomies soon after their diagnosis or chemotherapy treatment. However, our findings suggest that this surgery does not have to be immediately undertaken along with the other treatment."

She added, "In the longer term, risk-reducing surgery should be discussed as an option for BRCA1 mutation carriers in particular, to minimise their future risk of developing a new breast or ovarian cancer. Decisions about timing of additional surgery to reduce future cancer risks should take into account patient prognosis after their first cancer, and their personal preferences."

Commenting on the research, Fiona MacNeill, a consultant breast surgeon at the Royal Marsden NHS Foundation Trust, London, said, "Double mastectomy did not show any survival advantage at 10 years. However, it may be that any survival advantage to radical risk-reducing breast surgery in those already affected with breast cancer may not be demonstrated for 2-3 decades."

She added, "This study can reassure young women with breast cancer, particularly those with triple negative cancer or who are BRCA carriers, that breast conservation with radiotherapy is a safe option in the first decade after diagnosis and double mastectomy is not essential or mandatory at initial treatment. In view of this, younger women with breast cancer can take time to discuss whether radical breast surgery is the right choice for them as part of a longer term risk-reducing strategy."

1 CopsonEMAishmanTTapperW. Germline BRCA mutation and outcome in young-onset breast cancer (POSH): a prospective cohort study. *Lancet Oncol* 2018;(Jan). doi:10.1016/S1470-2045(17)30891-4.

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