

COMMENT OPEN



Comment: Survival after risk-reducing mastectomy in young BRCA1 carriers with breast cancer

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Women with breast cancer and a BRCA1 or BRCA2 mutation face high risks of contralateral breast cancer, and many opt for bilateral mastectomy. We used a simulation approach to predict the benefit of risk-reducing mastectomy (RRM) on 20-year survival.

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Reports regarding the impact of risk-reducing mastectomy (RRM) on breast cancer-specific mortality in breast cancer patients who carry a *BRCA1* mutation are conflicting [1]. Some studies have shown the benefit of RRM on mortality to be approach 50% [2]. To help resolve the uncertainty, we sought to estimate the expected benefit of RRM by simulating two cohorts of young women diagnosed with breast cancer who carried a *BRCA1* mutation. For this simulated analysis we assumed that; 1) the annual breast cancer mortality rate in women without an RRM was 2% per year [3]; 2) the annual risk of contralateral breast cancer in women with an intact contralateral breast was 2% per year [4, 5]; 3) after a contralateral breast cancer, the breast cancer-specific mortality rate increased from 2% per year to 4% per year; 4) RRM was 100% effective at preventing contralateral breast cancer. We simulated cohorts of 100,000 women each, with and without an RRM, and counted the number of deaths from breast cancer at 20 years in each cohort. In the first simulated cohort (no RRM), there were 27,833 incident cases of contralateral cancer and 37,410 deaths from breast cancer. In the second simulated cohort (RRM), there were no incident cases of contralateral cancer and 33,144 deaths from breast cancer. The hazard ratio associated with RRM (versus no RRM) was 0.87. This estimate is based on the premise that RRM prevents death from breast cancer in genetically predisposed women. In a recent article, we saw no overall survival benefit associated with bilateral mastectomy in a SEER-based analysis of breast cancer patients in the general (non-carrier) population [6]. The risk of death increased after a contralateral cancer, but preventing contralateral cancer through bilateral mastectomy did not reduce mortality.

A recent article by Blondeaux et al. estimated the (adjusted) hazard ratio for breast cancer mortality for women who underwent an RRM after breast cancer treatment—compared to those who did not—to be 0.65 [7]. This relative reduction of 35% is far greater than what we saw in our simulated analysis. It is unfortunate that the authors do not provide the number of

contralateral breast cancers experienced in the women in their study, with and without an RRM, nor did they list the causes of death. We were also surprised that they adjusted for distant recurrence, as this event lies on the causal pathway between cancer incidence and cancer death, and this adjustment may lead to a biased hazard ratio—women who experience a distant recurrence in the follow-up period are less likely to undergo a subsequent RRM. It is important that further studies be conducted in the carrier population to bring clarity to this issue in order to properly inform women who are newly diagnosed with breast cancer regarding the utility of genetic testing and how this might influence their treatment decisions.

DATA AVAILABILITY

No datasets were generated or analysed during the current study.

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AUTHOR CONTRIBUTIONS

All authors reviewed the manuscript. SN and VG wrote the main manuscript text.

COMPETING INTERESTS

The authors declare no competing interest.

ADDITIONAL INFORMATION

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