The risk of contralateral breast cancer in patients from BRCA1/2 negative high risk families as compared to patients from BRCA1 or BRCA2 positive families: a retrospective cohort study.

While it has been reported that the risk of contralateral breast cancer in patients from BRCA1 or BRCA2 positive families is elevated, little is known about contralateral breast cancer risk in patients from high risk families that tested negative for BRCA1/2 mutations. A retrospective, multicenter cohort study was performed from 1996 to 2011 and comprised 6,235 women with unilateral breast cancer from 6,230 high risk families that had tested positive for BRCA1 (n = 1,154) or BRCA2 (n = 575) mutations or tested negative (n = 4,501). Cumulative contralateral breast cancer risks were calculated using the Kaplan-Meier product-limit method and were compared between groups using the log-rank test. Cox regression analysis was applied to assess the impact of the age at first breast cancer and the familial history stratified by mutation status. The cumulative risk of contralateral breast cancer 25 years after first breast cancer was 44.1% (95%CI, 37.6% to 50.6%) for patients from BRCA1 positive families, 33.5% (95%CI, 22.4% to 44.7%) for patients from BRCA2 positive families and 17.2% (95%CI, 14.5% to 19.9%) for patients from families that tested negative for BRCA1/2 mutations.
Younger age at first breast cancer was associated with a higher risk of contralateral breast cancer. For women who had their first breast cancer before the age of 40 years, the cumulative risk of contralateral breast cancer after 25 years was 55.1% for BRCA1, 38.4% for BRCA2, and 28.4% for patients from BRCA1/2 negative families. If the first breast cancer was diagnosed at the age of 50 or later, 25-year cumulative risks were 21.6% for BRCA1, 15.5% for BRCA2, and 12.9% for BRCA1/2 negative families. Contralateral breast cancer risk in patients from high risk families that tested negative for BRCA1/2 mutations is similar to the risk in patients with sporadic breast cancer. Thus, the mutation status should guide decision making for contralateral mastectomy.