

New insights into the risk of breast cancer in childhood cancer survivors treated with chest radiation: A report from the Childhood Cancer Survivor Study (CCSS) and the Women's Environmental Cancer and Radiation Epidemiology (WECARE) Study.

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Background: The risk of breast cancer (BC) by age 50 among women treated for childhood cancer with chest radiation therapy (RT) and how this risk compares with that of *BRCA1* and *BRCA2* (*BRCA1/2*) mutation carriers is unknown.

Methods: We evaluated the risk of BC in a cohort of 1268 female 5-yr childhood cancer survivors treated with chest RT and estimated the cumulative incidence of BC non-parametrically treating death as a competing risk. The cumulative incidence of BC in *BRCA1/2* mutation carriers was estimated with the kin-cohort method using data from 4570 female first-degree relatives of women diagnosed with unilateral BC (probands) participating in the WECARE Study. Absolute Excess Risks (AERs) were estimated using population-based data from the SEER program.

Results: With a median follow-up of 26 yrs (range 5-39) for the CCSS cohort, 175 women were diagnosed with BC at a median age of 38 yrs (range 24-53) and a median latency of 23 yrs (range 7-38); the overall cumulative incidence of BC by age 50 was 24% (95% confidence interval [CI] 20-28%) and among Hodgkin lymphoma survivors was 30% (95% CI 25-35%). In comparison, among first-degree relatives of WECARE Study probands 324 were diagnosed with BC (median age at diagnosis, 55 yrs (range 26-90)). The estimated cumulative incidence by age 50 was 31% (95% CI 16-47%) and 10% (95% CI 2-23%) in carriers of *BRCA1* and *BRCA2* mutations, respectively. The population cumulative incidence of BC is 4% by age 50. Among the childhood cancer survivors, AERs for BCs diagnosed per 10,000 person-years of observation were respectively 34 (95% CI 18-52), 27 (95% CI 11-45), and 95 (95% CI 78-112) among women treated with 10-19 Gy (23%), 20-29 Gy (17%), and 30+ Gy (56%) of chest RT.

Conclusions: Women treated for childhood cancer with chest RT have a substantial risk of BC comparable to *BRCA1/2* mutation carriers and considerably greater than that of the general population. Women treated with 10-19 Gy RT had an increased excess risk warranting consideration of breast cancer surveillance strategies similar to the current recommendations for women treated with ≥ 20 Gy.

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