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.


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.

Corresponding Author: Chaya S. Moskowitz, PhD, Department of Epidemiology and Biostatistics, Memorial Sloan-Kettering Cancer Center, 307 East 63rd St, New York, NY, 10065 Phone: 646-735-8117; FAX: 646-735-0010; email: moskowc1@mskcc.org