Mortality following breast cancer in survivors of childhood cancer: A report from the Childhood Cancer Survivor Study

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Background: Female childhood cancer survivors have a high risk of subsequent breast cancer (BC). Little is known about mortality following BC in this population.

Methods: Risk of all-cause and BC-specific mortality were estimated in 274 5-year survivors of childhood cancer diagnosed with invasive (71% ER+) or in situ BC. Median age at first BC diagnosis was 38 years (range 20-58); median follow-up after BC was 8 years (range 0-26), 195 (71%) were treated with chest radiation (RT) for their primary cancer. Hazard ratios (HRs) were estimated from cause-specific proportional hazards frailty models comparing mortality with a population-based control group with BC selected in a 1:5 ratio from SEER matched on sex, race, stage, age and calendar year of BC diagnosis (69% ER+). Cumulative incidence was estimated accounting for competing risks.

Results: 92 childhood cancer survivors died, 49 from BC. Risk of death from any cause after a BC diagnosis was higher among childhood cancer survivors compared to controls (HR=2.2, 95% CI 1.7-3.0) and remained elevated after adjusting for BC treatment with RT (HR=2.2, 95% CI 1.7-3.1), chemotherapy (HR=2.3, 95% CI 1.8-3.2), or both (HR=2.4, 95% CI 1.7-3.2). Risk of death after diagnosis with early stage BC was elevated compared to controls (Stage 0, 1 & 2, n=200, HR=2.6, 95% CI 1.9-3.7) but BC-specific mortality was not significantly higher among survivors (HR=1.4, 95% CI 0.9-2.0). Ten-year cumulative incidence of all-cause mortality was 33% (95% CI 27-40%) among survivors and 16% among controls (95% CI 14-18%); for BC-specific mortality it was 20% (95% CI 15-25%) and 13% (95% CI 11-16%) and for deaths from other causes was 13% (95% CI 9-19%) and 3% (95% CI 2-4%), respectively. Other causes of deaths among childhood cancer survivors with BC included other subsequent neoplasms (44%) and cardiovascular disease (26%).

Conclusions: Mortality after BC is high in childhood cancer survivors compared to women with BC in the general population, even in the setting of early stage disease. Future research should determine if this increased mortality reflects co-morbidity, limited therapeutic options and/or missed opportunities for risk-reducing interventions at the time of BC diagnosis.