

Risk of subsequent breast cancer after radiotherapy according to hormone-receptor status: a nested case-control study in the Childhood Cancer Survivor Study (CCSS)

Background: Survivors of childhood cancer have a high absolute risk of subsequent breast cancer after chest-directed radiotherapy; however, it is not known if this risk differs by hormone-receptor status and radiation to the ovaries.

Methods: We conducted a nested case-control study within the CCSS of 282 five-year survivors of childhood cancer with subsequent breast cancer and 1202 matched controls. Radiation dose to the location of the breast tumor (or corresponding location for controls) and mean dose to the ovaries were estimated from treatment records for each patient. Risk of radiation-related breast cancer was measured with the Excess Odds Ratio per Gray (EOR/Gy) and corresponding 95% confidence interval (CI), derived from conditional logistic regression.

Results: The median age at subsequent breast cancer diagnosis was 39 years (range 21-58). Although 87% of cases and 70% of controls received radiotherapy, breast doses were higher in cases than controls (61% vs 24% breast dose >10Gy), whereas ovarian doses were lower (7% vs 13% ovary dose >5Gy). In the subset of cases (n=159) with currently available estrogen receptor (ER) status (76% cases ER+, 24% cases ER-), there was a linear dose-response relation with radiation dose to the breast that was similar for ER+ (EOR/Gy=0.51; 95%CI: 0.19-1.34) and ER- breast tumors (EOR/Gy=0.41; 95%CI: 0.05-2.88). If the patient received an ovarian dose >5Gy, this dose-response was significantly reduced for ER+ tumors but not for ER- tumors.

Conclusions: Preliminary analyses demonstrate that radiation exposure to the breast to treat childhood cancer results in an increased risk of both ER+ and ER- breast cancers. The novel finding that only the risk of ER+ breast cancer is lowered if the ovaries are also exposed is consistent with known differences by hormone receptor status in the biological mechanisms of breast carcinogenesis.

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