

Subsequent neoplasms in the 5th and 6th decades of life in the childhood cancer survivor study cohort.

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Background: The risk of subsequent neoplasms (SN) in childhood cancer survivors increases over time, but only limited data exist on risk beyond 40 years of age. **Methods:** Occurrence of SN was evaluated in 3171 5-year adult survivors of childhood cancer ≥ 40 years of age (median 44 years, range 40-58) following cancer diagnosed < 21 years of age, between 1970-1986. Cumulative incidence and standardized incidence ratio (SIR), with corresponding 95% confidence intervals (CI) were used to evaluate risk of SN and subsequent invasive malignant neoplasm (SMN), respectively. SIR were calculated using age-, sex- and calendar year-specific incidence from the NCI Surveillance, Epidemiology and End Results program. Survivors with a history of SN prior to age 40 (SN_{pos}) were also compared to those without previous SN (SN_{neg}). **Results:** A total of 371 SN were diagnosed ≥ 40 years of age, including 136 SMN (SIR=2.2, CI 1.9-2.5), 191 non-melanoma skin cancers (NMSC), and 44 meningiomas and other non-invasive neoplasms. Cumulative incidence of a new SN after age 40 was 34.6% (CI 28.7-40.6) at age 55, with SN_{pos} having a higher incidence compared to SN_{neg} 57.6% (CI 46.7-68.6) versus 30.4% (CI 23.8-37). While cumulative incidence of new SMN at age 55 was similar for SN_{neg} and SN_{pos} (15.4% (CI 10.2-20.5) vs. 20.8% (CI 12.5-29.1)), SN_{pos} experienced more NMSC compared to SN_{neg} (cumulative incidence 16.2% (CI 10.8-21.6) vs. 38.2% (CI 27.9-48.5)). Compared to the U.S. population, risk of a SMN was elevated for both SN_{neg} and SN_{pos} (SIR=2.0, CI 1.7-2.4 vs. SIR=3.0, CI 2.2-4.0). Breast cancer was the most common SMN beyond age 40, and also carried the largest risk (SIR=5.5, CI 4.5-6.7). Significantly elevated risks were also seen for renal cancer (SIR=3.9, CI 2.0-7.5), soft tissue sarcoma (SIR=2.6, CI 1.5-4.4) and thyroid carcinoma (SIR=1.9, CI 1.0-3.5). Hodgkin lymphoma (SIR=3.6, CI 3.0-4.4) and radiation therapy (SIR=2.6, CI 2.2-3.1) were associated with high risk of SMN although the magnitude of risk for SN_{neg} and SN_{pos} did not differ substantially. **Conclusions:** Risk of SN remains significantly elevated after age 40. These data have important implications for screening and should inform anticipatory guidance provided to childhood cancer survivors.