Identification of childhood cancer survivors at highest risk of developing subsequent thyroid cancer: A report from the Childhood Cancer Survivor Study

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Abstract

Background/Purpose

Prior treatment with radiotherapy is a well-established risk factor for the increased risk of subsequent thyroid cancer (STC) observed among childhood cancer survivors. Current thyroid cancer screening guidelines for survivors are primarily based on radiotherapy exposure, while the role of other factors and their potential joint effects with radiotherapy on STC risk remain poorly understood. Using data from the Childhood Cancer Survivor Study (CCSS), we aimed to elucidate the interplay among potential STC risk factors and identify survivors at the highest risk of developing STC to inform potential further risk-stratification of the current thyroid cancer screening guidelines for childhood cancer survivors.

Methods

The study included 20,590 five-year survivors diagnosed with a first primary cancer between 1970-1999 at ages <21 years and with complete information about chemotherapy and thyroid radiation dose. Mean dose to the left and right lobes of the thyroid was estimated based on radiotherapy records. We estimated relative risks (RRs) and 95% confidence intervals (CIs) using Poisson regression models adjusting for sex, attained age, thyroid radiation dose, and age at exposure, overall and stratified by thyroid radiation dose (no or <5 Gy versus ≥5 Gy). We then calculated cumulative STC risks stratified by risk factor, accounting for competing risk of death.

Results

During a median follow-up of 26.7 years (interquartile range (IQR) 21.1-34.7) since primary cancer diagnosis, 334 survivors developed an STC. Survivors who received ≥5 Gy of radiation to the thyroid (versus none) had a five-fold or greater increase in STC risk with the highest risks at 10-<20 Gy (RR 11.4, 95% CI 8.0-16.3), particularly among those exposed before age 10 (RR 15.6, 95% CI 9.6-25.3). In analyses stratified by thyroid radiation dose, female sex was consistently associated with increased STC risk compared to males ($RR_{no/<5Gy}$ 2.6, 95% CI 1.7-3.8; $RR_{\geq 5Gy}$ 1.5, 95% CI 1.1-1.9). Receipt of chemotherapy was associated with STC only among survivors with no thyroid radiation or <5 Gy (RR 2.3, 95% CI 1.5-3.5). No clear dose-response associations emerged for any of the chemotherapeutic classes. At age 50, the highest cumulative incidence of STC was observed for female survivors exposed to ≥5 Gy thyroid radiation at age <10 years (8.1%, 95% CI 0.0%-19.1%; Figure) and ≥10 years (7.7%, 95% CI 4.8%-10.6%), followed by males exposed to ≥5 Gy thyroid radiation at age <10 years (6.3%, 95% CI 3.8%-8.8%) and ≥10 years (4.9%, 95% CI 2.3%-7.4%). Among survivors with no thyroid radiation or <5 Gy, cumulative incidence of STC was <5.0% at age 50 years for females and males, regardless of chemotherapy exposure.

Conclusions

Beyond thyroid radiation exposure, sex and age at treatment exposure could be valuable factors for consideration in risk-stratified screening guidelines to optimize the long-term clinical care of childhood cancer survivors.

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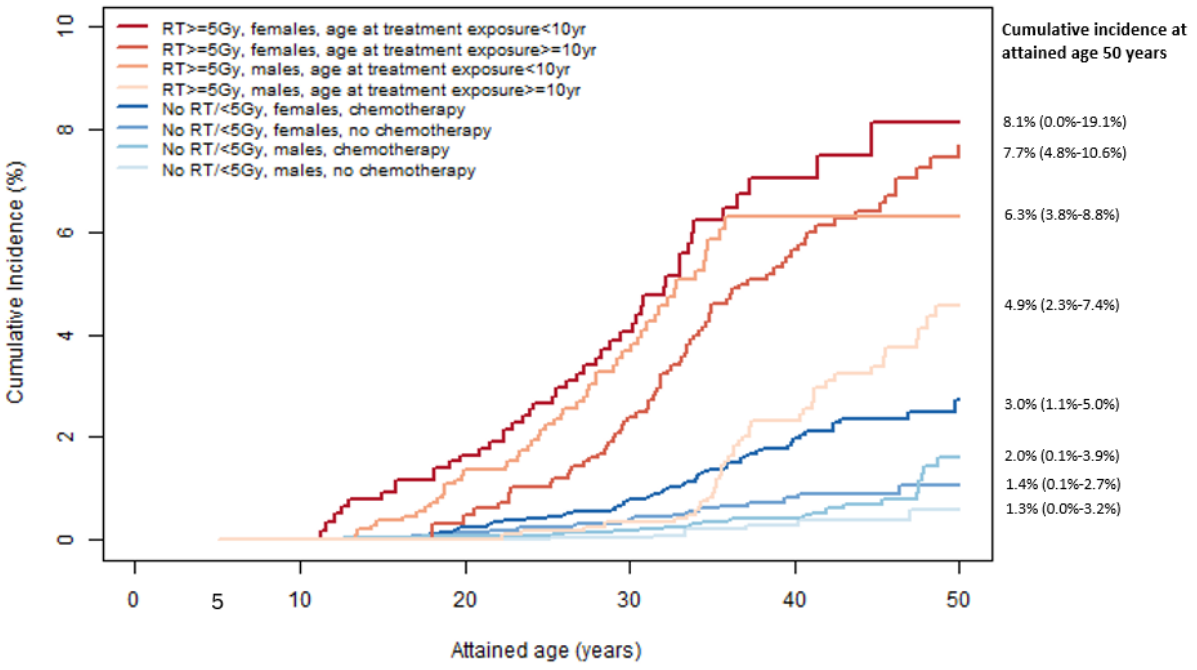

No. at risk at attained age	20 years	30 years	40 years	50 years
RT>=5Gy, females, age at treatment exposure<10yr	673	454	197	53
RT>=5Gy, females, age at treatment exposure≥10yr	581	1,083	716	321
RT>=5Gy, males, age at treatment exposure<10yr	945	588	222	72
RT>=5Gy, males, age at treatment exposure≥10yr	653	1,121	692	296
No RT/<5Gy, females, chemotherapy	3,608	3,053	1,466	405
No RT/<5Gy, females, no chemotherapy	2,649	2,122	1,094	334
No RT/<5Gy, males, chemotherapy	4,019	3,385	1,632	471
No RT/<5Gy, males, no chemotherapy	2,513	1,952	973	292