Abstract

ASCO annual meeting
May 31-June 4, 2019

Title: Frailty among childhood cancer survivors: A report from the Childhood Cancer Survivor Study (CCSS)

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Abstract

Background: Childhood cancer survivors are at increased risk for frailty, which is a loss of physiological capacity that is typically observed among older adults.

Aims: Estimate the prevalence of frailty among survivors, and examine direct and indirect effects of treatment, lifestyle, and chronic disease factors on frailty.

Methods: CCSS participants who were > 5-year survivors of childhood cancer, diagnosed between 1970-1999 at <21 years of age (n=10,899, 48% male), and siblings (n=2,097, 42% male) were included. Frailty was defined from self-reported data at mean ages of 37.6±9.4 and 42.9±9.8 years for survivors and siblings, respectively, as ≥3 of the following: low lean mass, exhaustion, low energy expenditure, slow walking, and weakness.

Results:

The prevalence of frailty among survivors was higher compared to siblings (5.8%, 95% CI: 5.4-6.3% vs. 1.9%, 95% CI 1.4-2.5%). Prevalence was highest in survivors of CNS tumors (9.5%, 5.2-13.8%), bone sarcomas (8.1%, 5.1-11.1%) and Hodgkin lymphoma (7.5%, 4.9-10.1%). In models adjusted for sex, age at assessment, and race/ethnicity, treatment exposures were associated with frailty (Table). After adjusting for the presence of chronic diseases and lifestyle factors, these associations were attenuated.

Table 1: Direct and indirect effects of treatment on frailty (n=681)

	Adjusted for Demographics		**Adjusted for Demographics, Chronic Disease and Lifestyle**	
	PRR[1]	**(95%CI)**	**PRR[2]**	**(95%CI)**
Cranial radiation	1.44	(1.32-1.58)	1.21	(1.10-1.33)
Abdominal radiation dose >40 Gy	1.38	(0.98-1.96)	1.15	(0.80-1.64)
Pelvic radiation dose ≥34 Gy	1.46	(1.20-1.80)	1.39	(1.13-1.71)

Cisplatin dose ≥600 mg/m²	1.51	(1.07-2.12)	1.24	(0.88-1.75)
Amputation	1.36	(1.13-1.63)	1.17	(0.92-1.47)
Thoracotomy	1.47	(1.26-1.73)	1.35	(1.14-1.58)

[1]Adjusted for sex, race and age at assessment. [2]Adjusted for sex, race, age at assessment, CTCAE graded 3-4 chronic diseases, smoking, physical activity and obesity.

Conclusions: The prevalence of frailty among survivors (6.0% at 38 years of age) was similar to the general population aged ≥65 years (9.0%). Radiation, platinum, amputation and thoracotomy increased risk for frailty. Findings suggest interventions to prevent, delay onset, or remediate chronic disease and/or promote healthy lifestyle are needed to preserve function in this population.