3000 characters including spaces, one table or graphic

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Accelerated Aging among Long-Term Survivors of Childhood Cancer: A Report from the Childhood Cancer Survivor Study (CCSS)

Background: Cross-sectional studies have suggested childhood cancer survivors demonstrate a pattern of functional limitations and morbidity consistent with premature aging, but cannot confirm if aging is accelerated relative to peers without cancer. We used longitudinal data to characterize aging using a Deficit Accumulation Index (DAI) which examines the accumulation of multiple aging-related deficits.

Methods: We included 5+ year survivors of childhood cancer (N=21,856; at entry mean age 26.7 [SD 6.1], 18.7 [4.7] years post diagnosis) and siblings (N=4,628, mean age 29.1 [7.1]) from the CCSS, a longitudinal prospective cohort study. Participants completed questionnaires at up to five timepoints (mean [SD] follow-up 9.5[8.9] years), with DAI scores generated as the proportion of deficits out of 30 items related to aging, including chronic conditions (e.g. hearing loss, hypertension), psychosocial and physical function, and activities of daily living. The total score range is 0 to 1; and a moderate clinically meaningful difference is 0.02. As survivors completed multiple surveys at varying intervals, attained age was used as the time scale. Linear mixed models with random subject-specific intercept and age slope compared DAI in survivors to siblings with an attained age x survivor/sibling interaction term to determine if DAI was increasing faster in survivors, adjusted for the first DAI score, age at first DAI and sex. Similar models examined DAI changes associated with treatments among survivors.

Results: Across all time points, the adjusted mean [95%CI] DAI was 0.195[0.195, 0.196] for survivors and 0.180[0.178,0.182] for siblings ($p<0.001$). Survivors experienced more rapid increase in DAI over time compared to siblings ($p<0.001$). For example, at age 20 there was no difference in DAI between survivors and siblings, however the mean difference [95%CI] in DAI between survivors and siblings steadily increased with age to 0.008[0.006, 0.010] at 30 years, 0.021[0.019, 0.024] at 40 years, 0.040[0.037, 0.044] at 50 years, 0.064[0.058, 0.071] at 60 years, and 0.093[0.082, 0.105] at 70 years; all p's<0.001 (Figure). Survivors who received abdominal, cranial, or chest radiation experienced more rapid increase in DAI over time compared to those who did not (p's<0.001). Survivors who received platinum agents also experienced a more rapid increase in DAI over time (p's<0.001).

Conclusions: Our data confirm survivors of childhood cancer experience significant age acceleration relative to peers. Given the ease of measuring DAI using self-reported data, this tool may be used to routinely monitor survivors and identify those at risk for adverse aging-related outcomes so that we may intervene and mitigate their accelerated aging trajectory.

Figure: Mean Deficit Accumulation Index (DAI) and 95%CI for survivors (Blue) and Siblings (Black) at each time point.