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Accelerated aging among survivors of childhood leukemia and lymphoma: Estimates of early onset and excess morbidity from the COMPASS model

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Background: Cohort studies have detected an increased risk of accelerated aging among survivors of childhood cancer but the timing and magnitude are not known.

Methods: To predict the clinical course of diseases of aging— cancer and cardiovascular disease — among survivors of childhood leukemia and lymphoma compared to the general population, we developed the Cancer Outcomes Microsimulation: Pediatric and Adolescent SurvivorShip (COMPASS) model. The model simulates 8 severe, disabling or life-threatening chronic health conditions (CHCs), including 4 subsequent cancers (breast, colorectal, glial tumors, sarcomas) and 4 cardiovascular diseases (heart failure, myocardial infarction/coronary artery disease, valvular disease, stroke), and excess mortality risks among survivors diagnosed between 1970 and 1999 over the course of their lifetimes. Treatment-related risks varied by patient characteristics (sex, age at diagnosis, diagnosis) and treatment exposures (chemotherapy, radiation dose) and were based on data from the Childhood Cancer Survivor Study (CCSS). Age-related risks and competing mortality were based on national databases (SEER, NHLBI, CDC Wonder). We used model calibration to identify parameter sets that generated outcomes consistent with observed data. Model outcomes included cumulative CHC risk. For comparisons to the general population, age-, sex, and diagnosis year-matched individuals who faced only age-related risks were simulated.

Results: Among survivors representative of CCSS participants, the model estimated that 45% of leukemia and 65% of lymphoma survivors will develop at least 1 of the 8 CHCs by age 65. Compared to the estimated 20% cumulative risk for the general population, this represented a two- to three-fold excess morbidity risk among survivors. The age at which 20% of survivors developed at least 1 CHC was 51 years for leukemia and 42 years for lymphoma, suggesting an early onset of 14 and 21 years compared to the general population. Outcomes varied by diagnosis and treatment era due to competing risk changes. Among leukemia survivors diagnosed in the 1990s vs. 1970s, cumulative late recurrence mortality by age 40 (11% to 1%) declined. This combined with a reduction in radiation exposure (79% to 24%) resulted in a greater proportion living into adulthood and developing CHCs by age 65 (38% to 48%). In contrast, among lymphoma survivors, the proportion projected to develop a CHC by age 65 remained stable during the same period (62% to 65%) as late recurrence mortality risk declined (8% to 1%), but almost half still received radiation (90% to 49%).

Conclusions: Despite improvements in therapy, leukemia and lymphoma survivors are projected to experience CHC early onset and excess morbidity, underscoring the importance of prevention-focused survivorship care and continued efforts to develop more targeted therapies.