Risks of mortality in 5 year survivors of Hodgkin's Lymphoma (HL) in the Childhood Cancer Survivor Study (CCSS).


[Abstract]

Background: Paradoxically, HL is the paradigm of treatment success, yet HL survivors are at an increased risk of premature death. We aimed to characterize risks factors associated with mortality in a cohort of HL survivors treated in childhood. Methods: The CCSS tracks long-term outcomes in childhood cancer survivors diagnosed between 1970 and 1986. This analysis explored the impact of treatment, recurrence, second malignancies, and potential adverse treatment effects on overall survival following HL. Hazard ratios (HR) and 95% confidence intervals (CI) were calculated from Cox proportional hazards models. Results: The CCSS includes 1,927 HL survivors followed for a median of 23 years; the median age at diagnosis is 14 years and 54% are male. There have been 320 deaths at median of 31 yrs of age; 30% are due to recurrence, 26% to second malignancy, and 19% to cardiovascular events. Because treatment patterns and causes of death varied by sex, we analyzed males and females separately in models adjusted for host demographics. Overall mortality is associated with supra- and infra-diaphragmatic radiotherapy (RT) at higher doses (>30Gy) in males (versus chemotherapy only: HR=2.7, CI=1.1-6.9), and all doses in females (versus chemotherapy only, <30Gy: HR=6.9, CI=1.4-33.5; >30Gy: HR=5.2, CI=1.2-22.0). Chemotherapy regimens including anthracycline significantly impact survival in males (versus radiotherapy only: HR=3.2, CI=1.8-5.6). Second malignancies decreased survival, with a stronger effect in males (HR=6.9, CI=4.0-11.7) than females (HR=5.4, CI=3.3-8.6). Grade 3-4 cardiovascular condition was also associated with mortality (males: HR= 2.5, CI=1.3-4.7; females: HR=2.1, CI=1.0-4.4). Conclusions: Childhood HL survivors who received anthracycline therapy and higher dose, extended field RT experience increased risk for premature death long after their therapy ends. The impact of treatment on mortality varies based on host sex.