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Reduction in Cardiac Events for Survivors of Childhood Cancer Treated in More Recent Eras: A Report from the Childhood Cancer Survivor Study

Background: Contemporary cancer protocols have incorporated modifications to minimize cardiotoxic exposures and preserve long-term health. We investigated the impact of these changes on late cardiac outcomes in a large cohort of adult survivors of childhood cancer.

Methods: Congestive heart failure (CHF), myocardial infarction (MI), valvular disease, pericardial disease, and arrhythmias were graded by the National Cancer Institute's Common Terminology Criteria for Adverse Events among 23,462 five-year cancer survivors [6,193 (26%) treated in the 1970s, 9,363 (40%) in the 1980s, and 7,906 (34%) in the 1990s] and 5,057 siblings. Cumulative incidence and 95% confidence intervals (95% CI) were estimated by treatment decade. Adjusted multivariable subdistribution hazard models were used to estimate hazard ratios (HR) and 95% CI for cardiac outcomes by decade. Mediation analysis examined risks with and without cardiotoxic exposures.

Results: For survivors [median age 6 years (range: 0-21) at diagnosis, 28 years (8.2-58) at follow-up], cardiac radiation (RT) exposure declined from 77% of those treated in the 1970s to 55% and 40% in the 1980s and 1990s. Anthracycline exposure increased from 28% to 50% to 64%. The 20-year cumulative incidence of CHF (0.69% for those treated in 1970s, 0.74% in the 1980s, 0.54% in the 1990s) and MI (0.38%, 0.24%, 0.19%) declined in more recent treatment eras ($p < 0.01$). This change was not seen for valvular disease (0.06%, 0.06%, 0.05%), pericardial disease (0.04%, 0.02%, 0.03%) or arrhythmias (0.08%, 0.09%, 0.13%). Compared to survivors diagnosed in the 1970s, the risk of CHF, MI, and valvular disease decreased in the 1980s and 1990s, but only significantly for MI (HR 0.64 95% CI 0.47-0.89 and 0.52 95% CI 0.32-0.83). The overall MI risk was attenuated by adjustment for cardiac RT exposure (HR 0.94 95% CI 0.80-1.11), mostly among Hodgkin lymphoma (HL) survivors (HR 0.82 95% CI 0.69-0.98 [unadjusted for RT]; 1.03 95% CI 0.83-1.28 [adjusted for RT]).

Conclusions: Reductions in exposure to cardiotoxic cancer therapies have resulted in declines in adverse cardiac outcomes, particularly for the RT-associated risk of myocardial infarction among HL survivors.