

**Cardiovascular Disease in Adult Survivors of Childhood and Adolescent Cancer: A Report from the Childhood Cancer Survivor Study (CCSS)** Daniel A. Mulrooney, M.D., M.S., Mark Yeazel, M.D., M.P.H., Pauline Mitby, M.S. Toana Kawashima, M.S., Wendy M Leisenring, Ph.D., Marilyn Stovall, Ph.D., Daniel M. Green, M.D., Charles A. Sklar, M.D., Leslie L. Robison, Ph.D., Ann C. Mertens, Ph.D.; University of Minnesota, Minneapolis, MN; Fred Hutchinson Cancer Research Center, Seattle, WA; University of Texas MD Anderson Cancer Center, Houston, TX; Roswell Park Cancer Inst., Buffalo, NY; Memorial Sloan-Kettering Cancer Center, New York, NY; St. Jude Children's Research Hospital, Memphis, TN; Emory University, Atlanta, GA

**Background:** Previous research has shown that cardiovascular disease contributes to significant morbidity and mortality among survivors of childhood and adolescent cancer. Few studies have reported risk factors in long-term survivors who are now adults.

**Methods:** This analysis includes 14,358 five-yr cancer survivors of the CCSS diagnosed  $\leq$  age 21, between 1970-1986, with one of eight childhood cancers [leukemia, CNS tumors, Hodgkin's (HD) or non-Hodgkin's lymphomas (NHL), renal tumors, neuroblastoma, soft-tissue sarcomas (STS), bone cancers]. Self-reported cardiac outcomes occurring at least 5-yrs post-dx are compared to a sibling control group (N=3899) and across treatment groups using Cox proportional hazards models to estimate relative risks (RR) adjusted for age, gender, race, sociodemographic factors, and smoking status.

**Results:** Survivors (54% males) were on average 7.8 yrs (0-20) at diagnosis, and 27.5 yrs (8-51) at follow-up. Compared to siblings, survivors were more likely to report congestive heart failure (CHF) (RR 5.7 95% CI 3.4-9.6), myocardial infarction (MI) (RR 4.9 95% CI 2.3-10.4), atherosclerosis (RR 10.2 95% CI 3.7-28.3), pericardial (RR 6.3 95% CI 3.3-11.9) and valvular disease (RR 4.8 95% CI 3.0-7.6), and coronary angiography (RR 8.2 95% CI 4.2-16.1). Anthracycline exposure  $\geq$  250 mg/m<sup>2</sup> increased the risk of reported CHF (RR 4.1 95% CI 3.0-5.6), pericardial (RR 1.9 95% CI 1.3-2.9) and valvular disease (RR 1.8 95% CI 1.3-2.5), and angiography (RR 2.6 95% CI 1.8-3.7) compared to unexposed survivors. Radiation (RT) to the heart also increased the risk of CHF (RR 2.0 95% CI 1.4-2.8), MI (RR 1.9 95% CI 1.1-3.2), atherosclerosis (RR 5.3 95% CI 2.5-11.0), pericardial (RR 2.2 95% CI 1.4-3.3) and valvular disease (RR 2.8 95% CI 1.9-4.0), and angiography (RR 2.2 95% CI 1.5-3.2) compared to those survivors without cardiac directed RT.

**Conclusion:** The occurrence of premature cardiovascular diseases is substantial in this young adult population of cancer survivors.