

## **Impact of Traditional Cardiovascular Disease Risk Factors on Long-term Cardiovascular Outcomes in Adult Survivors of Childhood Cancer: A Report from the Childhood Cancer Survivor Study**

**Background:** Childhood cancer survivors have an increased risk of late-onset treatment-related cardiotoxicity. How traditional cardiovascular disease risk factors (CVRFs) modify this risk is unknown.

**Methods:** Analyses included 14,358  $\geq 5$  yr survivors of childhood cancer diagnosed 1970-86 (median age at last follow-up 31.9 yrs, range 5.6-58.9). Rates of obesity (BMI $\geq 30$ ), CVRFs requiring medical treatment (diabetes, hypertension, dyslipidemia) and cardiac outcomes (coronary artery disease, congestive heart failure, valvular abnormality, stroke and arrhythmia) were collected at baseline and subsequent follow-up questionnaires and compared to a sibling cohort (n=4,023). Associations between CVRFs and cardiac outcomes and the predictive ability of CVRFs for future cardiac events were assessed.

**Results:** Survivors reported higher rates of diabetes (3.7% vs. 2.5%, OR= 1.7, 95% CI 1.4-2.1), hypertension (15.1% vs. 9.7%, OR= 2.1, 95% CI 1.9-2.4), dyslipidemia (8.2% vs. 5.7%, OR= 1.9, 95% CI 1.7-2.3), but not obesity (24.3% vs. 25.4%, OR= 1.0, 95% CI 0.9-1.1), and a higher rate of clustering of CVDRFs (any 3 of 4 CRFs, 2.5% vs. 1.9%, OR= 1.7, 95% CI 1.3-2.2) compared to siblings. Cumulative incidence (CI) at 45 years of age for coronary artery disease, congestive heart failure, valvular abnormality, stroke and arrhythmia was 4.2%, 6.7%, 6.2%, 2.5%, and 11.7%, respectively. The 45-yr CI for cardiac-related mortality was 1.6% (95% CI 1.2-1.9; standardized mortality ratio = 4.4, 95% CI 3.6-5.3). Presence of a CVRF cluster was associated with an increased risk of congestive heart failure (RR= 4.2, 95% CI 2.6-6.7) among survivors treated with anthracyclines ( $>250\text{mg/m}^2$ ) and of coronary artery disease (RR= 4.6, 95% CI 3.0-7.0) among those who received chest-directed radiotherapy. Presence of hypertension (RR=2.2, 95% CI 1.6-3.1) and obesity (RR=1.3, 95% CI 1.1-1.6) were predictive of future cardiac events.

**Conclusion:** Among adult survivors of childhood cancer exposed to cardiotoxic therapy, presence of traditional cardiovascular disease risk factors further increase the risk for poor cardiovascular outcome.

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