

Individual risk prediction of major cardiovascular events after cancer: A childhood cancer survivor study report.

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Background: Childhood cancer survivors are at increased risk of cardiovascular (CV) events. Models that combine information on cancer treatment exposures and conventional CV risk factors to estimate an individual's probability of developing major CV events would be clinically important. **Methods:** Cohort study of 10,521 five-year survivors of childhood cancer diagnosed 1970-86, free of CV disease at initial baseline survey, and who were followed with longitudinal surveys. Poisson regression models estimated the risk of the developing severe, life-threatening, or fatal CV events: 1) congestive heart failure (CHF), 2) coronary heart disease (CHD), 3) stroke, and 4) any CV-related death. Models accounted for sex, age at cancer diagnosis, and select chemo- and radiotherapy exposures. Secondary models accounted for late relapse and second cancers occurring beyond 5 years, and the effect of conventional CV risk factors (current smoking, alcohol use, physical activity, obesity, and any treatment for hypertension, dyslipidemia, or diabetes). Model prediction and discrimination were assessed via area under the curve (AUC) and the concordance (C) index. **Results:** After a median follow-up period of 25.8 years (range 7.4-39.2) since cancer diagnosis, the cohort experienced 182 (1.7%) CHF, 186 (1.8%) CHD, 159 (1.5%) stroke, and 66 (0.6%) deaths related to CV events. Models based on primary cancer treatment exposures predicted CHF, CHD, stroke, and CV death risk at/through age 40 with AUC and C-statistics ranging from 0.71-0.77. Adjusting for late relapse/second cancers and conventional CV risk factors further improved prediction (AUC/C-statistics 0.73-0.78; improvement in model prediction, $p=0.01$ to 0.07). The predictive weights assigned to hypertension and diabetes were similar to those assigned to high-level anthracycline or chest radiotherapy exposures. **Conclusions:** The predictive models we generated offer the potential for individual risk assessment of serious CV diseases at/through age 40. Once validated in other cohorts, these models may become important clinical tools in helping care for long-term childhood cancer survivors.