

PREDICTING CARDIOVASCULAR DISEASE AFTER CANCER: A CHILDHOOD CANCER SURVIVOR STUDY REPORT

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Background: Various factors are associated with an increased risk of cardiovascular (CV) disease among childhood cancer survivors at the population level. Models that combine selected risk factors to estimate an individual's probability of developing such complications would be clinically important.

Methods: Cohort study of 14,138 childhood cancer survivors diagnosed 1970-1986, free of CV disease at cohort entry 5 yrs from cancer diagnosis, and followed through 2009. Poisson regression models estimated the risk of developing subsequent severe/life-threatening 1) congestive heart failure (CHF), 2) coronary heart disease (CHD), and 3) CV-related death, in association with sex, ethnicity, cancer diagnosis age, and select chemotherapy and radiotherapy exposures. Discrimination was assessed via the concordance (c) index.

Results: Over a median follow-up of 19 yrs (range 0-34), the cohort experienced 312 (2.2%) CHF, 285 (2.0%) CHD, and 132 (0.9%) CV-related deaths. The magnitude of associations with selected factors varied by outcome (Table), but included female sex (CHF), older diagnosis age (CHD, CV-related death), increased anthracyclines (CHF, CV-related death), increased chest radiotherapy (all outcomes), and any neck (CHF) or abdominal radiotherapy (CHD). Overall, models predicting CHF, CHD, and CV-related death risk at 30 yrs after cancer diagnosis had excellent discrimination (c index 0.81, 0.80, and 0.79, respectively). C indices of models based on the same factors for outcomes at 15 yrs varied only by 0.01.

Conclusions: Readily available clinical factors predicted individual risk of CHF, CHD, and CV-related death in childhood cancer survivors with good discrimination 30 yrs after diagnosis. If validated in other populations, this may lead to more personalized long-term surveillance and counseling of survivors.

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Presentation: oral preferred

Category(s): heart

Chow, et al. Cardiovascular disease prediction.

Predictive factors	Congestive heart failure		Coronary heart disease		Cardiovascular-related death	
	RR	95% CI	RR	95% CI	RR	95% CI
Female	1.6	1.3-2.1	0.8	0.6-1.0	0.8	0.6-1.2
Diagnosis age						
<5 (ref)						
5-9	1.0	0.7-1.5	2.2	1.4-3.7	1.2	0.6-2.5
10-14	1.0	0.7-1.4	2.5	1.6-4.2	1.7	0.9-3.2
≥15	1.1	0.8-1.6	5.1	3.2-8.2	2.4	1.3-4.6
Anthracycline*, mg/m ²						
None (ref)						
<100	1.7	0.6-4.8			0.7	0.1-5.3
100-299	3.5	2.4-5.1			1.8	1.0-3.2
≥300	8.3	6.1-11.3			3.0	1.8-4.9
Radiotherapy field						
Chest, Gy						
<1 (ref)						
1-9	0.8	0.5-1.4	1.0	0.5-1.8	1.1	0.5-2.7
10-19	1.8	1.1-3.0	1.7	0.9-3.5	2.0	0.7-5.8
20-34	1.7	1.0-2.7	2.8	1.8-4.4	2.8	1.3-5.8
≥35	3.9	2.5-6.1	5.1	3.5-7.5	8.8	5.2-14.7
Neck, any*	2.1	1.4-3.1				
Abdomen, any*			1.5	1.1 - 2.1		

*Only estimates meeting model selection criteria shown