The spectrum of cardiovascular disease (CVD) after early stage breast cancer (ESBC)

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Background: There are limited data on the incidence of heart failure (HF) relative to other forms of CVD after ESBC. The temporal relationship of HF to other types of CVD is also unclear.

Methods: We used the Ontario Cancer registry to identify 124,733 women diagnosed with ESBC between April 1 1998 and March 31 2015. Clinical data were obtained by linkage to administrative databases. Women were matched 1:3 on birth year to 374199 controls who were alive without cancer history on the index date. We identified all hospital presentations for CVD through available follow-up. Cumulative incidence function curves were used to estimate CVD incidence, with all-cause death treated as a competing risk. This was also done separately for HF, ischemic heart disease (IHD), cerebrovascular disease, and arrhythmias. Cause-specific regression models were used to compare the hazard of CVD between event-free women and age-matched controls. We tested the proportional hazards assumption for the ESBC indicator variable by allowing the natural logarithm of the HR to change linearly over time. The time-interaction term was significant, so HRs are presented at 1 and 5 years. Analyses were repeated after dividing the ESBC cohort based on chemotherapy receipt.

Results: Ten-year all-cause survival was 71% in the ESBC cohort and 80% in controls. At ten years, the cumulative incidence of CVD hospitalization was 11.7% after ESBC and 10.6% in controls. The cause-specific HR for ESBC relative to controls was 1.07 (95% CI 1.04-1.10) at 1 year and 1.17 (95% CI 1.02 - 1.34) at 5 years. The HR was higher in chemotherapy-treated women, but was also significantly elevated without chemotherapy. Patients were most commonly hospitalized for IHD (28% of hospitalizations), followed by HF (24%), cerebrovascular disease (18%) and arrhythmias (17%). Of 4,531 women with hospital presentation for HF, 36% had a prior hospital presentation with another CVD.

Conclusion: ESBC is associated with higher rates of CVD compared to age-matched controls. The HR increases with time from ESBC diagnosis. HF is often preceded by alternate forms of CVD. These data support the "multiple-hit hypothesis" for HF after cancer, and mandate more intensive screening and management of global CVD risk in survivors.
Figure: cumulative incidence of diagnoses responsible for the first cardiovascular hospitalization after early stage breast cancer