Comparing the impact of insufficient physical activity on cardiovascular disease in survivors of childhood Hodgkin lymphoma and sibling controls: a report from the Childhood Cancer Survivor Study (CCSS)

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Abstract text ASCO:

Background: Survivors of childhood Hodgkin lymphoma are at increased risk of cardiovascular disease (CVD) from anthracycline and radiation exposures. Whether the treatment-induced risk can be mitigated with physical activity is not known. We aimed to compare the impact of insufficient physical activity on CVD in Hodgkin lymphoma survivors and controls.

Methods: Participants in the Childhood Cancer Survivor Study (CCSS) reported physical activity, which was translated into metabolic equivalent of task hours/week (MET) and categorized as 0, 1-8, or ≥9 METs. We estimated rate ratios (RR) for new onset (incident) congestive heart failure and any CVD (including heart attack, congestive heart failure, arrhythmia, and valvular disease requiring interventions) during follow-up, accounting for age, sex, race/ethnicity, smoking, risky drinking, overweight/obesity, and treatment exposures (survivors only). Then we calculated population attributable fractions (PAF) for insufficient physical activity (<9 METs). The attributable relative rate (ARR) was calculated by multiplying the PAF in survivors with the RR for CVD incidence in survivors compared to controls, resulting in an ARR for survivors that was compared to the PAF in controls.

Results: In 2,357 Hodgkin survivors [50% female; [mean (SD)] 14.3 (4.1) years at diagnosis; 31.6 (5.8) years at start of follow-up, and 17.8 (7.6) years from diagnosis] and 3,949 sibling controls, 233 survivors and 19 controls developed congestive heart failure. 462 survivors and 95 controls developed any CVD. The PAF for congestive heart failure attributable to

insufficient physical activity was larger in controls (38.0%) than survivors (22.3%). However, with RR 20.3 (95% CI 12.6-32.5) for congestive heart failure for survivors compared to controls, the ARR in survivors (452.1%) revealed a 12 times higher incidence of congestive heart failure attributable to insufficient physical activity in Hodgkin survivors than in controls (452.1%/38.0%). The ARR indicates that 4.5 of the 20-fold higher risk of congestive heart failure in survivors vs. siblings is attributable to insufficient physical activity in the survivors. For any CVD, the PAFs were comparable in survivors (13.7%) and controls (11.7%). With RR 10.2 (95% CI 8.2-12.7) for any CVD for survivors compared to controls, the ARR for any CVD in survivors (139.7%) was also 12 times higher than the incidence attributable to insufficient physical activity in controls (139.7%/11.7%).

Conclusion: Our results suggest that the magnitude of treatment-induced CVD risk that can be mitigated by physical activity is considerable. This offers a modifiable target and provides rationale for exercise interventions aimed at reducing CVD in survivors at high risk.

Abstract text ISLCCC:

Background: Survivors of childhood Hodgkin lymphoma are at increased risk of congestive heart failure (CHF) from anthracycline and radiation exposures. Whether the treatment-induced risk can be mitigated with physical activity is not known. We aimed to compare the impact of insufficient physical activity on CHF in Hodgkin survivors and controls.

Methods: Participants in the CCSS reported physical activity (categorized as 0, 1-8, or ≥9 metabolic equivalent of task hours/week). We estimated rate ratios (RR) for new onset (incident) CHF during follow-up, accounting for age, sex, race/ethnicity, smoking, risky drinking, overweight/obesity, and treatment exposures (survivors). Then we calculated population attributable fractions (PAF). The attributable relative rate (ARR) was calculated by multiplying the PAF in survivors with the RR for CHF incidence in survivors compared to controls, resulting in an ARR for survivors that was compared to the PAF in controls.

Results: In 2,357 Hodgkin survivors [50% female; [mean (SD)] 14.3 (4.1) years at diagnosis; 31.6 (5.8) years at start of follow-up, with 17.8 (7.6) years of follow-up] and 3,949 sibling controls, 233 survivors and 19 controls developed severe CHF during follow-up. The PAF for CHF attributable to insufficient physical activity was larger in controls (38.0%) than survivors (22.3%). However, with RR 20.3 (95% CI 12.6-32.5) for CHF for survivors compared to controls, the ARR in survivors (452.1%) revealed a 12 times higher incidence CHF attributable to insufficient physical activity in Hodgkin survivors than in controls (452.1%/38.0%). The ARR indicates that 4.5 of the 20-fold higher risk of CHF in survivors vs. siblings is attributable to insufficient physical activity in the survivors.

Conclusion: Our results suggest that the magnitude of treatment-induced CHF risk that can be mitigated by physical activity is considerable. This offers a modifiable target and provides rationale for exercise interventions aimed at reducing CHF in survivors at high risk.