**Relationship between Coronary Artery Radiation Doses and Risk of Late Coronary Artery Disease: A Report from the Childhood Cancer Survivor Study (CCSS)**

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*Purpose*:

Among childhood cancer survivors, heart dose from radiotherapy (RT) is an established risk factor for coronary artery disease (CAD). Since contemporary RT can be optimized for individual substructures, coronary artery-specific dose-response relationships could refine cardiac dose constraints beyond whole heart metrics. We investigated associations between coronary artery doses and risk of CAD.

*Methods*:

We estimated 35-year cumulative incidence and incidence rate ratios (RR) of Common Terminology Criteria for Adverse Events grade 3-5 CAD for 25,481 5-year cancer survivors in the CCSS diagnosed at median age 6.1 years (0-20 years) between 1970-1999 at 32 institutions. For the 12,228 individuals treated with RT, fields were reconstructed on an age-scaled computational phantom with a detailed heart model with four coronary arteries. Mean doses to the left main (LMA), left anterior descending (LAD), left circumflex (LCX), and right coronary (RCA) arteries and whole heart were calculated. Associations of heart and artery doses with CAD were evaluated with piecewise exponential models adjusted for demographic, treatment-related characteristics, and cumulative anthracycline dose.

*Results*:

For all arteries and whole heart, mean doses ≥10 Gy were associated with significantly increased CAD risk. After a mean dose of 10-<20 Gy to the LMA, LAD, LCX, and RCA respectively, 35-year cumulative incidences were 4.7% (95%CI:2.7-6.7), 10.7% (95%CI:7.7-13.7), 6.8% (95%CI:4.8-8.7), and 12.6% (95%CI:10.3-15.0); RR values were 2.5-5.3 times higher than for survivors unexposed to RT. Lower doses (5-<10 Gy) to the LAD (RR 1.9, 95%CI:1.6-4.1, p<0.001) and RCA (RR 2.6, 95%CI:1.6-4.1, p<0.001) were also associated with significantly increased risk.

*Conclusions*:

This study expands our understanding of RT-related CAD beyond whole heart doses and establishes relationships between dose to specific coronary arteries and CAD. We uniquely identified that RCA and LAD doses as low as 5 Gy were associated with increased risk. These data can guide contemporary pediatric RT to prioritize coronary artery dose constraints.