

Title: Cumulative Burden of Late, Major Surgical Intervention in Survivors of Childhood Cancer: A Report from the Childhood Cancer Survivor Study (CCSS)

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ABSTRACT

Background The cumulative burden of late (>five years from cancer diagnosis), major surgical intervention among childhood cancer survivors has not been evaluated.

Methods 25,656 survivors diagnosed 1970-1999 (median follow-up 22.2 years, interquartile range [IQR]=16.5-29.7; median diagnosis age 6.1 years [IQR]=3.0-12.4) and 5,045 siblings from the CCSS self-reported late, major surgical interventions, defined as anesthesia-requiring operations occurring >5 years after cancer diagnosis. Cumulative burden was assessed using mean cumulative counts (MCC) of late, major surgical interventions. Piecewise exponential regression models evaluated associations between treatment exposures and late, major surgical interventions.

Results Survivors underwent 28,202 late major surgical interventions. The 35-year MCC was 206.7 (95% confidence interval [CI]=202.7-210.8) per 100 survivors compared to 128.9 (95%CI=123.0-134.7) per 100 siblings (adjusted rate ratio [RR]=1.8, 95%CI=1.7-1.9). Survivors diagnosed in the 1990s (RR=1.4, 95%CI=1.3-1.5) experienced an increased rate of late surgery versus the 1970s. Survivors underwent life-altering late operations at higher rates relative to siblings including heart valve replacement (RR=12.6, 95%CI=4.8-33.1), lung resection (RR=8.5, 95%CI=4.6-15.6), mastectomy (RR=6.2, 95%CI=3.8-10.2), coronary artery bypass (RR=6.1, 95%CI=2.4-14.5), colectomy (RR=2.9, 95%CI=1.8-4.8), scoliosis correction (RR=2.9, 95%CI=1.9-4.4), and amputation (RR=2.8, 95%CI=1.7-4.5). Hodgkin lymphoma (35-year MCC=333.3 per 100 survivors, 95%CI=320.1-346.6), Ewing sarcoma (MCC=322.9, 95%CI=294.5-351.3), and osteosarcoma (MCC=269.6, 95%CI=250.1-289.2) survivors experienced the highest burden. Treatment involving locoregional surgery and/or radiotherapy at the time of original cancer diagnosis was associated with undergoing late surgical intervention in the same body region or organ system, even when corrected for development of grade 3-4 chronic health conditions in that organ system: (central nervous system surgery + cranial radiotherapy RR=19.9, 95%CI 15.3-25.8; cardiovascular/respiratory surgery + chest radiotherapy RR=4.1, 95%CI=2.8-6.1; gastrointestinal surgery + abdomen/pelvis radiotherapy RR=1.7, 95%CI=1.5-1.9; musculoskeletal surgery + radiotherapy RR=2.5, 95%CI=2.1-2.8).

Conclusions Survivors of childhood cancer have a significant burden of late, major surgical interventions, a late-effect that has previously been poorly quantified. Survivors would benefit from regular healthcare evaluations aiming to anticipate impending surgical issues and to intervene early in the disease course when feasible.