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Abstract limits - 50 (18) word title/ 300 (300) word body

Title - Late Morbidity and Mortality in Survivors of Childhood Ependymoma: A Report from the Childhood Cancer Survivor Study (CCSS)

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Background: Between the 1970s and 1990s, therapy for childhood ependymoma evolved to include chemotherapy and focal rather than whole-brain radiation. The impact of these changes on health outcomes is unknown.

Methods: 404 five-year survivors of ependymoma (52.5% male, median 6 [range 0-20] years old at diagnosis, 22 [5-49] years from diagnosis) were evaluated for cumulative incidence of late mortality, subsequent neoplasms, and chronic health conditions (CHC). Outcomes were analyzed by diagnosis decade and brain radiation and chemotherapy exposures. Fine-Gray's test compared cumulative incidence curves. Relative Risks (RRs) with 95% CIs estimated outcomes using multivariable piecewise exponential models.

Results: Throughout the three decades whole brain radiation exposure decreased (32.7% to 2.3%) while focal brain radiation increased (16.4% to 59.2%), and chemotherapy use increased (23.6% to 47.9%). Fifteen-year all-cause late mortality (incidence, 95% CI) estimates were similar across treatment eras: 1970s (9.3%, 3.4-18.8%), 1980s (14.7%, 9.4-21.2%), 1990s (10.3%, 6.7-14.9%), (p=0.9). Mortality was higher with whole brain radiation (22.5%, 11.2-36.5%) compared to focal radiation (11.4%, 7.5-16.1%) or no brain radiation (3.5%, 0.9-9.1%), (p <0.001). Mortality was also higher with chemotherapy (14.4%, 9.6-20.0%) compared to no chemotherapy (6.8%, 3.8-11.0%) (p=0.004). Differences in mortality were due to recurrence/progression of the primary cancer and health-related causes. Compared to no brain radiation, there were increased risks (RR, 95% CI) of any grade 3-4 CHCs for focal (2.6, 1.3-5.4) and whole brain radiation (3.5, 1.5-8.1) and >1 Grade 3-4 CHCs for whole brain radiation

(6.5, 1.3-31.6). There were no differences in CHCs or subsequent neoplasms by chemotherapy exposure.
Conclusions: Despite the treatment changes over the 1970s to 1990s, late morbidity and mortality in pediatric ependymoma remained unchanged. Whole and focal brain radiation were associated with increased risk of grade 3-4 CHCs compared to no radiation. Future therapies for childhood ependymoma should target reductions in late morbidity and mortality.