Increasing risk of severe, life-threatening and fatal chronic health conditions in aging survivors of childhood CNS tumors: A report from the Childhood Cancer Survivor Study

Gregory T. Armstrong, MD, MSCE, Toana Kawashima, MS, Wendy Leisenring, ScD, Marilyn Stovall, PhD, Charles A. Sklar, MD, Leslie L Robison, PhD, Kevin C. Oeffinger, MD

Background The incidence, severity, and spectrum of chronic health conditions in the third and fourth decades of life among survivors of childhood CNS tumors have not been well studied.

Methods Analyses included 14,358 ≥5 yr survivors of childhood cancer including 1876 (13.1%) survivors of CNS tumors (median age at last follow-up 31.0 yrs, range 6.0-56.0; 45.8% ≥30 years) and a sibling comparison group (n=4,023). Self-reported health conditions were classified using the NCI CTCAE 4.0 grading system. Analyses focused on serious conditions (SC) defined as severe/life-threatening/fatal, grades 3-5. Hazard ratios (HR) and 95% confidence intervals (CI) were calculated using Cox proportional hazards models adjusted for gender and race, using age as the time scale.

Results Among survivors of CNS tumors with no previous SC through age 25, the cumulative incidence for a new SC by age 40 compared to non-CNS tumor survivors and to siblings was 25.1% (95% CI 25.1-25.2) vs. 23.7% (95% CI 23.7-23.7) vs. 6.2%, (95% CI 6.2-6.3), respectively. Survivors of CNS tumors ≥30 yrs of age had a 6.1-fold (95% CI 5.4-6.8) increased risk of a SC compared to same age siblings, in contrast to non-CNS survivors (HR 4.3, 95% CI 3.9-4.7). Compared to siblings, CNS tumor survivors had a significantly increased risk for: stroke (HR 26.7, 95% CI 15.9-45.1), myocardial infarction (HR 2.1, 95% CI 1.1-4.2), hypothyroidism (HR 4.8, 95% CI 3.6-6.3), ovarian or testicular dysfunction (HR 4.5, 95% CI 3.0-6.9) and renal failure (HR 5.9, 95% CI 2.0-17.3) among other serious conditions. Compared to non-CNS survivors, CNS tumor survivors had significantly higher risks of stroke ($p<0.001$), hypothyroidism ($p=0.004$) and growth hormone deficiency ($p<0.001$).

Conclusions As they age, adult survivors of childhood CNS tumors continue to develop new SC at overall rates that are comparable to non-CNS survivors, but at substantially higher rates than siblings.

Department of Epidemiology and Cancer Control and Department of Biostatistics, St. Jude Children's Research Hospital, Memphis, TN;

Corresponding Author: Gregory T. Armstrong, Department of Epidemiology and Cancer Control, St. Jude Children's Research Hospital, 262 Danny Thomas Place, Mail Stop 735, Memphis, TN; Phone: 901-595-5892, Fax: 901-595-5845, Email: greg.armtrong@stjude.org