

Temporal Trends in Late-Onset Morbidity and Mortality After Medulloblastoma Diagnosed Across Three Decades: A Report from the Childhood Cancer Survivor Study (CCSS)

Ralph Salloum, Yan Chen, Yutaka Yasui, Roger Packer, Wendy Leisenring, Elizabeth Wells, Allison King, Rebecca Howell, Todd M. Gibson, Kevin R. Krull, Leslie L. Robison, Kevin C. Oeffinger, Maryam Fouladi, Gregory T. Armstrong

Background: Therapy for medulloblastoma and primitive neuroectodermal tumor has evolved from surgery and adjuvant radiotherapy to risk-adapted multimodal regimens. The impact of these changes in treatment on long-term outcomes remains unknown.

Methods: Cumulative incidence of late mortality (>5 years from diagnosis), subsequent malignant neoplasms (SMN), chronic health conditions and psychosocial functioning were evaluated among 5-year survivors in CCSS diagnosed between 1970 and 1999. Survivors were stratified according to treatment decade (1970s, 1980s, 1990s) and treatment exposure (surgery + craniospinal irradiation [CSI] ≥ 30 Gy, no chemotherapy; surgery + CSI ≥ 30 Gy + chemotherapy [high-risk therapy], surgery + CSI < 30 Gy + chemotherapy [standard-risk therapy]). Rate ratios (RRs), odds ratios (ORs) and 95% confidence intervals (CIs) were estimated for long-term outcomes among treatment eras and exposure groups using multivariable piecewise-exponential models.

Results: Among 1,380 eligible survivors (median [range] age 29 [6-20] years; 21.4 [5-44] years from diagnosis), the 15-year cumulative incidence of all-cause (21.9% 1970s vs. 12.8% 1990s; $p=0.003$) and recurrence-related (16.2% vs 9.6%, $p=0.03$) late mortality decreased with no reduction in mortality attributable to late effects of therapy including SMN. Among 959 participants, the incidence of SMN did not decrease by era or by treatment group. However, survivors treated in the 1990s had an increased cumulative incidence of severe, life-threatening and fatal health conditions (16.9% 1970s vs 25.4% 1990s; $p=0.03$), and were more likely to develop multiple severe or life-threatening health conditions, RR=2.98 (95% CI, 1.10-8.07). Survivors of standard-risk therapy were less likely to use special education services than high-risk therapy patients, OR =0.51 (95% CI, 0.33-0.78).

Conclusions: Historical changes in therapy have improved 5-year survival, reduced risk of late mortality due to disease recurrence, and reduced special education utilization, at the cost of increased risk for multiple, severe and life-threatening chronic health conditions.