TEMPORAL CHANGES IN THERAPY AND NEUROCOGNITIVE OUTCOMES IN ADULT SURVIVORS OF PEDIATRIC EPENDYMOMA: A REPORT FROM THE CHILDHOOD CANCER SURVIVOR STUDY (CCSS)

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Background and aims: Treatment for childhood ependymoma has evolved to reduce exposure to cranial radiation (CRT) to prevent late effects. The impact of these changes and of chronic health conditions (CHCs) on neurocognition remains unknown.

Methods: Survivors of childhood ependymoma (n=185; 53% female; median[minimum-maximum] 28[18-49] years at survey, 21[15-34] years from diagnosis) and siblings (n=727; 44% males; 32[18-58] years at survey) completed the CCSS Neurocognitive Questionnaire assessing task efficiency, emotional regulation, organization, and memory (impairment: scores >90th percentile of siblings). Treatment exposure categories reflected temporal changes in CRT: whole-brain CRT (≥30Gy), focal CRT (≥30Gy), and no CRT. Self-reported CHCs were graded by organ system using the NCI's CTCAE v4.3. Multivariable models estimated risk of neurocognitive impairment in survivors compared to siblings, and risk associated with treatment exposures and moderate to life-threatening CHCs among survivors, adjusting for demographic and clinical factors. Relative risk (RR) and 95% confidence interval (95% CI) were reported.

Results: Across decades, whole-brain CRT exposure decreased (1970s, 38.5%; 1980s, 30.6%; 1990s, 11.3%) whereas focal CRT increased (1970s, 7.7%; 1980s, 40.3%; 1990s, 56.7%). Compared to siblings, all treatment categories demonstrated elevated risk of impaired task efficiency and memory (e.g., task efficiency: no CRT RR [95% CI] 1.78 [1.01-3.14]; focal CRT 3.03 [2.17-4.21]; whole-brain CRT 5.19 [3.93-6.83]). Whole-brain CRT was associated with more impaired task efficiency (2.68 [1.50-4.79]) and memory (2.14 [1.02-4.50]) compared to no CRT, whereas focal CRT was not. Seizures were associated with more impaired task efficiency (1.86 [1.33-2.61]), memory (2.33 [1.42-3.81]) and organization (2.23 [1.20-4.15]). Hearing deficits were associated with organization impairment (2.03 [1.02-4.04]). These associations remained significant after adjusting for CRT treatment exposure groups.

Conclusions: Despite reduced CRT exposure, long-term survivors of childhood ependymoma remain at-risk for neurocognitive impairment in adulthood. Otoprotective agents and epilepsy management may be potential interventions to mitigate late neurocognitive problems associated with early neurotoxic exposures.