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Late Mortality and Morbidity of Adult Survivors of Childhood Glioma Treated Across Three Decades: A Report from the Childhood Cancer Survivor Study

PURPOSE: Pediatric low-grade glioma therapy has evolved to delay or eliminate radiation. The impact of therapy changes on long-term outcomes remains unknown.

METHODS: Cumulative incidence of late mortality (death >5 years from diagnosis), subsequent neoplasms (SNs), and chronic health conditions (CHCs, CTCAE grading criteria) were evaluated in the Childhood Cancer Survivor Study among 5-year survivors of glioma diagnosed 1970-1999. Outcomes were evaluated by diagnosis decade and by treatment exposures received ≤5 years following diagnosis (surgery-only, chemotherapy ± surgery, and cranial radiation ± surgery or chemotherapy). Relative risk (RRs) with 95%CIs estimated long-term outcomes using multivariable piecewise exponential models.

RESULTS: Among 2,684 eligible survivors (age at diagnosis (median [range]), 7 years [0-20 years]; time from diagnosis, 24 years [5-48 years]), exposure to cranial radiation decreased [51% (1970s), 45% (1980s), 25% (1990s)] along with late tumor recurrence (>5 & ≤15 years from diagnosis) [9.8% (1970s), 8.8% (1980s), 5.0% (1990s)]. The 15-year cumulative incidence of late mortality was 10.3% (1970s), 6.5% (1980s), and 6.0% (1990s) (p<0.001, comparison of cumulative incidence curves). The 15-year cumulative incidence of grade 3-5 CHCs was 19.7% (1970s), 17.8% (1980s), and 14.2% (1990s) (p<0.0001). A reduction in SN incidence was not
observed. In multivariable analyses excluding treatment exposure, later diagnosis (1990s vs. 1970s) was associated with lower risk of late mortality, grade 3-5 CHCs and SNs. Inclusion of treatment exposure in the model attenuated the effect of diagnosis decade. Radiation or chemotherapy exposure increased risk compared to surgery alone for late mortality (radiation RR 4.95, 95%CI 3.79-6.47; chemotherapy RR 2.88, 95%CI 1.85-4.48), CHCs (radiation RR 4.02, 95%CI 3.28-4.94; chemotherapy RR 1.66, 95%CI 1.13-2.45), and SNs (radiation RR 4.02, 95%CI 3.06-6.13, chemotherapy RR 2.08, 95%CI 1.03-4.23)).

CONCLUSION: Late mortality and CHCs decreased in childhood glioma survivors diagnosed from 1970-1999 largely due to therapy changes, particularly avoidance of cranial radiation, without increased late recurrence.