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Title: Neurologic morbidities, emotional distress, and functional independence in adult survivors of childhood cancer treated with CNS-directed therapies: A report from the Childhood Cancer Survivor Study

Background: Survivors of childhood cancer who received CNS-directed therapies are at risk for neurologic sequelae, which may adversely impact psychological functioning and independence in adulthood.

Methods: Participants included 7,942 survivors of childhood cancer treated from 1970-99 with cranial radiation, intrathecal methotrexate or cytarabine (59% leukemia; 27% CNS tumor; 11% non-Hodgkin; 3% other; mean[SD] age = 25.5[5.8] yrs, time since diagnosis = 17.7[4.6] yrs). Self-reported neurologic conditions included stroke, seizure, sensory deficits, focal neurologic dysfunction, and severe headaches. Emotional distress symptoms (BSI-18) included anxiety, depression, and suicide ideation (SI). Functional independence was assessed using latent class analysis with six indicators (independent living, assistance with routine needs, assistance with personal care needs, ability to attend work/school, driver's license, marital status). Multivariable regression models, adjusted for age, sex, race, pain, and health status, estimated relative risks (RR) and odds ratios (OR) for associations of neurologic morbidity with emotional distress and functional independence.

Results: Prevalence of neurologic conditions was: 3% stroke; 11% seizure; 25% sensory deficits; 29% focal neurologic dysfunction; 31% severe headaches. In multivariable models, risk of emotional distress was associated with focal neurologic dysfunction (anxiety: RR 1.6; 95% CI 1.3-2.1; depression: RR 1.4; CI 1.2-1.7), sensory deficits (anxiety: RR 1.3; CI 1.0-1.6; depression: RR 1.3; CI 1.1-1.5; SI: RR 1.3; CI 1.0-1.6), and severe headaches (anxiety: RR 1.5; CI 1.2-1.9; depression: RR 1.6; CI 1.4-2.0; SI: RR 1.5; CI 1.2-1.8). Stroke (OR 0.3, CI 0.2-0.5), seizure (OR 0.2, CI 0.2-0.3), and focal neurologic deficits (OR 0.26, CI 0.2-0.3) were associated with decreased likelihood of functional independence.

Conclusion: Childhood cancer survivors who develop neurologic morbidities are at-risk of emotional distress symptoms, including suicide ideation, and failure to attain independence in adulthood.