

Title: Neuromuscular dysfunction and associated health/socioeconomic outcomes: A report from the Childhood Cancer Survivor Study

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Background: Childhood cancer survivors are at risk for neuromuscular dysfunction. We estimated the prevalence and cumulative incidence of neuromuscular dysfunction in a cohort of childhood cancer survivors and examined associations with treatment exposures and health/socioeconomic outcomes.

Methods: CCSS participants ≥ 5 years from cancer diagnosed between 1970-1999 ($n=25,583$, 46.5% female, median [range] age 54.4 [15.1-57.6] years) and siblings ($n=5,044$, 52.3% female, median [range] age 54.1 [32.5-57.0] years) were included. Neuromuscular dysfunction was identified by self-report of 1) motor dysfunction: impaired balance, tremor, or extremity weakness; 2) sensory dysfunction: impaired touch sensation. Multivariable analyses examined predictors of dysfunction by diagnosis.

Results: Cumulative incidence of neuromuscular dysfunction was elevated at 20 years from diagnosis in survivors (24.3%, 95% CI 23.8-24.8; motor 18.2%, sensory 13.5%) versus siblings (8.9%, 95% CI 8.1-9.7). In survivors five years from diagnosis, motor dysfunction was associated with exposure to cytarabine (OR=1.39, 95% CI 1.10-1.77) and spinal radiation (OR=2.11, 95% CI 1.31-3.41) in acute lymphoblastic leukemia/non-hodgkin lymphoma (ALL/NHL), vinca alkaloids (OR 1.29, 95% CI 1.03-1.60) and brain radiation (OR=1.58, 95% CI 1.35-1.85) in central nervous system tumors, and cytarabine (OR=3.73, 95% CI 1.62-8.57) and non-brain/spine radiation (OR=1.84, 95% CI 1.42-2.40) in bone/soft tissue tumors. Sensory dysfunction was associated with exposure to vinca alkaloids (OR=3.45, 95% CI 1.06-11.22) in ALL/NHL, and platinum agents (OR=1.31, 95% CI 1.03-1.67) and spinal radiation (OR=3.71, 95% CI 1.24-11.11) in bone/soft tissue tumors. Survivors with neuromuscular dysfunction were at increased risk for adverse health/socioeconomic outcomes (Table).

Conclusions: Neuromuscular dysfunction is a prevalent morbidity in childhood cancer survivors, associated with specific therapies within a particular diagnosis. Interventions are needed to identify

and improve neuromuscular dysfunction given its association with adverse health/socioeconomic outcomes.

Table: Health/socioeconomic outcomes in survivors with neuromuscular dysfunction compared with those without dysfunction

	OR	95% CI
College or Higher Degree	0.72	0.67 – 0.78
Ever Employed	0.46	0.37 - 0.56
Anxiety	2.76	2.40 - 3.18
Depression	2.27	2.02 - 2.55
Obesity	1.15	1.06 - 1.24

Model adjusted for sex, race/ethnicity, age, presence of any grade 3/4 chronic condition