Title: Neuromuscular dysfunction and associated health/socioeconomic outcomes in survivors of childhood cancer

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Background: Childhood cancer survivors are at risk for neuromuscular dysfunction as an acute side effect of treatment with vinca alkaloids and platinating agents. We estimated the prevalence and cumulative incidence of neuromuscular dysfunction in childhood cancer survivors, and examined associations with treatment and health/socioeconomic outcomes.

Methods: Childhood Cancer Survivor Study participants ≥5 years from cancer diagnosed between 1970-1999 (n=25,583, 46.5% female, median age 54.4 [range 15.1-57.6] years) and siblings (n=5,044, 52.3% female, median age 54.1 [range 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 treatment/demographic associations with 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, 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 platinating 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 had increased risk for adverse health/socioeconomic outcomes (Table).

Conclusions: Neuromuscular dysfunction is a prevalent morbidity in childhood cancer survivors. In addition to vinca alkaloids and platinating agents, we found cytarabine, and radiation were also associated with neuromuscular dysfunction and associations varied by cancer diagnosis. Interventions are needed to identify and treat neuromuscular dysfunction given its association with adverse health/socioeconomic outcomes.
**Table:** Health/socioeconomic outcomes in survivors with neuromuscular dysfunction compared with those without dysfunction

<table>
<thead>
<tr>
<th></th>
<th>OR</th>
<th>95% CI</th>
</tr>
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<tbody>
<tr>
<td>College/graduate degree</td>
<td>0.72</td>
<td>0.67 – 0.78</td>
</tr>
<tr>
<td>Employed</td>
<td>0.46</td>
<td>0.37 – 0.56</td>
</tr>
<tr>
<td>Anxiety</td>
<td>2.76</td>
<td>2.40 – 3.18</td>
</tr>
<tr>
<td>Depression</td>
<td>2.27</td>
<td>2.02 – 2.55</td>
</tr>
<tr>
<td>Obesity</td>
<td>1.15</td>
<td>1.06 – 1.24</td>
</tr>
</tbody>
</table>

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

Word Count: 299