

Background: Neuroblastoma (NB) survivors can develop many complications from their treatment. We evaluated long-term morbidity and mortality in a large cohort of NB survivors.

Procedures: Late effects data from 5-year NB survivors diagnosed between 1970-86 enrolled in the Childhood Cancer Survivor Study (CCSS) were collected from self-administered questionnaires. 832 survivors and 3899 siblings were included. Treatment data were abstracted from the medical records of all survivors. Late mortality, second malignant neoplasm (SMN), and chronic health conditions were analyzed in relation to treatment factors.

Results: 42 survivors (6%) died more than 5 years after their diagnosis (standardized mortality ratio [SMR]:4.8; 95% CI 3.5-6.5). Causes of late mortality included: disease recurrence (n=23), SMN (n=6) (SMR: 8.5; 95% CI 3.1-18.4), cardiac (n=1) (SMR 2.9; 95% CI 0.04-16.0), pulmonary (n=1) (SMR 4.8; 95% CI 0.1-26.5), external causes (n=4), other and unknown (n=11). 33 developed a SMN (standardized incidence ratio [SIR] 8.6; 95% CI 5.9-12.1): thyroid (n=7), renal (n=6), soft tissue sarcomas (n=3), acute myeloid leukemia (n=2), breast cancer (n=2) and other (n=13). Exposure to radiation therapy (RT) ($p=0.003$) and to VP-16 ($p=0.04$) were significant risk factors for SMN.

38% of the survivors reported at least one chronic health condition. Compared to siblings, they were more likely to report any chronic condition (risk ratio [RR] 14.7; 95% CI, 12.4-17.6). The highest relative risks were related to the following systems: musculoskeletal (RR 49.8; 95% CI, 27.9-88.8), endocrine (RR 36.2; 95% CI 24.1-54.5), sensory (RR 21.5; 95% CI, 14.6-31.7) and neurological (RR 13.1; 95% CI 10.8-16). A multivariable Poisson regression analysis revealed the following associations: laminectomy (RR 8.6; 95% CI 3.5-21) and chest RT (RR 2.8; 95% CI 1.3-6.5) as risk factors for scoliosis; age < 1 year at diagnosis (RR 1.9; 95% CI 1.4-2.6) and laminectomy (RR 3.5; 95% CI 2.4-5.3) for neurological complications; for hearing loss, increasing cumulative dose of cisplatin (for ≥ 600 mg/m² RR 52.8; 95% CI 10.2-272.5); and RT to the neck (RR 6.6; 95% CI 2.4-18) for hypothyroidism.

Conclusions: NB survivors are at risk of developing chronic health conditions. Long-term surveillance is required for early detection of these complications.