

Hearing Impairment among Long-term Survivors of Childhood Cancer: A Report from the Childhood Cancer Survivor Study (CCSS)

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Background/Objectives: Cisplatin, carboplatin, and cranial radiotherapy (CRT) ≥ 30 Gy is associated with ototoxicity; however, information on the magnitude of risk and latency associated with treatment combinations is limited.

Design/Methods: Presence or absence of hearing impairment (requiring a hearing aid or deafness) was reported by 24,306 ≥ 5 year childhood cancer survivors (mean years from diagnosis=24.1, standard deviation=8.9). Age- and sex-adjusted prevalence ratios (PR) and hazard ratios (HR), with corresponding 95% confidence intervals (CI), were estimated for early-onset (< 5 years post-diagnosis) and late-onset (≥ 5 years post-diagnosis) hearing impairment, respectively.

Results: Among all survivors, the prevalence of hearing impairment was 3.1% (95% CI: 2.9-3.4) at 5 years post-diagnosis, and the 15-year cumulative incidence was 4.8% (95% CI: 4.5-5.1). Any cisplatin exposure was associated with early-onset impairment, even at doses < 200 mg/m² (PR[95% CI]=14.6 [7.6-28.0]), while higher doses remained associated with late-onset impairment (e.g., HR[95% CI]: 3.7 [1.7-8.0] for 200-300 mg/m²). In contrast, early-onset impairment was associated with carboplatin doses ≥ 4.0 g/m² (PR[95% CI]=8.6 [4.1-18.1]), while lower doses were associated with late-onset impairment (e.g., HR[95% CI]: 4.6 [1.1-18.7] for 0.1-1.9 g/m²). Hearing impairment was more strongly associated with exposure to CRT ≥ 30 Gy combined with platinum (PR[95% CI]: 49.5 [36.5-67.3] for CRT ≥ 30 Gy + 400-599 mg/m² cisplatin; 22.2 [10.8-45.7] for CRT ≥ 30 Gy + 2-3.9 g/m² carboplatin) than comparable doses of CRT (9.4 [7.0-12.6]), cisplatin (19.2 [12.9-28.4]), or carboplatin (2.0 [0.3-14.1]) alone. Impairment occurred in 50.1% (95% CI: 45.3-54.8) of survivors treated with CRT ≥ 30 Gy and ≥ 200 mg/m² cisplatin and 33.5% (95% CI: 22.5-44.5) with CRT ≥ 30 Gy and ≥ 2 g/m² carboplatin by 15 years post-diagnosis.

Conclusion: Hearing impairment in survivors of childhood cancer evolves over decades following treatment. Although the incidence is greatest in survivors exposed to multiple ototoxic therapies, survivors treated with platinum therapy, even at low doses, have a high likelihood of profound ototoxicity.