Journal of Cancer Survivorship (2023) 17:1–3
https://doi.org/10.1007/s11764-022-01302-z

EDITORIAL

Introduction to the special section: treatment-related hearing loss and its impact on cancer survivors

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Received: 2 November 2022 / Accepted: 11 November 2022 / Published online: 13 January 2023

Late effects experienced by cancer survivors often depend on the site of the disease, the treatment regimen, comorbid conditions, health behaviors, and prevention and/or management strategies. While platinum-based therapies and cranial radiation are effective at treating a number of pediatric and adult cancers, including sarcomas, central nervous system tumors, head and neck, and testicular and ovarian cancers, certain recipients of these therapies are at risk for developing permanent hearing loss [1, 2]. Cisplatin chemotherapy regimens appear to pose the most consistently reported risk with 40–80% of adult and 50% of pediatric recipients experiencing hearing loss [3–5]. Hearing loss has been associated with impaired communication, social isolation, delayed language development, decreased educational performance, cognitive limitations, employment challenges, and an overall decreased health-related quality of life [6, 7]. Although hearing loss is a known late effect of platinum-based cancer treatment, hearing loss in cancer survivors remains an enigma to both researchers and practitioners. As a result, there is a substantial opportunity to improve our understanding of this functional loss. There is much to learn about prevention, screening, assessment, and treatment of cancer-treatment related hearing loss in order to better improve the quality of life for cancer survivors who experience this impairment.

This special section features research on hearing loss mechanisms and prevention efforts as well as research that illustrates the burden of hearing loss, including its impact on quality of life and aspects of daily living. Opportunities to engage clinicians from diverse disciplines to improve care delivery are also highlighted. We hope that this special section increases awareness of hearing loss in cancer survivors and provides areas where future research seems promising.

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Phillips et al. [8] conducted a literature review to appreciate the long-term impact of ototoxicity (including hearing loss and tinnitus) on cancer survivors. The authors identified 16 original articles and two systematic reviews describing many of the deficits, lifestyle disruptions, and mental health impacts of ototoxicity in cancer survivors. The review identified opportunities to improve patient-provider communication, monitor at-risk patients, and coordinate across disciplines (e.g., audiology, oncology). Sanchez et al. [9] surveyed testicular cancer survivors and identified age, dose, cardiovascular risk factors, and family history of hearing loss as risk factors in survivors experiencing hearing loss and tinnitus. These findings lend support for routine assessments when caring for cancer survivors with a history of testicular cancer and likely apply to other cancer survivors who were treated with platinum agents.

Miaskowski and colleagues [10] indicated that the prevalence of self-reported hearing loss was lower than hearing loss confirmed on the audiogram. This gap may demonstrate an under-appreciation for the survivor's ability to compensate for (or disregard) hearing deficits. The investigators also reported co-occurring symptoms including depression, sleep disturbances, anxiety, and cognitive impairment supporting the need for comprehensive routine assessments that include self-assessment and formal evaluation by a multidisciplinary team. Appreciating the significant effect hearing loss has on cancer survivors, future research to understand the pathology and develop prevention strategies is recommended.

DeBacker and colleagues [11] conducted a systematic review of predictive models to determine the risk of developing ototoxicity after platinum regimens and/or cranial radiation. The review identified cancer treatment, genetic, auditory, and demographic risk predictors which can be incorporated into clinical practice to inform treatment planning.

In terms of providing a better understanding of cisplatin-induced ototoxicity, Guthrie and Spankovich [12] provided a comprehensive overview of mechanisms and presented

various prevention strategies such as the use of alternative therapies, dose modifications, antioxidants, and non-oxidant therapies. They also discussed future research prospects incorporating both concomitant pharmacological and non-pharmacological approaches.

Evaluation of various otoprotective agents while not compromising the therapeutic benefit of a treatment regimen remains a significant challenge. Freyer and colleagues [13] reviewed two landmark sodium thiosulfate efficacy trials conducted in pediatric oncology populations and discussed the benefits and challenges of free-standing versus embedded trials as well as considerations for future trials testing preventative agents. Sodium thiosulfate was recently approved by the Food and Drug Administration (FDA) as the first otoprotective agent for children receiving cisplatin-based therapy [14]. This FDA approval now allows sodium thiosulfate to be routinely incorporated as the standard of care; with widespread use, sodium thiosulfate is expected to decrease the incidence of hearing loss in childhood cancer survivors receiving cisplatin-based therapy. As the authors describe, however, this agent cannot be incorporated into some cisplatin regimens, such that developing and testing other strategies remains a critical need.

A cross-sectional study of audiologists and service chiefs in the Veteran's Administration by Konrad-Martin et al. [15] found that all respondents reported observing significant decreases in quality of life among those with hearing loss. About half of the respondents indicated they routinely provided services for "at-risk" cancer survivors, but cited barriers related to referral and care coordination between audiology and oncology, including limited access due to the insufficient audiology workforce. Audiologists in this study also mentioned a lack of protocols and standards of practice for survivors with a history of potentially ototoxic therapy, limiting the ability or capacity for audiological follow-up.

Survivors experiencing hearing loss may encounter a number of challenges participating in everyday activities. Safety is of utmost concern as emergency alarms, warning sounds, and routine sounds may go undetected. Childhood cancer survivors may encounter delayed language development, lack of access to accommodations, and struggle for academic success. A partnership among survivors, caregivers, oncology team members, pediatricians, and educators allows for a proactive approach to minimize barriers and harness a student's full potential. Depending on the work environment, returning to and maintaining employment may be difficult if the job requires telephone communication, hearing and understanding spoken words, or discerning sounds in a noisy environment [16]. Workplace accommodations to address the specific needs of the employee may require supporting documentation from the oncology team [17]. In addition, social isolation and withdrawal can occur as a result of any one or a number of these experiences.

The intention of this special section of the Journal of Cancer Survivorship was to highlight the importance of hearing loss as a potential late effect in cancer treatment, urge routine testing for at-risk survivors, and emphasize the importance of and suggest strategies for future research.

Future research opportunities span from basic mechanistic to multilevel care delivery studies. FDA approval of the first otoprotective agent is an encouraging step toward prevention and emphasizes the need for clinical trials identifying additional preventive treatments. Also, it is interesting to note that exposure to hearing aids is related to brain plasticity, suggesting flexibility in brain processes may subsequently result in functional improvement (e.g., cognitive function and/or work) [18]. Routine collection of DNA samples to understand individual susceptibility and inclusion of ototoxicity endpoints in population science and cancer control studies may support improved long-term outcomes. While cisplatin and/or radiation therapy represent cancer treatments that continue to be used in the treatment of cancer, current and future survivors are very likely to be exposed to other ototoxic therapies. The 2019 cancer survivorship statistics showed nearly two-thirds of cancer survivors were over the age of 65 [19]. Aging increases the likelihood of co-morbid illnesses with functional loss, such as cognitive impairment, that may be related to cancer treatments and contribute to hearing loss-associated disability [20, 21]. There is a critical need for research to identify these interactions. Research in prevention, detection, and treatment across age, treatment exposures, and cancer types represents important next steps. Lastly, as each contribution to this special section illustrates, research considering ototoxicity from the perspective of multiple disciplines has the potential to maximize symptomatic, functional, and quality of life outcomes for survivors experiencing therapy-related hearing loss.

Declarations

Conflict of interest The authors declare no competing interests.

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