ORIGINAL ARTICLE

Hearing Loss and Complaint in Patients With Head and Neck Cancer Treated With Radiotherapy

Christiane Schultz, MS; Maria Valéria Schmidt Goffi-Gomez, PhD; Patrícia Helena Pecora Liberman, MS; Antonio Cássio de Assis Pellizzon, MD, PhD; André Lopes Carvalho, MD, PhD

Objective: To investigate occurrences of hearing loss and hearing complaints among patients with head and neck tumors who underwent radiotherapy.

Design: Prospective case-control study.

Setting: Tertiary care hospital.

Participants: Two hundred eighty-two participants underwent evaluation, including 141 with head and neck tumors and 141 as an age-matched control group. The controls had never undergone oncological treatment that put their hearing at risk.

Main Outcome Measures: Results of audiological evaluation, including the Hearing Handicap Inventory for the Elderly questionnaire and pure-tone, speech, and immittance audiometry, and radiation dose received by the auditory system (based on the percentage of the external auditory canal included in the radiation field).

Results: We observed occurrences of hearing loss in 102 (72.3%) of the participants exposed to radiotherapy and 69 (48.9%) of the control group ($P < .001$). Hearing losses were mostly sensorineural and of mild degree, but those exposed to radiotherapy more frequently presented with severe and mixed-type hearing losses ($P < .001$). Of the participants exposed to radiotherapy, 19.1% had a severe handicap ($P < .001$).

Conclusion: Patients undergoing radiotherapy in the head and neck region have a higher incidence of hearing loss and more severe hearing handicap.

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Author Affiliations: Departments of Audiology (Mss Schultz and Pecora Liberman and Dr Goffi-Gomez) and Radiation Oncology (Dr Pellizzon), Hospital do Câncer A. C. Camargo, São Paulo, and Head and Neck Surgery and Otorhinolaryngology Department, Hospital de Cancer de Barretos, Barretos (Dr Carvalho), Brazil.

HEARING IS AN IMPORTANT sense for life because it is through hearing that interactions between the environment and society are established. Although there are different degrees of hearing loss, any impediment in conduction of sounds to the auditory nervous system signifies loss of message content, and this may give rise to emotional and social limitations and/or restrictions.

Head and neck cancer is the sixth most prevalent type of cancer worldwide. The treatment methods include surgery, chemotherapy, and radiotherapy, singly or in combination. Among other factors, the choice of treatment depends on the size and location of the tumor, the disease stage, the patient's condition, and, above all, the aim of the treatment (ie, curative or palliative).

Any of these treatment methods may affect the auditory system and cause transitory or permanent hearing losses. In surgical treatment, removal of the tumor and neck dissection may cause hearing losses. Chemotherapy with the use of ototoxic drugs such as cisplatin and carboplatin, when used at high doses, may lead to sensorineural hearing losses.[1-3]

Irradiation of head and neck tumors is increasingly used and usually involves the region of the temporal bone in cases of primary tumors and cervical metastases. Sequelae from this treatment and its clinical manifestations may occur during the treatment, just after finishing it,[4] or even many years after finishing it.[5,6]

Depending on the location and size of the tumor, the irradiation dose that reaches the structures of the auditory system may be almost 100%, such as in cases of nasopharyngeal tumors, in which the auditory tube and the mucosa of the middle ear receive practically the same dose as the tumor.[7] With intensity-modulated radiotherapy, some authors found that hearing can be protected by administering limited radiation doses to the inner and middle ear.[8]

However, when the inner ear is included in the irradiation field, permanent sensorineural hearing loss as a consequence of radiotherapy involving the cochlea is much more harmful and of great concern. This may result in cognitive deficit, depression, and even diminished living conditions for the individual.

Sensorineural hearing loss occurs after a latent period ranging from 1½ to 5 years after conventional fractionated radiotherapy.[9] Such hearing reduction seems to result from the loss of ciliated cells in the cochlea, especially in the basal turn, and/or damage to the spiral ganglion. The etiology of these losses is thought to relate to insufficient vascularization, thus leading to progressive degeneration and atrophy of the sensory structures of the inner ear, fibrosis and even ossification of the fluids of the inner ear,[10] and abnormalities of the cochlear nerve.

The quality of life of patients with cancer has become a matter of growing concern because of higher survival rates. Therefore, we should determine and understand the hearing difficulties that might have a negative impact and may impose changes or restrictions that affect the lives of patients with cancer. Recognizing these patients' problems, limitations, and reactions when faced with communication difficulties will enable better rehabilitation.

In 1982, the Hearing Handicap Inventory for the Elderly (HHIE) was drawn up and standardized with the aim of identifying and grading hearing difficulties and disabilities, as well as the emotional and social aspects of hearing loss. It was translated and adapted to Brazilian Portuguese in 1997 and has been in use since then.

The aims of the present study were to evaluate the frequency of hearing complaints and abnormalities and to characterize such problems among patients with head and neck cancer who have undergone radiotherapy alone or in association with chemotherapy or surgery.

METHODS

PARTICIPANTS

This was a prospective, transversal, case-control study in which the individuals in the exposed (study) and control groups were selected in accordance with the following criteria. The group of exposed individuals consisted of patients with a disease-free survival interval of at least 2 years subsequent to treatment for head and neck cancer that was based on radiotherapy alone or in combination and in which the auditory system was included in the field of irradiation.

The group of nonexposed individuals (control group) was composed of patients with cancer and volunteers who were invited to participate in a study and signed the informed consent without being asked whether they had any previous hearing problems or complaints. The patients with cancer underwent local surgery only, with no chemotherapy or radiotherapy. The volunteers (members of the health care volunteers' team of the Hospital do Câncer A. C. Camargo, a tertiary care hospital) were invited to participate according to their age to complete the age-matched groups (±2 years). The protocol was approved by the internal review board and all of these individuals.

EVALUATIONS

Before each evaluation, the patients answered the question "Do you think you are hearing well?" to detect and characterize the presence of hearing complaints. The HHIE questionnaire[11] was also applied. Audiological evaluation was performed between 2 and 29 years after the end of treatment, with a median of 7 years.

For the audiological evaluation, the following procedures were used: otoscopy; pure-tone threshold audiometry through the airways or, if necessary, through bones; and vocal audiometry, using the speech reception threshold and the speech recognition index. Acoustic immittance measurements were made, along with tympanometry and contralateral measurements of the stapedius acoustic reflex thresholds, at the frequencies of 500, 1000, 2000, and 4000 Hz.

All the patients in the exposed group had undergone standardized radiotherapy, that is, once a day with a fraction of the dose of 180 or 200 cGy. This was administered 5 days a week using photons of 4 or 6 MV. The fields of irradiation used (amount, shape, and entry point) and the incident plane depended on the location of the primary lesion and its areas of drainage.

We studied the simulation of radiotherapy planning to localize the external acoustic meatus.[12] A 2.5-cm-diameter circle was drawn to include the auditory system. Hence, the percentage of the area of the circle reached by the radiation field was considered for the statistical analysis. When the acoustic meatus was far from the radiation field (ie, contralateral ear), it was given a 3% value of the radiation total dose as a reference by suggestion of the radiotherapist (A.C. de A.P.). Thus, the results from the audiological evaluation were analyzed per ear.

The degree of hearing handicap was divided into the following 3 categories in accordance with the scoring from the HHIE questionnaire, as suggested by the authors: category 0, with scores from 0% to 16%; category 1, with scores from 18% to 42%; and category 2, with scores of more than 42%.

STATISTICAL ANALYSIS

We used commercially available software (SPSS for Windows, version 12.0; SPSS, Inc, Chicago, Illinois) for the statistical analysis. This analysis consisted of calculating means, medians, and standard deviations for the quantitative variables and absolute and relative frequencies for the qualitative variables. To compare hearing losses and their characteristics between the groups, we used the χ^2 test. For all statistical test results, $P \leq .05$ was considered statistically significant.

RESULTS

In the group exposed to radiotherapy, 141 patients underwent evaluation, including 98 male (69.5%) and 43 female (30.5%) patients. Their ages ranged from 13 to 84 (mean, 61.9) years. In the control group, 141 patients underwent evaluation, including 82 male (58.2%) and 59 female (41.8%) participants. Their ages ranged from 11 to 84 (mean, 61.5) years (**Table 1**). The most common tumor location was the larynx (23.4%), followed by the nasopharynx (14.8%) and tongue (10.6%). Other sites included the hypopharynx, parotid, soft palate, hard palate, and lower lip (58.2%). Some patients had tumors in multiple locations. After clinical staging, 31.2% of the tumors were designated T1 or T2 and 62.5% were designated T3 or T4. In addition, 2.8% of the tumors were recurrent, and for 3.5% the information was not available. After node staging, 75.2% of the tumors were designated N0 or N1, 3.5% were N2 or N3, and for 21.3% the information was not available. One patient in the sample (0.7%) had M1 stage cancer.

Table 1. Demographic and Hearing Loss Distribution[a]

Characteristic	Study Group, No. (%) Normal Hearing	Study Group, No. (%) Hearing Loss	*P* Value	Control Group, No. (%) Normal Hearing	Control Group, No. (%) Hearing Loss	*P* Value
Sex						
Male	29 (74.3)	69 (67.6)	.44	36 (50.0)	46 (66.7)	.045
Female	10 (25.6)	33 (32.4)		36 (50.0)	23 (33.3)	
Age, y						
<50	3 (7.7)	21 (20.6)	.07	21 (29.2)	2 (2.9)	<.001
≥50	36 (92.3)	81 (79.4)		51 (70.8)	67 (97.1)	

[a] Percentages have been rounded and may not total 100.

Table 2. Type and Classification of Hearing Loss[a]

Variable	Group, No. (%)[b] Study Right Ear	Study Left Ear	Control Right Ear	Control Left Ear	*P* Value
Hearing status					
Hearing loss	90 (63.8)	96 (68.1)	61 (43.3)	63 (44.7)	<.001
Normal hearing	51 (36.2)	45 (31.9)	80 (56.7)	78 (55.3)	<.001
Type of hearing loss					
Normal hearing	51 (36.2)	45 (31.9)	80 (56.7)	78 (55.3)	<.001
Sensorineural	72 (51.1)	72 (51.1)	58 (41.1)	60 (42.6)	
Mixed	17 (12.0)	23 (16.3)	2 (1.4)	3 (2.1)	
Conductive	1 (0.7)	1 (0.7)	1 (0.7)	0	
Hearing loss classification					
Normal hearing	51 (36.2)	45 (31.9)	80 (56.7)	78 (55.3)	<.001
Mild/moderate	81 (57.4)	84 (59.6)	60 (42.6)	61 (43.3)	
Severe/profound	9 (6.4)	12 (8.5)	1 (0.7)	2 (1.4)	

[a] The classification of hearing loss was determined using the International Bureau for Autophonology criteria.[13]
[b] Percentages have been rounded and may not total 100.

Hearing losses of the sensorineural type predominated, but occurrences of conductive hearing losses (≤0.7%) and mixed-type hearing losses (≤16.3%) were also seen in either ear and in both groups. In the group of individuals exposed to radiotherapy, mild to moderate hearing losses were observed in 57.4% of right ears and 59.6% of left ears. In the control group, hearing abilities were within normal limits in 56.7% of right ears and 55.3% of left ears, and there were mild to moderate hearing losses in 42.6% and 43.3% of right and left ears, respectively; that is, the exposed group presented with hearing losses 20% more frequently (**Table 2**). In addition, severe or profound hearing losses or anakusis occurred in the exposed group in 6.4% of right ears and 8.5% of left ears compared with only 0.7% and 1.4%, respectively, in the control group (Table 2).

The tympanometric curve was normal in 75.0% of the ears in the group of individuals exposed to radiotherapy and in 95.0% of the ears in the control group. The stapedius reflex was absent in around 65.0% of the ears in the exposed group, and this was inverted in the control group, in which the stapedius reflex was present in 65.0% of the ears.

Table 3. Distribution of Patients in the Study Group With and Without Hearing Loss According to the Treatment Protocol

Hearing Loss	Treatment, No. (%) of Patients: Radiotherapy Only (n=102)	Chemotherapy: Carboplatin (n=6)	Chemotherapy: Cisplatin (n=33)	*P* Value
Absent	31 (30.4)	4 (66.7)	4 (12.1)	<.001
Present	71 (69.6)	2 (33.3)	29 (87.9)	

Table 4. Total Dose of Radiotherapy in Each Ear Related to Hearing Loss in the Study Group

Radiotherapy Dose, cGy	No. (%) of Patients: Normal Hearing	Hearing Loss	*P* Value
Right ear			
<6500	20 (44.4)	25 (55.6)	.02
≥6500	5 (17.2)	24 (82.8)	
Left ear			
<6500	21 (46.7)	24 (53.3)	.01
≥6500	5 (17.2)	24 (82.8)	

Although only a small number of patients underwent chemotherapy with carboplatin, most of the patients who took this drug did not present with hearing loss. Most of the patients who underwent chemotherapy with cisplatin presented with hearing loss (**Table 3**). The total dose of 6500 cGy was statistically significant with regard to hearing losses for both ears (**Table 4**), but there was no statistically significant association between the percentage of the area of the auditory system that had been included in the field of irradiation and the presence of hearing losses for either ear.

There was a correlation between the degree of hearing loss and score on the HHIE questionnaire. Patients with a higher degree of hearing loss had higher scores on the questionnaire, that is, greater hearing loss was a major hearing handicap independent of group. Among the individuals who presented hearing losses of the most severe grade in both ears, 7 (70%) had a score of 2 on the HHIE questionnaire, demonstrating a major hearing handicap (**Table 5**).

Furthermore, severe handicap was observed in 2.8% of the participants in the control group vs 19.1% of the patients in the group exposed to radiotherapy. This indicates that, when present, hearing losses were substantially greater and more incapacitating after the radiotherapy.

COMMENT

In the vocal audiometry of the present study, the speech reception threshold that accompanied the degree of loss identified from tone audiometry and its values were mostly within normal limits, that is, greater than 88%, which suggests that the observed sensorineural hearing loss was cochlear.[7]

The control group was recruited by preferentially selecting individuals of the same sex and age as the ex-

Table 5. Correlation Between Degree of Hearing Loss[a] and HHIE Score for Both Groups and Both Ears

Hearing Loss	HHIE Score,[b] No. (%) of Patients[c] 0	1	2	P Value
Right ear				
Normal hearing	113 (86.9)	12 (9.2)	5 (3.8)	
Mild/moderate hearing loss	99 (69.7)	24 (16.9)	19 (13.4)	<.001
Severe/profound hearing loss	2 (20.0)	1 (10.0)	7 (70.0)	
Left ear				
Normal hearing	109 (88.6)	10 (8.1)	4 (3.3)	
Mild/moderate hearing loss	104 (71.7)	24 (16.6)	17 (11.7)	<.001
Severe/profound hearing loss	1 (7.1)	3 (21.4)	10 (71.4)	

Abbreviation: HHIE, Hearing Handicap Inventory for the Elderly.
[a]The classification of hearing loss was determined using the International Bureau for Autophonology criteria.[13]
[b]An HHIE score of 0 indicates no hearing handicap; 1, mild to moderate hearing handicap; and 2, severe hearing handicap.
[c]Percentages have been rounded and may not total 100.

posed individuals. Male patients and individuals who were 50 years or older predominated in the study population. Hearing losses occurred in both sexes and in the 2 age group categories, but we could not conclude that sex and age were independent risk factors for hearing loss. In the control group, however, being 50 years or older was the only independent risk factor for hearing loss (Table 1). Auditory thresholds do not typically undergo significant change until 80 to 89 years of age.[14] Hearing becomes severely impaired after the age of 90 years in both sexes,[15] and sex has no influence on occurrences of hearing loss after radiotherapy. Such losses occur because of vascular damage in the ear, thereby leading to atrophy of the vascular striae in the basal turn of the cochlear duct and causing greater sensorineural hearing loss of high-pitched sounds. A study of the incidence of ototoxic effects after radiotherapy for head and neck tumors concluded that sex did not influence the development of this complication in univariate or multivariate analysis.[16]

Some authors have observed clinically significant hearing loss in older patients with green eyes and unfavorable pretreatment hearing after they were treated with intensity-modulated radiotherapy for head and neck tumors.[17]

Hearing loss associated with aging is a highly prevalent phenomenon among the elderly population, and it may lead to a series of difficulties in communication. In Brazil, presbycusis has been indicated as the most frequent cause of hearing deficiencies among elderly people. Based on the international literature, the National Policy for the Handicapped[18,19] mentions a prevalence of hearing loss of about 30% in persons older than 65 years. Unfortunately, there is a large gap in the Brazilian literature regarding epidemiological population-based studies and data on hearing loss according to age and sex among the Brazilian population. Gates and Mills[18] determined that, among the general population, the incidence of hearing loss sufficiently severe to impair communication is 10% of all individuals. They also stated that this percentage rose to 40% among individuals older than 65 years. In the present study, individuals in both groups presented with lower hearing thresholds, particularly with regard to high-frequency sounds. However, the individuals exposed to radiotherapy presented with even lower thresholds than those of the control group. This suggests that, despite the ages and the physiological changes inherent to aging, their auditory systems were exposed to aggressive agents that caused the hearing loss to be greater as a consequence of the treatment received. Another study[20] described cochlear implantation in 3 patients treated for meduloblastoma who then experienced profound sensorineural hearing loss and chronic ear disease following treatment, suggesting that the hearing loss and auditory damage after oncological treatment can be very extensive.

In the study by Chen et al,[21] radiation doses of greater than 6000 cGy in the cochlea were the most significant factor for the presence of sensorineural hearing loss. Doses of 2000 to 3000 cGy in the cochlea led to notable hearing losses in 50% of patients in a study by Hermann et al,[15] and ototoxic effects occurred in 41.8% of their patients with head and neck tumors after radiotherapy, of whom 33.2% presented with complications in the outer ear, 28.6% in the middle ear, and 26.8% in the inner ear. In a study by Bhandare et al,[16] complications were attributed to the dose of radiotherapy that reached the auditory system, and the authors reported that the incidence of ototoxic effects increased with increasing doses of radiotherapy, particularly with doses ranging from 6000 to 6600 cGy. In the present study, the total dose ranged from 2000 to 9580 cGy, and the percentage of the auditory system that was included in the radiotherapy field ranged from 40% during the first phase of treatment to 16% during the second phase for both ears. A total dose of 6500 cGy was statistically significant for the presence of hearing loss.

In the general population, hearing complaints and the impact of hearing losses vary greatly and depend on individuals' lifestyles, their expectations, and even their general physical health. Among patients with cancer, much has been said about quality of life, but few studies have dealt with hearing loss and the limitations and difficulties encountered because of it.

After analyzing our 2 groups separately, we found that the individuals in the exposed group had more complaints, as shown by their answers on the HHIE questionnaire, than did individuals in the control group. In parallel, the individuals in the exposed group also presented with hearing losses more frequently, including losses of higher grade, thus demonstrating the same relationship as that observed by several other authors[22,23] who proved a statistically significant association between higher degrees of hearing loss and higher scores in the HHIE questionnaire. This suggests that the HHIE questionnaire is also capable of measuring hearing handicaps among patients with cancer.

Individuals with untreated hearing losses were more sorrowful, with more feelings of loneliness, depression, worry, anxiety, and paranoia.[22,24] They had fewer social activities and were less able to integrate information regarding their environment. Hearing loss affects individuals' psychosocial situation and, if untreated, contributes to social isolation, depression, and low self-esteem. It also seems to be a cofactor related to senile dementia.[17] As could be seen from the present study, the group of participants exposed to radiotherapy presented with greater hearing losses of higher grade and with more complaints. This is extremely important because behavioral patterns that are more depressive or that present greater tendencies for social isolation can sometimes be attributed to the cancer or to the functional sequelae of the treatment. Nonetheless, one must remember that hearing loss and hearing handicap may also lead to such behavior.

Hearing loss is still given little recognition and little value, and, for this reason, it is not always treated as a health abnormality. However, it is one of the biggest chronic problems among elderly people, and, as seen from the present study, the population with cancer is even more affected by this. Concern for the quality of life of patients undergoing cancer treatment is necessarily growing, and determination of hearing loss should form part of such investigations to enable better rehabilitation.

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Correspondence: Christiane Schultz, MS, Department of Audiology, Hospital do Câncer A. C. Camargo, Rua Professor Antonio Prudente 211, 01509-900 São Paulo, Brazil (chris_schultz1@yahoo.com.br; chris@hcancer.org.br).
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