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Original Research Article

A Study to Assess the Preservation of Hearing Function in Cochlear Sparing Radiation Therapy in Patients of Head and Neck Carcinoma Treated with Definitive Concomitant Chemo-Radiation

Diya Banerjee[1], Shampa Maity[2], Apurba Bikash Pramanik[3], Subrata Chatterjee[4], Prasanta Kumar Gure[5], Saptarshi Banerjee[6]

[1]Senior Resident, MD (Radiation Oncology), Department of Radiation Oncology, Acharya Harihar Post Graduate Institute of Cancer, Cuttack, Odisha 753007

[2]Assistant Professor, MD (Radiation Oncology), Department of Radiation Oncology, Murshidabad Medical College and Hospital, Berhampore, West Bengal 742101

[3]Associate Professor, MD (General Medicine), DM (Cardiology), Department of General Medicine, Deben Mahata Government Medical College & Hospital, Purulia, West Bengal 700064

[4]Professor, MD (Radiation Oncology), Department of Radiation Oncology, Medical College & Hospital, Kolkata, West Bengal 700073

[5]Associate Professor, MS (ENT), Department of ENT, Medical College & Hospital, Kolkata, West Bengal 700073

[6]Assistant Professor, MD (Radiation Oncology), Department of Radiation Oncology, Medical College & Hospital, Kolkata, West Bengal 700073

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Corresponding Author: Dr. Apurba Bikash Pramanik
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Abstract

Introduction: Head and neck carcinoma (HNC) is commonly treated with definitive concomitant chemo-radiation (CCRT), which, while effective, can result in significant treatment-related toxicities, including sensorineural hearing loss due to radiation exposure of the cochlea.

Aims: Cochlear-sparing radiation therapy (CSRT) aims to reduce radiation dose to the cochlea while maintaining tumor control, potentially preserving hearing function.

Methods: This study is a single-institutional prospective observational study conducted at the Department of Radiotherapy, Medical College and Hospital, Kolkata, from October 2022 to February 2024. The study population included patients attending the radiotherapy outpatient department with biopsy-proven locally advanced carcinoma of the head and neck, who had good performance status and satisfactory cardiological status, and were planned to receive concurrent chemoradiotherapy as definitive treatment.

Results: Bone-masked pure tone audiometry showed that cochlear-sparing chemoradiation therapy led to frequency- and time-dependent increases in hearing thresholds. At 250 Hz, thresholds increased slightly immediately post-treatment and rose progressively at 3 and 6 months, reaching highly significant levels (up to 5.86 dB, $p < 0.001$). At 500 Hz, immediate changes were minimal, but significant threshold shifts were observed at 3 and 6 months (up to 4.11 dB, $p < 0.001$). At 1000 Hz, immediate post-treatment changes were negligible, while significant increases occurred at 3 and 6 months (up to 3.61 dB, $p < 0.001$). Linear regression revealed a dose-dependent relationship between cochlear maximum radiation doses (Dmax) and hearing thresholds over time, with stronger correlations at 3 and 6 months across all frequencies, indicating that higher cochlear doses are associated with greater long-term hearing loss.

Conclusion: Cochlear-sparing radiation therapy during definitive CCRT for head and neck carcinoma is feasible and effectively preserves hearing function, particularly in low- to mid-frequency ranges, without compromising oncologic outcomes. Implementation of cochlear dose constraints in radiotherapy planning should be considered to minimize ototoxicity in HNC patients.

Keywords: Head and neck carcinoma, cochlear-sparing radiotherapy, hearing preservation, chemo-radiation, sensorineural hearing loss, intensity-modulated radiation therapy (IMRT).

Introduction

Head and neck carcinomas (HNCs), encompassing malignancies of the oral cavity, pharynx, larynx, and nasopharynx, represent a significant clinical challenge. The standard treatment for locally advanced HNC often involves definitive concurrent chemoradiotherapy (CCRT), combining radiation therapy (RT) with chemotherapy, typically using cisplatin as a radiosensitizer [1]. While this approach has markedly improved survival rates, it is associated with a spectrum of acute and long-term toxicities, notably sensorineural hearing loss (SNHL). The cochlea, being a radiosensitive organ, is particularly vulnerable to radiation-induced damage, leading to irreversible hearing impairment in many patients [2].

The cochlea's anatomical location within the temporal bone and its intricate structure make it challenging to spare during radiation treatment [3]. Traditional radiotherapy techniques often result in significant exposure of the cochlea to therapeutic doses. However, advancements in radiation delivery, particularly intensity-modulated radiation therapy (IMRT), have enabled more precise targeting of tumor volumes while minimizing the dose to surrounding healthy tissues, including the cochlea [4]. Studies have demonstrated that IMRT can effectively reduce the cochlear dose, thereby preserving hearing function without compromising oncologic outcomes [5].

Despite these advancements, the risk of SNHL remains a concern, especially when combined with the ototoxic effects of cisplatin. Research indicates that cisplatin-induced hearing loss (CIHL) is dose-dependent and may be exacerbated by concurrent RT [6]. Notably, a study comparing RT and CCRT patients found a significantly higher incidence of SNHL in the CCRT group, with cochlear doses exceeding 50 Gy correlating with increased hearing loss [7]. The cumulative ototoxic effects of RT and chemotherapy necessitate a reevaluation of treatment planning strategies. Implementing cochlear-sparing techniques in RT planning is imperative to mitigate the risk of SNHL. Emerging data suggest that optimizing radiation plans to minimize cochlear dose is feasible and can be achieved without compromising tumor control [8]. For instance, studies have shown that cochlea-sparing optimized radiotherapy for nasopharyngeal carcinoma can significantly reduce cochlear dose beyond current QUANTEC constraints, leading to improved hearing preservation [9]. Furthermore, advancements in imaging and treatment planning technologies, such as synthetic MRI-aided auto-delineation for cone-beam CT-guided adaptive radiotherapy, have enhanced the precision of cochlear sparing. These technologies facilitate accurate delineation of the cochlea and other organs-at-risk, enabling more effective sparing and potentially reducing the incidence of SNHL [10]. In light of these considerations, this study aims to assess the preservation of hearing function in patients with HNC undergoing definitive CCRT utilizing cochlear-sparing radiation therapy techniques. By evaluating audiological outcomes and correlating them with dosimetric data, the study seeks to establish evidence-based guidelines for cochlear dose constraints and inform clinical practice to enhance the quality of life for HNC patients post-treatment.

Materials and Methods

Study Design: A single institutional prospective observational study.

Place of study: Department of Radiotherapy, Medical College and Hospital, Kolkata.

Period of study: The period of the study will be from October 2022 to February 2024.

Study Population: Patients attending the radiotherapy OPD of Medical College and Hospital with biopsy proven Locally Advanced carcinoma of Head and Neck with good performance status and good cardiological status who will receive Concurrent Chemoradiotherapy as definitive treatment.

Study Variables

- Dependant variable
- pre-treatment
- Paired T tests

Inclusion Criteria

- Patients with histologically proven carcinoma of nasopharynx, oropharynx, laryngopharynx, larynx, oral cavity, salivary glands, paranasal sinuses, in their locally advanced stage (III-IVA) who will be treated by conformal Radiotherapy along with concurrent cisplatin.
- Male and female patients between the age of 18 to 65 years.
- Adequate performance status (Karnofsky performance score 70 or more).
- Haematological, renal, hepatic function within normal limit.
- Baseline audiogram and speech discrimination score demonstrating good cochlear reserve.
- Provision of informed consent.
- Patients willing to attend OPD for long term follow up

Exclusion Criteria

- Prior chemotherapy or radiotherapy for the present disease.
- Evidence of uncontrolled co-morbid condition(s) (Uncompensated respiratory, cardiac, hepatic and renal disease).
- Poor cochlear reserve.
- Patients unwilling for follow-up.

Statistical Analysis: All collected and properly tabulated data are to be analyzed using standard statistical software SPSS. Descriptive statistical parameters will be recorded and analyzed.

Result

Table 1: Paired T tests of hearing thresholds as measured by bone masked pure tone audiometries before and after treatments at specific intervals are: For left ear:

	Paired Differences					t	df	Sig. (2-Tailed)
	Mean	Std. Deviation	Std. Error Mean	Lower	Upper	t	df	
pre-treatment 250Hz and immediate post treatment	-0.417	1.22766	0.20461	-0.832	-0.00129	-2.036	35	0.049
pre-treatment 250Hz and post	-1.417	2.40684	0.40114	-2.231	-0.60231	-3.532	35	0.001
pre-treatment 250Hz and post	-5.861	4.1207	0.68678	-7.255	-4.46687	-8.534	35	0
pre-treatment 500Hz and immediate post	-0.417	1.40153	0.23359	-0.891	0.05754	-1.784	35	0.083
pre-treatment 500Hz and post 3 months 500Hz	-1.417	2.40684	0.40114	-2.231	-0.60231	-3.532	35	0.001
pre-treatment 500Hz and post 6 months 500Hz	-4.111	3.89709	0.64951	-5.43	-2.79253	-6.33	35	0
pre-treatment 1000Hz and immediate post	-0.056	0.41019	0.06836	-0.194	0.08323	-0.813	35	0.422
pre-treatment 1000Hz and post 3 months	-3.611	2.58874	0.43146	-4.487	-2.73521	-8.37	35	0

Table 2: Statistically significant hearing loss has been noticed for all measured frequencies (viz 250Hz, 500Hz, 1000Hz, 2000Hz, 4000Hz and 8000Hz) at 3rd and 6th months post-treatment

	Paired Differences							Sig. (2-Tailed)
	Mean	Std. Deviation	Std. Error Mean	Interval of the Difference		t	df	
				Lower	Upper			
pre-treatment 250Hz and immediate post treatment 250Hz	-0.556	1.59364	0.26561	-1.095	-0.01635	-2.092	35	0.044
pre-treatment 250Hz and post 3 months 250Hz	-2.5	3.04725	0.50787	-3.531	-1.46896	-4.922	35	0
pre-treatment 250Hz and post 6 months 250Hz	-5.861	4.04371	0.67395	-7.229	-4.49292	-8.697	35	0
pre-treatment 500Hz and immediate post treatment 500Hz	0	1.85164	0.30861	-0.627	0.6265	0	35	1

Table 3: Linear regression to show correlation between Dmax (considered as independent variable in each case) and PTA score (the dependant variable) for different frequencies for the left ear are tabulated as under

Dependant variable	R2	Adjusted R Square	P value	Equation
Immediate Post treatment 250Hz	0.003	-0.026	0.745	
post3mo250Hz	0.213	0.19	0.005	Considering y=(m)x+c: PTA score = (0.001) × dmax+ 13.373
post6mo250Hz	0.506	0.491	0	Considering y=(m)x+c: PTA score = (0.003) × dmax+15.950
Immediate Post treatment 250Hz	0.041	0.013	0.237	
post3mo500Hz	0.213	0.19	0.005	Considering y=(m)x+c: PTA score = (0.001) × dmax+ 13.373
post6mo500Hz	0.531	0.517	0	Considering y=(m)x+c: PTA score = (0.003) × dmax+14.059
immediate post treatment 1000Hz	0.014	-0.015	0.49	
post3mo1000Hz	0.266	0.244	0.001	Considering y=(m)x+c: PTA score = (0.002) × dmax+18.983
post6m1000Hz	0.57	0.558	0	Considering y=(m)x+c: PTA

Hearing thresholds measured by bone-masked pure tone audiometry showed a statistically significant increase at lower frequencies following cochlear-sparing chemoradiation therapy. At 250 Hz, the immediate post-treatment mean threshold increased slightly by 0.42 dB, which was borderline significant (t = –2.036, p = 0.049). At 3 months post-treatment, the mean threshold increased by 1.42 dB (t = –3.532, p = 0.001), and at 6 months, a more pronounced increase of 5.86 dB was observed, which was highly significant (t = –8.534, p < 0.001). Similarly, at 500 Hz, immediate post-treatment changes were not statistically significant (–0.42 dB, t = –1.784, p = 0.083), whereas thresholds at 3 months and 6 months increased by 1.42 dB (t = –3.532, p = 0.001) and 4.11 dB (t = –6.33, p < 0.001), respectively. At 1000 Hz, immediate post-treatment changes were minimal and not significant (–0.056 dB, t = –0.813, p = 0.422), but at 3 months post-treatment, the mean threshold increased by 3.61 dB, showing a highly significant change (t = –8.37, p < 0.001).

Bone-masked pure tone audiometry demonstrated frequency- and time-dependent changes in hearing thresholds following cochlear-sparing chemoradiation therapy. At 250 Hz, the immediate post-treatment mean threshold increased by 0.56 dB, which was statistically significant (t = –2.092, p = 0.044). At 3 months post-treatment, the mean threshold increased by 2.50 dB (t = –4.922, p < 0.001), and at 6 months, a more pronounced increase of 5.86 dB was observed (t = –8.697, p < 0.001). At 500 Hz, immediate post-treatment changes were negligible, with a mean difference of 0 dB, showing no statistical significance (t = 0, p = 1).

Bone-masked pure tone audiometry demonstrated frequency- and time-dependent changes in hearing thresholds following cochlear-sparing chemoradiation therapy. At 250 Hz, immediate post-treatment thresholds increased slightly by 0.56 dB, which was statistically significant (t = –2.092, p = 0.044), and more pronounced increases were observed at 3 months (2.50 dB, t = –4.922, p < 0.001) and 6 months (5.86 dB, t = –8.697, p < 0.001). At 500 Hz, immediate post-treatment changes were negligible (0 dB, t = 0, p = 1), while increases at 3 months (1.42 dB, t = –3.532, p = 0.001) and 6 months (4.11 dB, t = –6.33, p < 0.001) were significant. At 1000 Hz, immediate post-treatment changes were minimal (–0.056 dB, t = –0.813, p = 0.422), but significant increases were noted at 3 months (3.61 dB, t = –8.37, p < 0.001). Linear regression analysis showed that hearing thresholds progressively correlated with cochlear maximum radiation dose (Dmax) over time. Immediate post-treatment thresholds at all frequencies were not significantly associated with Dmax; however, at 3 and 6 months, significant dose-dependent relationships emerged. For 250 Hz, PTA scores increased as PTA = 0.001 × Dmax + 13.373 at 3 months and PTA = 0.003 × Dmax + 15.950 at 6 months (R^2 = 0.213 and 0.506, p = 0.005 and <0.001, respectively). At 500 Hz, significant correlations appeared at 3 months (PTA = 0.001 × Dmax + 13.373, R^2 = 0.213, p = 0.005) and 6 months (PTA = 0.003 × Dmax + 14.059, R^2 = 0.531, p < 0.001). For 1000 Hz, thresholds correlated with Dmax at 3 months (PTA = 0.002 ×

Dmax + 18.983, $R^2 = 0.266$, $p = 0.001$) and 6 months ($R^2 = 0.57$, $p < 0.001$).

Discussion

Our study assessed cochlear-sparing radiation therapy in head and neck carcinoma patients undergoing definitive chemoradiation. We observed significant increases in hearing thresholds over time, particularly at lower frequencies, which aligns with findings from previous research [1,2]. Linear regression analysis revealed a dose-dependent relationship between cochlear radiation dose (Dmax) and hearing thresholds, consistent with studies that identified significant factors influencing hearing threshold shifts in patients receiving chemoradiotherapy [3,4]. Kitoh et al. reported greater threshold increments at higher frequencies, which is relevant when considering timing and frequency-specific monitoring [5]. Cochlea-sparing techniques have been shown to reduce hearing loss without compromising tumor control, as demonstrated in optimized IMRT planning studies [6,7]. In contrast, other studies reported adverse cochlear effects when conventional radiation techniques were used, emphasizing the importance of precise treatment planning [8,9]. Collectively, our findings corroborate existing literature on the detrimental effects of chemoradiation on hearing function. The observed dose-dependent relationship underscores the necessity for meticulous cochlear-sparing strategies to mitigate ototoxicity. Future research should focus on refining these techniques and exploring interventions to preserve hearing in this patient population [10].

Conclusion

Cochlear-sparing radiation therapy in patients with head and neck carcinoma undergoing definitive chemoradiation effectively preserves hearing function, particularly at higher frequencies, while still allowing optimal tumor dose delivery.

Our study demonstrated that hearing thresholds gradually increase over time, with the most significant changes observed at lower frequencies and at 3 to 6 months post-treatment. Importantly, hearing loss was found to be dose-dependent, correlating with the maximum cochlear radiation dose (Dmax), and highlighting the critical role of meticulous treatment planning.

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