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The Effects of Tympanomastoid Paragangliomas on Hearing and the Audiological Outcomes after Surgery over a Long-Term Follow-Up

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Key Words
Tympanomastoid paraganglioma · Preoperative hearing · Audiological outcomes · Surgical treatment · Glomus tumor

Abstract
The primary goals of surgery of tympanomastoid paragangliomas (TMPs) are tumor eradication and hearing preservation. Though the surgical management of TMPs has been dealt with widely in the literature, the effects of TMPs themselves on preoperative hearing and the audiological outcomes after surgery have not been analyzed in detail. This article comprehensively evaluates the preoperative hearing and the long-term hearing outcomes after surgery of TMPs. This study is based on a study population of 145 patients which is the largest reported in the literature. The surgical approaches for all patients with TMPs were formulated according to an algorithm developed by the authors. Complete tumor removal with excellent hearing results can be achieved by approaching the tumor classes by the right surgical technique. TMPs could possibly induce sensorineural hearing loss in higher frequencies, and future studies could be directed towards this.

Introduction

Temporal bone paragangliomas can be classified as tympanomastoid paragangliomas (TMPs) and tympanojugular paragangliomas. TMPs, commonly referred to as 'glomus tympanicum' tumors, are the most common primary neoplasm of the temporal bone [Forest et al., 2001]. The term 'glomus' itself is inaccurate [Fisch and Chang, 2001; Gulya, 1993], and therefore its use must be discouraged. We maintain that the above terminology be consistently used to replace 'glomus' while reporting in the literature.

Despite the fact that the management of TMPs is challenging, surgery remains the most effective treatment in the management of all types of TMPs, and any reference to radiotherapy in the management of this group of tumors must be disregarded. The primary goals of surgery are tumor eradication and hearing preservation. In the past, it was difficult to achieve this twin objective, and most surgeons performed radical surgeries to achieve complete eradication or opted for radiotherapy in an attempt to preserve hearing. However, with the advent of modern microsurgical and imaging tools, it is today pos-

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Table 1. Modified Fisch and Mattox classification of TMPs

Class		Description
A		Tumors limited entirely to the middle ear
	A1	Tumors completely visible on otoscopic examination
	A2	Tumor margins are not visible on otoscopy; tumor may extend anteriorly up to the eustachian tube and/or to the posterior mesotympanum
B		Tumors limited to the tympanomastoid segment (middle ear cleft) of the temporal bone
	B1	Tumors filling the middle ear with extension into the hypotympanum and tympanic sinus
	B2	Tumors filling the middle ear with extension into the mastoid and medially to the mastoid segment of the facial nerve
	B3	Tumors filling the middle ear with extension into the mastoid with erosion of the carotid canal

Table 2. Algorithm for the management of TMPs at the Gruppo Otologico

Class A	A1	Transcanal approach
	A2	Postauricular transcanal approach
Class B	B1	Canal wall up mastoidectomy with posterior tympanotomy
	B2	Canal wall up mastoidectomy with posterior tympanotomy and subfacial recess tympanotomy
	B3	Subtotal petrosectomy with middle ear obliteration

sible to precisely locate the tumor and accurately plan a surgical strategy, thereby affecting good outcomes both in terms of tumor control and hearing. In this direction, we modified the Fisch and Mattox classification [1988] (table 1) to make it surgically relevant and suggested an algorithm for the management of this set of tumors (table 2) [Sanna et al., 2010]. This algorithm describes precise surgical approaches for specific tumor classes. Details of the surgical approaches and techniques are described elsewhere [Sanna et al., 2010, 2012, 2013]. Though the surgical management of TMPs has been dealt with widely in the literature, the effects of TMPs themselves on preoperative hearing and the audiological outcomes after surgery have not been analyzed in detail. In this paper, we discuss in detail the preoperative hearing and the postoperative audiological results with reference to tumor class, surgical approaches and hearing frequencies in the largest series of TMPs presented in the modern English literature.

Materials and Methods

This retrospective study was conducted according to the code of ethics in the Declaration of Helsinki. The medical records of 145 patients who were diagnosed with TMPs and managed at the Gruppo Otologico, Piacenza-Rome (Italy), between December 1988 and July 2013 were reviewed. The clinical and radiological findings were recorded in all patients. The class of tumor and the type of surgery performed were noted. Tumors were staged according to the modified Fisch and Mattox classification [1988] (table 1). At the Gruppo Otologico the surgical approaches for all patients with TMPs are formulated according to our management algorithm as shown in table 2. The surgical techniques have been described elsewhere [Sanna et al., 2010, 2012, 2013]. In class A1–B2 tumors where the ossicular chain was eroded, the tympanic membrane was reconstructed with a temporalis fascia graft with a Silastic sheet placed between the graft and the medial wall of the middle ear, and an ossicular reconstruction with autologous incus was planned as a second stage surgery after 6 months. Pure tone averages were noted for air conduction (AC) and bone conduction (BC) calculated before surgery and at the last available follow-up as the mean of 500-, 1,000-, 2,000- and 4,000-Hz thresholds. Air-bone gaps (ABGs) were calculated using AC and BC values determined at the same time. The follow-up records were noted. Follow-up period was defined as period of time from surgery to the most recent office visit.

Statistical Analysis

Data was analyzed with a statistical software program (SPSS Statistics for Windows, version 20, Chicago, Ill., USA). Continuous data was summarized as mean with 95% confidence intervals (95% CIs). Categorical data was presented as frequencies and percentages. Kolmogorov-Smirnov and Shapiro-Wilk tests were used to verify data for normal distribution. p values below 0.05 were considered significant.

Results and Observations

Of a total of 382 patients with temporal bone paragangliomas who were managed at the Gruppo Otologico, a quaternary referral center for otology and skull base surgery, 145 were diagnosed to have TMPs (modified Fisch and Mattox classes A and B); 138 (95%) of the study population were females, and the rest were males. The median age of the population was 55 years (range, 13–82 years).

Tumor Class and Surgical Procedure

Thirty-four (23.5%) patients were diagnosed to have TMP class A1 tumors, 46 (31.7%) to have class A2 tumors, 22 (15.2%) to have class B1, 18 (12.4%) to have class B2 and 25 (17.2%) to have class B3 tumors. All class A1 tumors were operated with a transcanal approach, class A2 with a postauricular transcanal approach and class B1 with a canal wall up mastoidectomy with a posterior tympanotomy. Ten of the 18 patients with class B2 tumors underwent a canal wall up mastoidectomy with a posterior tympanotomy and a subfacial recess tympanotomy, and the remaining 8 patients underwent subtotal petrosectomy (STP) with middle ear obliteration. All but 1 of the patients with a class B3 tumor underwent STP with middle ear obliteration. In the remaining case, an infratemporal fossa approach class A was performed combined with a transcochlear approach for a large class B3 tumor which had infiltrated the facial nerve which was sacrificed and reconstructed using a sural nerve graft. In another patient who underwent STP, the facial nerve was sacrificed and a facial-hypoglossal anastomosis was made later. One patient who had undergone radiotherapy elsewhere for a class B3 tumor also underwent STP.

Follow-Up

The follow-up (consisting of clinical evaluation, hearing tests and serial CT scans) of the series ranged from 6 to 230 months (mean, 48.4 ± 51.1 months).

Hearing Results

Hearing results were available for analysis in 131 patients. Eleven patients with previous anacusis on the side of the tumor were excluded from the study. Three patients who were followed up in their countries of origin were excluded from the postoperative hearing results analysis. The ossicular chain was found to be intact in all cases of A1 and A2 tumors. In B1 tumors, 6 cases were found to have ossicular erosion and were reconstructed in a second stage.

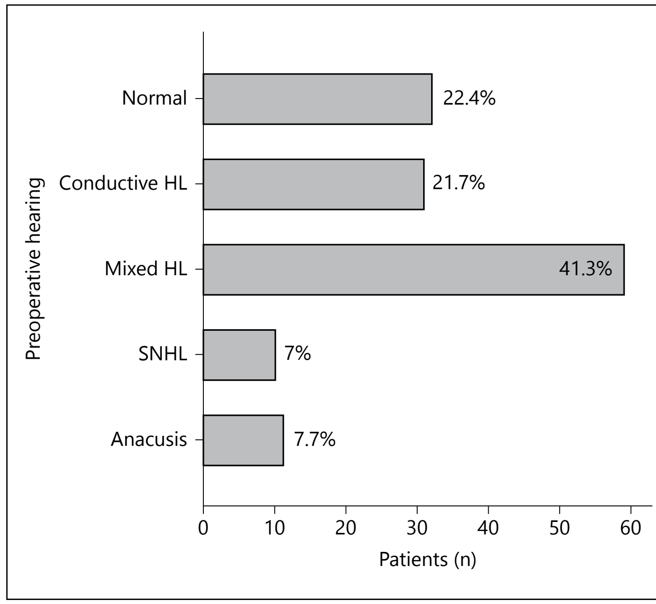

Fig. 1. Bar diagram showing the type of preoperative hearing in the study sample. HL = Hearing loss.

Preoperative Type of Hearing

The incidence of normal hearing, conductive hearing loss, mixed hearing loss, sensorineural hearing loss (SNHL) and anacusis were 22.4, 21.7, 41.3, 7 and 7.7%, respectively (fig. 1). The distribution of the anacoustic patients was asymmetrical between tumor classes, with 1 patient in class A1, 2 patients in class A2, 1 patient in class B2 and 7 patients in class B3. Four of these patients had anacusis due to previous surgery and 7 due to tumor erosion of the cochlea.

Analysis by Tumor Class

Preoperative and postoperative hearing analyses were done according to the modified Fisch and Mattox classification of TMPs. Table 3 shows means and 95% CIs for preoperative and postoperative mean AC, mean BC and the ABG in comparison with individual tumor classes. The AC and BC results are also graphically visualized in figure 2. It can be observed that preoperative hearing worsened with progression of tumor class. Postoperatively, the mean AC showed an improvement in all categories except in classes B2 and B3, which corresponded to the classes where STP patients were included. In class B3 there was a significant worsening of the AC ($p = 0.001$, Wilcoxon test). There was no statistically significant difference in the improvement of postoperative AC among the classes A1–B1 ($p = 0.27$, Kruskal-Wallis test). Postop-

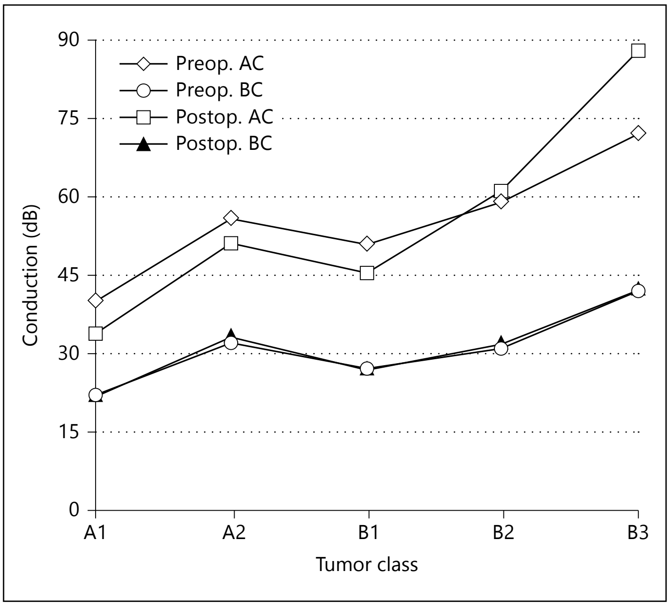

Fig. 2. Line chart representing the preoperative and postoperative AC and BC for each tumor class.

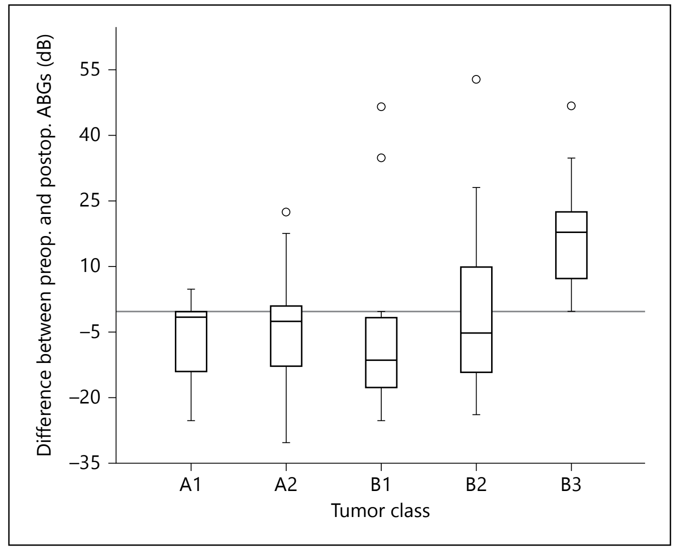

Fig. 3. Boxplot showing the difference between pre- and postoperative ABGs according to tumor class. Boxes show median, interquartile range, maximum and minimum. The horizontal line represents the value 0 dB.

Table 3. Means and 95% CIs for pre- and postoperative AC and BC, and differences of values before and after surgery in AC and BC in individual tumor classes

Tumor class	AC			BC			ABG		
	preop.	postop.	difference	preop.	postop.	difference	preop.	postop.	difference
A1	40.56 33 to 48	34.69 29 to 40	–5.87 –9 to –2	22.42 17 to 27	22.27 17 to 27	–0.15 –1.4 to 1	18.14 13 to 23	12.42 10 to 15	–5.72 –9 to –3
A2	56.09 47 to 63	51.58 44 to 59	–4.51 –9 to –2	32.40 27 to 37	33.07 28 to 38	0.67 0.04 to 1	23.69 19 to 28	18.50 14 to 23	–5.18 –9 to –1
B1	51.84 43 to 61	45.20 34 to 56	–6.64 –14 to 1	27.56 20 to 35	27.61 20 to 35	0.05 –0.8 to 0.9	24.28 19 to 29	17.58 10 to 25	–6.70 –15 to 1
B2	59.55 48 to 71	61.63 48 to 75	2.07 –8.5 to 13	31.39 24 to 39	32.92 26 to 40	1.52 –0.2 to 3	28.16 23 to 33	28.70 19 to 38	0.5 –10 to 11
B3	72.36 64 to 80	88.27 79 to 98	15.91 9 to 23	42.70 37 to 49	42.77 37 to 48	0.06 –1.6 to 1.8	29.65 25 to 34	45.50 40 to 51	15.84 9 to 23

eratively, the mean BC showed a slight deterioration in all classes, ranging from 0.05 to 1.5 dB by average, with the exception of class A1 where there was an average improvement of 0.1 dB.

Regarding the ABG, there was a statistically significant reduction in classes A1, A2 and B1 ($p < 0.05$, Wilcoxon test) In class B2, there was a minimum deterioration, which was not statistically significant ($p = 0.81$), whereas in class B3, there was a significant deterioration in ABG ($p = 0.002$) as a consequence of the surgical technique (fig. 3).

Analysis by Surgical Categories

We also sought to identify the impact of surgical techniques on hearing. For this we classified hearing preservation surgery (HPS) methods into one group and STP

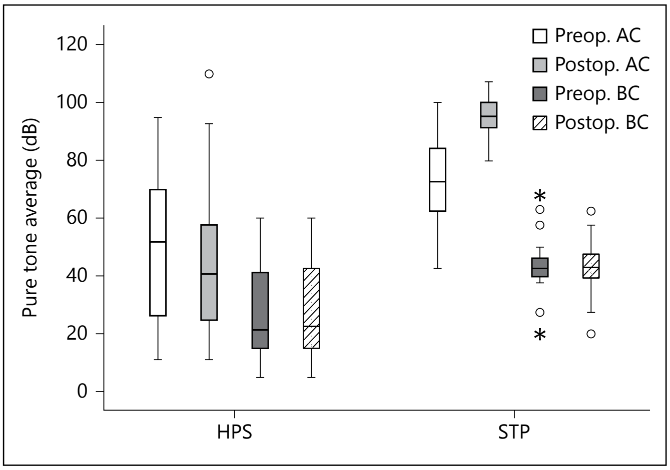

Fig. 4. Boxplots showing median pure tone average for AC and BC both pre- and postoperatively according to the surgical approach.

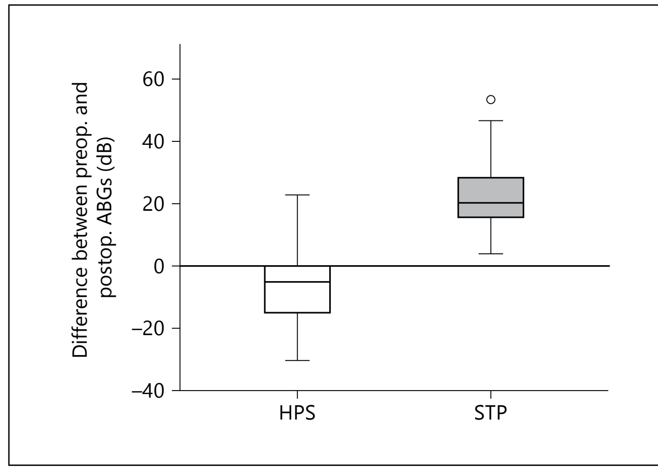

Fig. 5. Boxplot showing the difference between pre- and postoperative ABGs in patients who underwent HPS versus STP.

Table 4. Means and 95% CIs for preoperative and postoperative AC, BC and ABG according to the surgical approach

	AC			BC			ABG		
	preop.	postop.	difference	preop.	postop.	difference	preop.	postop.	difference
HPS	50.01 46 to 54	42.87 39 to 47	–7.13 –9 to –5	27.42 24 to 30	27.82 25 to 31	0.39 –0.1 to 0.9	22.58 20 to 25	15.04 13 to 17	–7.53 –9 to –6
STP	72.55 66 to 79	95.87 93 to 99	23.32 18 to 28	43.43 39 to 47	43.80 40 to 48	0.3 –1 to 2	29.11 25 to 33	52.07 49 to 55	22.95 17 to 28

into another and compared their effect on hearing. Table 4 shows the preoperative and postoperative hearing results according to the surgical approach. Figure 4 shows boxplots for pre- and postoperative AC and BC in both groups. Preoperatively, both AC and BC (mean pure tone averages) were significantly better in the HPS group when compared to patients who underwent STP ($p = 0.0001$, Mann-Whitney U test). Postoperatively, AC improved in the HPS group by 7.13 dB (95% CI, 5–9 dB) and deteriorated in the STP group by 23.32 dB (95% CI, 18–28 dB) as a logical consequence of the surgery. This difference was statistically significant ($p = 0.0001$, Mann-Whitney U test). However, it can be seen that STP caused a mean decrease in AC of only 23.32 dB because this group already had a greatly deteriorated AC as a consequence of the progressive disease. Postoperatively, BC remained unchanged in both groups ($p > 0.05$, Wilcoxon test), and there were no statistical differences in the average worsening in BC for either group ($p = 0.77$, Mann-Whitney U test), proving that STP does not imply any higher risk of worsening BC.

Figure 5 shows boxplots for the difference between preoperative and postoperative ABGs in both groups. It can be seen that most patients who underwent HPS experienced a reduction of ABG whereas all the patients who underwent STP experienced an increase in ABG. It can be observed from table 4 that, postoperatively, the ABG improved from 22.58 to 15.04 dB (with an average decrease of –7.53 dB) in the HPS group. In contrast, patients who underwent STP experienced an average deterioration of 22.95 dB in their ABG as an expected consequence of the surgery ($p = 0.0001$, Mann-Whitney U test). It can also be noted that the preoperative ABG was significantly higher (6.53 dB on average) in the STP group than in the HPS group ($p = 0.012$, Mann-Whitney U test).

Figure 6 shows the overall postoperative changes in ABG in patients after excluding those who underwent STP. Preoperatively, the average ABG was <10 dB in 29

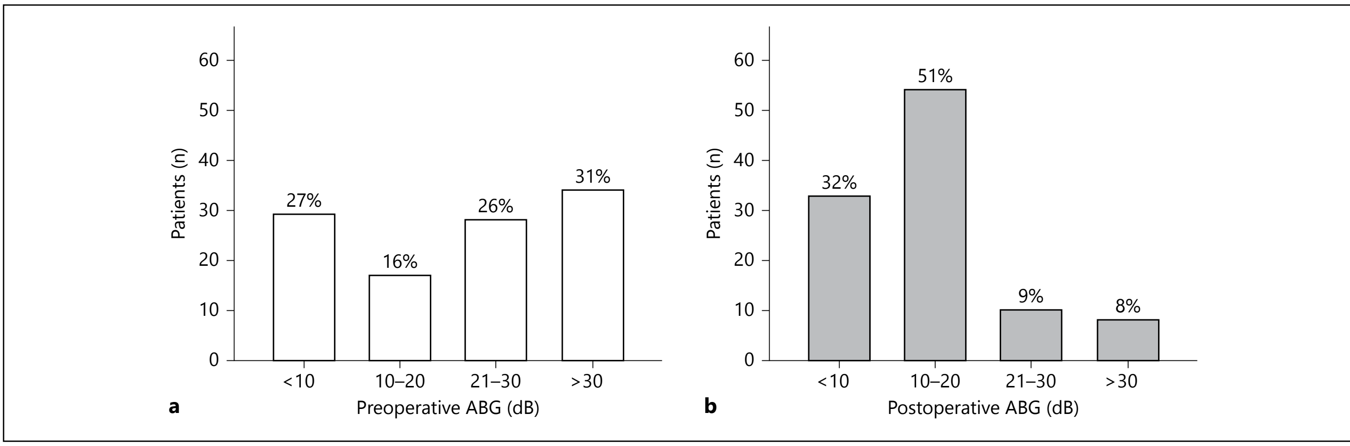

Fig. 6. a, **b** Overall pre- and postoperative ABG results in patients excluding STPs.

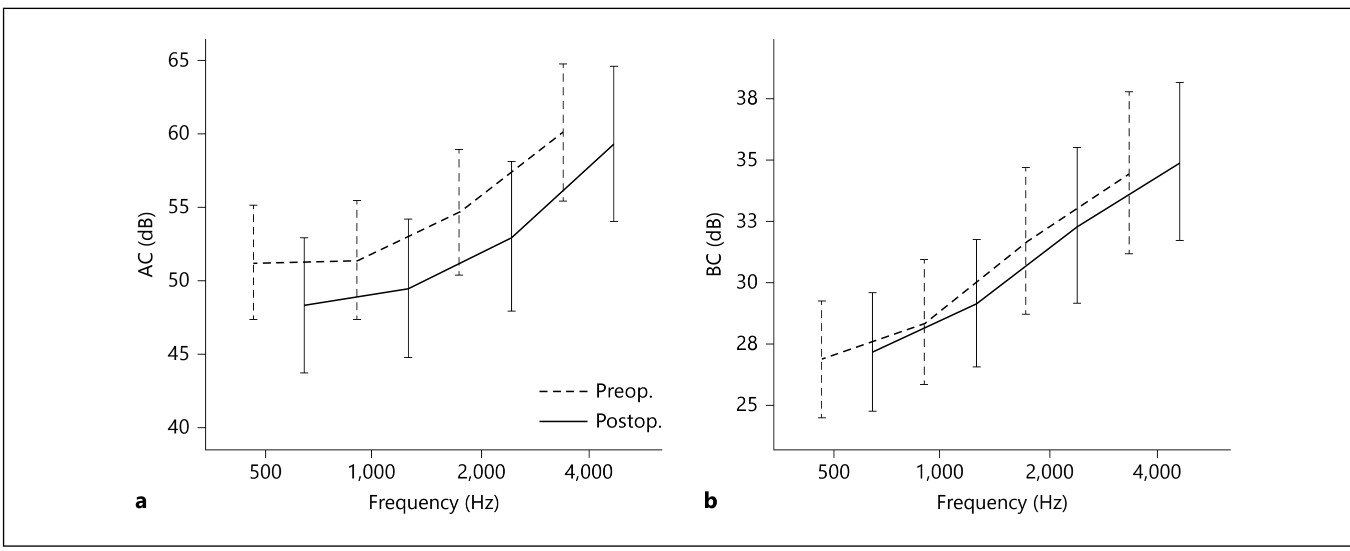

Fig. 7. Changes in AC (**a**) and BC (**b**) at frequencies of 500, 1,000, 2,000 and 4,000 Hz. The error bar plots represent the mean and the 95% CI.

(27%) patients, between 10 and 20 dB in 17 (16%) patients, between 21 and 30 dB in 28 (26%) patients and >30 dB in 34 (31%) patients. Postoperatively, the ABG was <10 dB in 33 (32%) patients, between 10 and 20 dB in 54 (51%) patients, between 21 and 30 dB in 10 (9%) patients and >30 dB in 8 (8%) patients. It can be noted that 83% of the patients had a recovery of ABG to less than 20 dB.

Analysis of Preoperative BC by Frequency

The postoperative changes in both AC and BC according to frequencies of 500, 1,000, 2,000 and 4,000 Hz are depicted in figure 7. It can be seen that AC was significantly improved in all frequencies after surgery ($p < 0.0001$, Wilcoxon test), with maximum improvement seen at 500 Hz (9.19 dB). On the other hand, minimum changes were observed in BC, ranging from –0.05 to +0.5 dB. These changes were not statistically significant in any of the hearing frequencies ($p > 0.05$, Wilcoxon test).

The preoperative BC at pure tone frequencies of 500, 1,000, 2,000 and 4,000 Hz was then analyzed according to tumor classes (fig. 8). It can be seen that across all classes there was a tendency to affect the higher frequencies more than the lower frequencies. In smaller tumors, e.g. class A1, the mean preoperative BC was 20.15 dB at

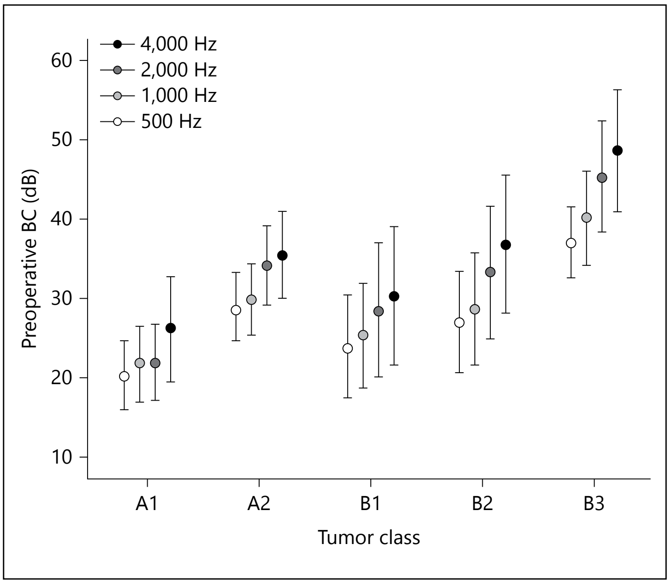

Fig. 8. Error bar plots showing preoperative BC at frequencies of 500, 1,000, 2,000 and 4,000 Hz for individual tumor classes. The bars represent the mean and the 95% CI.

500 Hz and 36.94 dB at 4,000 Hz. Similarly in class B3, the mean preoperative BC was 26.06 dB at 500 Hz and 48.61 dB at 4,000 Hz. This difference is statistically significant ($p < 0.02$) in all classes. It can also be appreciated from figure 8 that for each hearing frequency, the mean BC decreases with higher tumor classes. Thus, combining tumor class and hearing frequency we obtained a spectrum of audiograms in which it was seen that the principal afflictions were in big tumors in high frequencies and the least afflictions were found in small tumors in low frequencies ($p = 0.001$).

Discussion

Almost all articles on TMPs focus only on the surgical aspects conveying very little importance to the analysis of hearing before and after surgery. The reported incidence of normal hearing, conductive hearing loss, mixed hearing loss and SNHL in TMPs is 11.1–34, 49–50, 11–18.7 and 5–22.2%, respectively [Jackson et al., 1989; Forest et al., 2001; Mahadevaiah et al., 2007]. Similarly, in our series, their incidences were 22.4, 21.7, 41.3 and 7%. In addition, we had a 7.7% incidence of anacoustic patients (fig. 1).

While other series have not analyzed hearing according to tumor classes, it can be observed in our series that preoperative hearing worsened with progression of tumor class (table 3; fig. 2). Postoperatively, the mean AC showed an improvement in classes A1–B2. This points to the fact that despite the size of the tumors, the application of the appropriate surgical technique for tumor classes led to improvement in postoperative AC in all tumor classes. Similarly, there was an improvement in ABG in classes A1–B2 (fig. 3).

While classes A1–B2 can be managed by HPS, B3 tumors need a more radical approach by way of STP. However, our analysis of hearing results has shown that even in STP, the hearing loss before and after surgery is moderate and acceptable. As pointed out before (table 4; fig. 4, 5), STP caused a mean decrease in AC of only 22.95 dB because in this group patients already had a greatly deteriorated AC as a consequence of the progressive disease. Likewise, postoperatively there was no statistical difference in the average changes in BC between HPS and STP, proving that STP did not imply any higher risk of worsening BC either. The average postoperative improvement in ABG in the HPS group was 7.53 dB (range, 6–9 dB) while in the patients who underwent STP there was a deterioration of ABG by 22.95 dB postoperatively as an expected consequence of the surgery. It must also be noted that the preoperative ABG was significantly higher (6.53 dB on average) in the STP group than in the conservative surgery group.

In addition, in the HPS group, the percentage of patients with ABG <20 dB increased from 43% preoperatively to 83% postoperatively, without changes in BC. It can be inferred that good functional results in terms of ABG closure can be offered to a high percentage of patients with TMP from classes A1 to B2. Definitively, these hearing results cannot be offered by any other modalities of treatment like radiotherapy. Upon analyzing the postoperative improvement in both AC and BC according to frequencies of 500, 1,000, 2,000 and 4,000 Hz (table 5; fig. 7), it was seen that AC was significantly improved in all frequencies after surgery ($p < 0.0001$, Wilcoxon test), with maximum improvement occurring at 500 Hz. Changes were also observed in all frequencies in BC though they were not statistically significant. This points to the fact that the selection of surgeries for individual tumor classes was beneficial across all frequencies of hearing.

As mentioned above, all series reporting on TMPs have recorded various degrees of deterioration in BC in TMPs [Jackson et al., 1989; Forest et al., 2001; Mahadevaiah et al., 2007]. In our series, when the preoperative BC at pure tone frequencies of 500, 1,000, 2,000

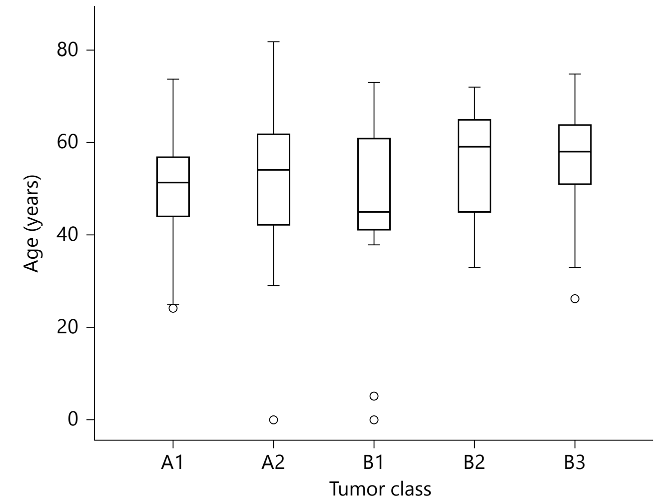

Fig. 9. This boxplot shows that the age distribution was homogeneous between tumor classes (p = 0.12, Kruskal-Wallis test).

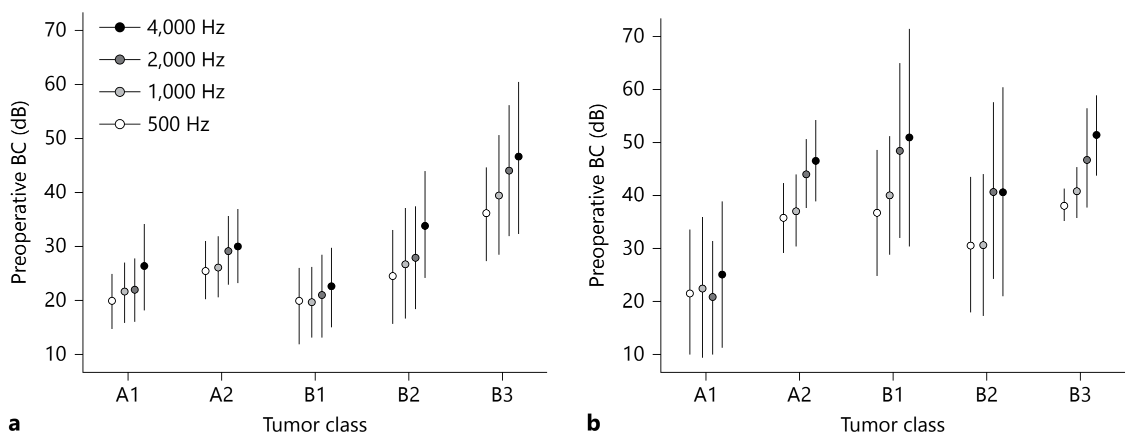

Fig. 10. Error bar diagrams showing mean BC pure tone average in patients below 60 years old (**a**) and above (**b**). It can be seen that once the sample is split by age higher frequencies remain affected to a greater extent than lower frequencies for every tumor class.

and 4,000 Hz was analyzed according to tumor classes (fig. 8), it was seen that the higher frequencies were affected more than the lower frequencies in all tumor classes. We tried to determine if this was an effect of the tumor per se or other confusing factors like presbyacusis, which is well known to predominantly affect high frequencies. To this end, we first confirmed the homogeneity of age distribution between tumor classes (p = 0.12, Kruskal-Wallis test; fig. 9). Secondly, we sought to eliminate the effect of presbyacusis. Considering the onset of presbyacusis to be around 60 years [Moscicki et al., 1985; Dayasiri et al., 2011], we analyzed if the pattern was maintained when the study sample was split at 60 years. It was seen that the results still remained statistically significant in the group of patients below 60 years, once the effect of presbyacusis was minimized (fig. 10). Hence it can be inferred that both big and small tumors affect higher frequencies more than lower frequencies once other potential confusing factors are eliminated.

Once it is established that there is a possibility that TMPs could induce a sensorineural damage at the higher frequencies, the probable reasons for this have to be ascertained. One potential cause could be the mass effect produced by the tumoral mass over the round window. The pressure of the tumor on the round window could have a role to play in the initiation of SNHL in TMP patients. In fact, it has been reported earlier that a SNHL produced by glomus tumors could be due to a cochlear or oval window fistula [Jackson et al., 1989]. Another possible reason could be catecholamine-secretion-induced SNHL. Based on the presence of catecholamines and neuropeptides, paraganglia are included in the amine precursor uptake and decarboxylase system, which has more recently been referred to as the diffuse neuroendocrine system [Kau and Arnold, 1996]. Though TMPs have been shown to contain intracellular granules suggestive of catecholamine secretion [Dickens et al., 1982], a functional endocrine output by them is speculative [O'Leary et al., 1991]. However, it can be conjectured that even small amounts of catecholamine secretion will be sufficient to induce a sensorineural damage due to the close proximity of the tumor to the round window. Catecholamines, especially epinephrine, are known to be capable of inducing sensorineural damage due to a vasoconstrictive effect [Miller et al., 1994]. Dopamine, another catecholamine, is also known to play a role in cochlear neurosecretory physiology [Puel, 1995]. Future studies could be directed towards this matter.

Conclusion

In this report we have comprehensively analyzed the hearing results in TMPs according to tumor class, surgical procedures and hearing frequencies. Surgery offers excellent hearing outcomes in terms of improved ABG and preservation of BC. Complete tumor removal with hearing preservation in TMPs can be achieved by approaching the tumors by the right surgical technique as described in our surgical algorithm. TMPs could possibly induce SNHL in higher frequencies, and future studies could be directed towards this.

Disclosure Statement

Conflict of interest and financial disclosures: none.

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