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Sporadic vestibular schwannoma: correlation between tumour size, hearing levels, age and radiologic features in 384 patients

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ABSTRACT

Objective: The aim of this study was to delineate characteristics of patients diagnosed with unilateral sporadic vestibular schwannoma. Symptomatology and MR imaging were correlated to hearing levels, tumour size, age, and radiologic features.

Methods: Retrospective study in a tertiary referral centre for neurotology and skull base surgery on 384 patients with a unilateral sporadic vestibular schwannoma in the cerebellopontine angle. Patients with intralabyrinthine schwannoma, neurofibromatosis type 2, meningiomas, and patients already treated elsewhere, were excluded from analyses.

Results: Age ranged from 11 to 92 years (mean age of 52 years). At presentation, 75% complained of ipsilateral subjective hearing loss, 56% of tinnitus, 41% of vertigo, 19% of ear fullness. A cystic component was observed in 21%, brainstem compression in 33%. Tumour size included 31% intracanalicular, 20% small, 28% medium, 13% moderately large, 6% large and 2% giant tumours. A weak positive correlation between tumour size and hearing loss was observed. We also noticed a weak negative correlation between age and tumour size.

Conclusion: Our series confirms subjective hearing loss being the main presenting complaint of sporadic vestibular schwannoma at any age. Nevertheless, more than half of our cases presented initially with tinnitus. This emphasizes the importance of imaging for tinnitus and hearing loss in patients. Although all sizes of tumour can present with all types of hearing loss, there is a weak positive correlation between size and hearing loss. Furthermore, we observed a significant negative correlation between age and tumour size. The presence of cystic components is associated with larger tumour size but not with hearing loss.

Keywords: Acoustic neuroma, age, hearing loss, symptomatology, vestibular schwannoma

Introduction

Vestibular schwannoma are benign tumours arising from Schwann cells of the eighth cranial nerve (vestibulocochlear nerve). Incidence rates are estimated between 19 per million and 42 per million (1,2) Since the popularisation of MR imaging in medicine, this pathology is probably diagnosed more often in a smaller stage as an incidentaloma. Before, auditory brainstem response (ABR) and computer tomography (CT) were the gold standard. Although an overall sensitivity of 90% to detect a vestibular schwannoma by ABR is estimated; multiple studies showed a decrease in sensitivity with tumour size. Tumours less than 1 cm can hardly be detected through ABR, in contrast to MR imaging (3). In general, MR imaging with gadolinium is considered to have a sensitivity and specificity of nearly 100% to detect vestibular schwannomata (4). Therefore, MR imaging of the cerebellopontine angle (CPA) is currently the gold standard to diagnose vestibular schwannomata (5). Sometimes, it concerns an incidental finding on the MR imaging scan performed for a different indication.

Vestibular schwannomata mostly expand slowly in the internal auditory canal as well as the cerebellopontine angle. However, large tumours are able to compress the brainstem (6). Vertigo, hearing loss, tinnitus, and ear fullness are the most common presenting symptoms among these patients. Concerning the hearing loss, different mechanisms were described in the literature. Thakur et al. (7) mentioned more specifically 4 patterns

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of hearing loss. Firstly, they delineated the mechanical and/or neurotoxic effect of a growing tumour on nearby neurovascular structures. Secondly, biochemical alterations in the inner ear fluid and accumulation of tumour toxic metabolites can cause hearing loss, even in non-growing tumours. Thirdly, an efferent olivocochlear bundle dysfunction can appear. Lastly, they described multiple causes of sudden deafness, like a vascular insult of the internal auditory artery or the labyrinthine artery and the earlier mentioned nerve compression and rapid accumulation of biochemical toxins. Likely, the etiology of hearing loss in vestibular schwannoma is multifactorial. We described and analysed the symptomatology and MR imaging characteristics among patients diagnosed with a unilateral sporadic vestibular schwannoma. Furthermore, we evaluated potential correlations between hearing levels, tumour size, age, and radiologic features such as cystic tumours or brainstem compression.

Methods

Ethical Considerations

The study was accepted by the ethical committe of the University of Antwerp and the Antwerp University Hospital. (EDGE number 000695) Ethical guidelines were followed, according to Belgian legal requirements.

Study Design and Patients

A retrospective study was performed on all patients diagnosed with a unilateral sporadic vestibular schwannoma between January 1998 and December 2017 at a tertiary referral centre for neurotology and skull base surgery. Patients with primary inner ear or intralabyrinthine schwannomas, neurofibromatosis type 2, meningiomas as well as patients already actively treated elsewhere (by radiotherapy, subtotal resection, or gross total resection) were excluded from this study. Finally, 384 patients met the inclusion criteria.

Demographic data and presenting symptoms were retrieved from the medical history taken at the tertiary centre, while maximal diameter in the CPA, the presence of cystic components and/or brainstem compression were studied on the first MR imaging performed in each patient. Concerning the presenting symptoms, we made a selection of four important presenting symptoms: hearing loss, tinnitus, vertigo, ear pressure. Other important clinical manifestations, like facial paraesthesia/paresis, were not included in this study.

Main Points:

- In our series, all sizes of tumour presented with all types of hearing levels: normal to profound hearing loss. Normal hearing does not exclude the presence of a vestibular schwannoma.
- We measured a weak correlation between tumour size and hearing loss.
- We noticed a weak negative correlation between age and size of tumours.
- Patients mainly present with hearing loss. Nevertheless, more than half of our cases presented initially with tinnitus. This emphasizes the importance of imaging for tinnitus and hearing loss patients.
- Brain stem compression can be caused by all sizes of tumour, ranging from small to giant tumours.

Tumour size was classified using the 2001 Consensus Meeting on Acoustic Neuroma guidelines: intracanalicular (not reaching the CPA), small (1-10 mm in the CPA), medium (11- 20 mm in the CPA), moderately large (21-30 mm in the CPA), large (31-40 mm in the CPA) and giant (over 40 mm in the CPA). REF The audiometric tests were performed with Hughson Westlake methodology in a sound-proof booth using a 2-channel Interacoustics AC-40 audiometer according to current clinical standards (ISO 8253-1, 2010). Pure-tone audiometry was obtained at 500, 1000, 2000, 3000, 4000 and 8000 Hz bilaterally in all cases. If the ear was deaf, a value of 120 dB was assigned.

Statistical Analysis

Data were further analysed with IBM SPSS version 25 using non-parametric multivariate analyses, incl. Spearman's rank correlation, Pearson ranking test and Mann-Whitney U test. A p-value of <0.05 was considered statistically significant. A correlation coefficient of -1.0 to -0.5 or 1.0 to 0.5 was considered as strong, while -0.5 to -0.3 or 0.3 to 0.5 was considered moderate, -0.3 to -0.1 or 0.1 to 0.3 as weak; and -0.1 to 0.1 as none to very weak.

Results

In our population, age ranged from 11 to 92 years with a mean age of 52 years. Gender was equally divided. Tumours were left-sided in 49%, right-sided in 51%. Tumour size included 31% intracanalicular, 20% small, 28% medium, 13% moderately large, 6% large and 2% giant tumours. At presentation, 75% of patients complained of ipsilateral subjective hearing loss, 56% presented with tinnitus, while 41% experienced vertigo and only 19% had ear fullness. Profound sensorineural hearing loss was identified in 3.9% of patients. This occurred in all sizes of tumour. Symptoms like vertigo and hearing loss seemed to increase with tumour size. (Table 1) After statistical analysis, a weak association was observed between tumour size class and appearance of hearing loss (correlation coefficient 0.22). No correlation was demonstrated with tinnitus, vertigo, nor ear fullness.

Generally, in our study population, all sizes of tumour can cause all types of hearing loss. (Figure 1) We used the Spearman's rank correlation to measure whether there was any further influence of tumour size on amount of hearing loss. Mild significant correlation

Table 1. Symptomatology at presentation presentation (in percentage) vs Size

Symptomatology vs size	Hearing loss	Tinnitus	Ear Fullness	Vertigo
Intercanalicular	62%	58%	16%	40%
Small	69%	67%	24%	42%
Medium	81%	55%	20%	29%
Moderately large	90%	44%	10%	54%
Large	86%	50%	32%	55%
Giant	78%	33%	11%	89%

CPA: Cerebellopontine angle
Tumour size: Classification 2001 Consensus Meeting on Acoustic Neuroma guidelines: Intracanalicular (not reaching the CPA*), Small (1-10 mm in the CPA), Medium (11- 20 mm in the CPA), Moderately large (21-30 mm in the CPA), Large (31-40 mm in the CPA), Giant (over 40 mm in the CPA)

was found between tumour size and hearing loss of the affected ear, both using Fletcher Index (FI) (The average of hearing levels at 500Hz, 1000Hz and 2000Hz) (correlation coefficient 0.152) and high Fletcher index (hFI) (The average of hearing levels at 1000Hz, 2000Hz and 4000Hz) (correlation coefficient 0.158).

The difference in hearing thresholds between the affected ear and the contralateral normal ear was also assessed. The mean asymmetry of FI was 23.6dB HL, at hFI it was 30dB HL. Using Wilcoxon Singed Rank test, there was a statistically significant asymmetry in Fletcher Index between both ears (Z=-15, p<0.01) and greater difference in hFI (Z=-16.1, p<0.01) Further statistical analysis concerning the correlation between tumour size and the difference in hearing thresholds between the affected ear and the normal ear, demonstrated a weak correlation between tumour size and the difference in hearing thresholds with Fletcher Index (correlation coefficient 0.230) and with high Fletcher Index (correlation coefficient 0.203) (Figures 4 and 5).

We also assessed the effect of brainstem compression on hearing loss. Tumours that only touched the brain stem were not included in this group. Brain stem compression was observed in 33% of tumours. Although brain stem is related to size, we remarked one small tumour and multiple medium-sized tumours causing brain stem compression (Table

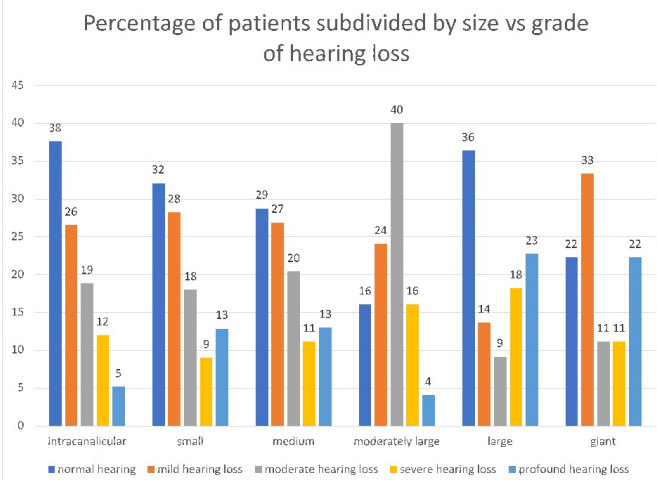

Figure 1. Size (percentage of patients per size group) versus level of hearing loss
Levels of hearing (FI, Fletcher index): Normal hearing: FI <20dB HL, Mild hearing loss: FI 20-40dB HL, Moderate hearing loss: FI 40-60dB HL, Severe hearing loss: FI 60-80dB HL, Profound hearing loss: FI >80dB HL

Table 2. Size of tumour vs brain stem compression. Amount of patients (total) divided by the presence or absence of brain stem compression. Percentage of patients with brainstem compression per size group

Size vs brainstem compression	No brain stem compression (n)	Brain stem compression (n)	Percentage of patients with brainstem compression (%)
Intercanalicular	117	0	0%
Small	77	1	1%
Medium	60	48	44%
Moderately large	5	45	90%
Large	0	22	100%
Giant	0	9	100%
Total	259	125	33%

CPA: Cerebellopontine angle
Tumour size: Classification 2001 Consensus Meeting on Acoustic Neuroma guidelines: Intracanalicular (not reaching the CPA*), Small (1-10 mm in the CPA), Medium (11- 20 mm in the CPA), Moderately large (21-30 mm in the CPA), Large (31-40 mm in the CPA), Giant (over 40 mm in the CPA)

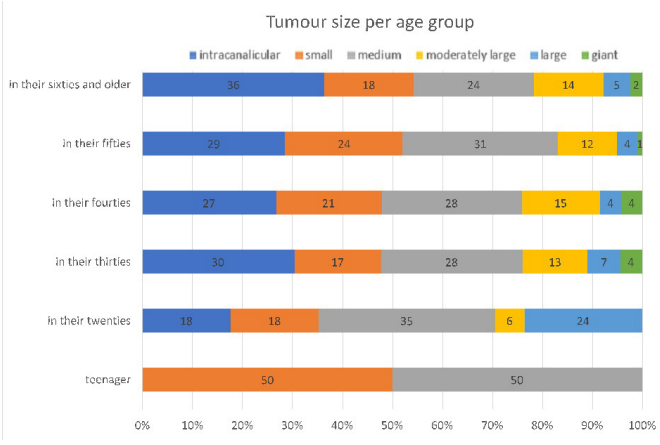

Figure 2. Amount of patients divided by size (in percentage) per age group
Age groups (y, years): Teenager: age 0-19y, In their twenties: age 20-29y, In their thirties: age 30-39y, In their fourties: age 40-49y, In their fifties: age 50-59y, In their sixties and older: age >60y

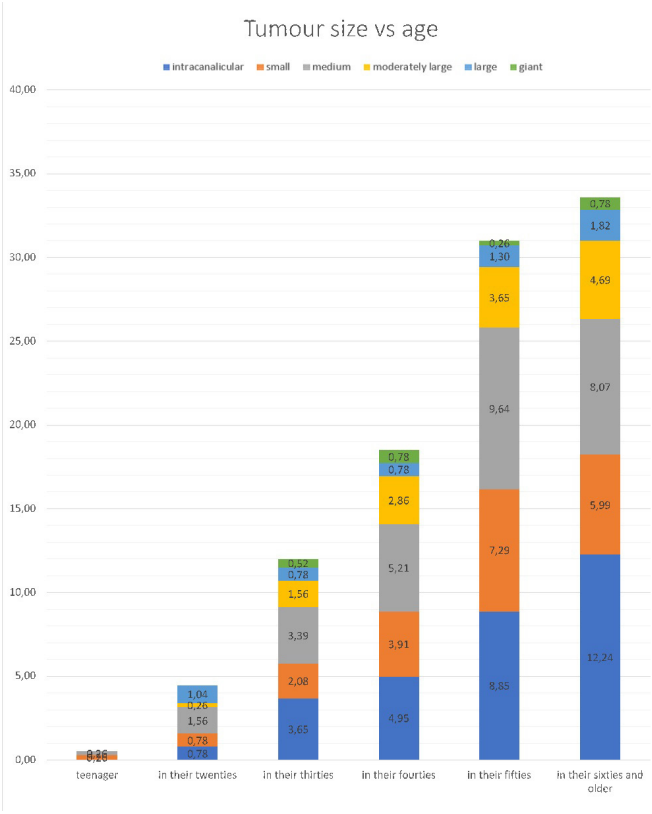

Figure 3. Amount of patients (of total patients, in percentage) with certain tumour size per age category
Age groups (y, years): Teenager: age 0-19y, In their twenties: age 20-29y, In their thirties: age 30-39y, In their fourties: age 40-49y, In their fifties: age 50-59y, In their sixties and older: age >60y

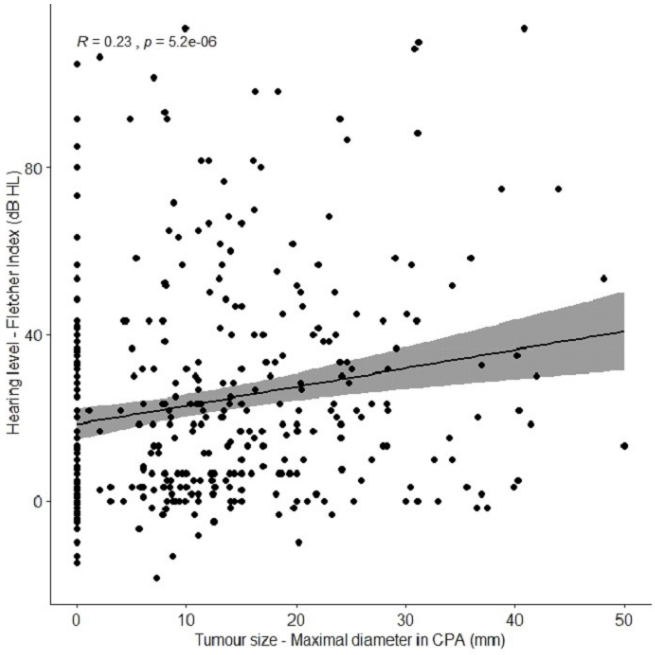

Figure 4. Difference between Fletcher Index of the affected ear and Fletcher Index of the normal ear
Fletcher Index (FI): The average of hearing levels at 500Hz, 1000Hz and 2000Hz; CPA: Cerebellopontine angle

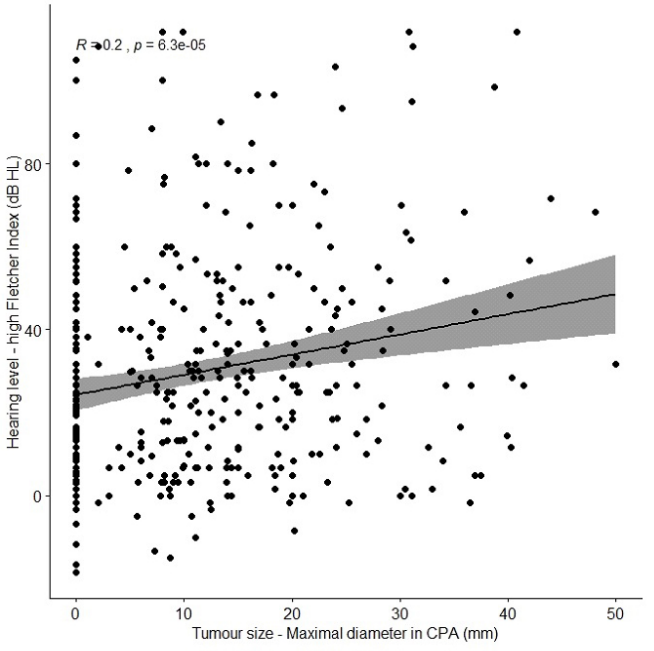

Figure 5. Difference between Fletcher Index of the affected ear and Fletcher Index of the normal ear
high Fletcher index (hFI): The average of hearing levels at 1000Hz, 2000Hz and 4000Hz; CPA: Cerebellopontine angle

2). We noticed no significantly increased hearing loss at the affected ear when brain compression was present. However, examining the difference between the normal ear and the affected ear, there was a significant increased asymmetry in hearing loss at FI (Z=-3, p=0.003) and hFI (Z=-2.65, p=0.008) in tumours with brainstem compression, compared to tumours without brainstem compression. Cystic components were observed in 21% of tumours. A statistically significant correlation between tumour size and the presence of cystic components in the tumour (correlation coefficient 0.49) was found. No statistically significant difference in hearing level could be observed between non-cystic and cystic tumours (p>0.05). A weak negative correlation between age of diagnosis and size of tumour (correlation coefficient -0.125) was observed. Younger patients presented with larger tumours (Figure 3).

Discussion

We investigated potential correlations between hearing levels, tumour size, age and radiologic features (cystic component, brainstem compression). In our series, all sizes of tumour presented with all types of hearing levels: normal to profound hearing loss. (Figure 1) Normal hearing levels were consequently measured at all tumour sizes. Caution, therefore, remains important: normal hearing or mild hearing loss does not exclude (large) tumoural pathology. Our results concerning the positive correlation between tumour size and hearing loss differ from what earlier studies published. Although we only found a weak correlation, most studies showed no correlation (8-11).

Nadol et al. (12) reported a correlation with the size and the severity of low-frequency sensorineural hearing loss. Day et al. (13) reported frequency-specific hearing loss related to tumour size, with pantonal frequency hearing loss in tumours larger than 2.5cm. Harner et al.(14) reported hearing deterioration with tumour size, with an increase at the level of 4.1-5cm.

In our study population, we marked a correlation with both low-to-mid frequencies (Fletcher Index) and mid-to-high frequencies (high Fletcher Index) with tumour size.

Age at diagnosis. Earlier studies reported a negative correlation between age at diagnosis and size of tumour (15). However, in absolute counts, more large tumours are detected at older age, which is reflected in the former correlation. But as the presence of a vestibular schwannoma is less frequent at a younger age, the tumours that were diagnosed in our study population, relatively had a greater diameter.(Figures 2 and 3) Different considerations have been made in literature before. Stranger et al. (1) stated that the negative correlation can be explained by the fact that, with easier access to MR scanning, the examination has also been offered to elderly patients, in whom the small and intrameatal tumours dominate. Another consideration is a real difference in tumour growth rate in function of the age. Ogawa K et al. (16) proclaimed a higher tumour growth rate in younger patients. This assumption might explain the presentation of larger tumours in younger patients.

Cystic tumours and brainstem compression. Cystic vestibular schwannomas are known for their unpredictable growth rate and different radiologic features (17). Cystic elements may easily expand very rapidly, causing acute neurologic symptoms (18, 19). This corresponds to the moderate significant correlation between tumour size and presence of cystic components in the tumour. In literature, incidence variate mainly between 6%-24% (19, 20), we had an incidence of 21%. Earlier literature described more aggressive, shorter symptomatic period (19, 21), but no objectivation of hearing loss seems to be investigated. Our results showed no correlation between the presence of cystic components and hearing levels.

Samii et al. (22) already prescribed an increase in trigeminal and facial nerve impairment, intracranial hypertension, hydrocephalus with large and giant tumours. Besides, cerebellar compression aggravates vestibular dysfunction. Harari et al. (23) examined vestibular schwannomata with brainstem expression, confirming these higher rate of associated complications. Besides, 50% presented with hyperacusis, 35% with complete hearing loss and 11% with moderate hearing loss. Though these earlier studies did no comparative investigation between tumours with and without brainstem compression. In our study, we measured no additionally increased hearing loss due to brainstem compression. But we did notice a significant increased asymmetry in hearing loss between both ears. Furthermore, it is remarkable that different sizes of tumour can cause brain stem compression (Table 2), which suggests the importance of exact location of the tumour on the vestibular nerve. Further research on this subject may be very interesting.

Limitations

Demographic data and presenting symptoms were retrieved from the medical history. This retrospective approach limited us to the information that was available in the patient files. Information was acquired through different doctors and no standardized questionnaires were used. Therefore, not all patients may have reported all relevant symptoms and interpretation bias of the doctors may have occurred. Moreover, as we mentioned earlier, we focused in this study on ENT symptomatology, selecting four important clinical manifestations. Consequently, the presence of other potential symptoms like headache, hydrocephaly and facial palsy, was not investigated.

Besides maximal diameter in the CPA and specific MR imaging features were studied on the first MR imaging scan performed in each patient and the audiometric tests were done at time of diagnosis of the tumours. These tumours all had already an intrameatal growth period, and some even an extrameatal growth period before diagnosis. Consequently, no conclusions/data can be retrieved of the effective beginning of these tumours. In our measurements, we used the largest extrameatal diameter of the tumour. We can question whether the use of the volumetric dimensions might be more accurate, but as it is the absolute size that determines the risk of brainstem or adjacent cranial nerve compression, this seems to be an adequate measuring unit (6). Although some studies claim tumour growth as being a better predictor of hearing loss than the initial tumour size, we did not investigate tumour growth patterns in our study (11).

In our series, sporadic vestibular schwannomas are diagnosed at all ages and mainly present with hearing loss. Nevertheless more than half of our cases presented initially with tinnitus. This emphasizes the importance of imaging for tinnitus and hearing loss patients. Although all sizes of tumour can present with all types of hearing loss, there is a weak correlation between size and hearing loss. All tumour sizes can present with hearing loss, while we could only find a weak correlation between tumour size and hearing loss. Larger tumours generally presented with slightly worse hearing levels. Furthermore, we noticed a weak negative correlation between age and size of tumours. Presence of cystic components is associated to larger tumour size, but not to hearing loss. Brain stem compression can be caused by small up to giant sized tumours.

Ethics Committee Approval: This study was approved by the institutional Ethics committee of the University of Antwerp and the Antwerp University Hospital. (Approval No: 000695).

Informed Consent: Informed consent is not necessary due to the retrospective nature of this study.

Peer-review: Externally peer-reviewed.

Author Contributions: Supervision – V.V., P.V., V.T., T.M.; Design – E.G.,V.V.; Resources – E.G.,V.V.; Materials – V.V, E.G.; Data Collection and/or Processing – E.G., B.I.,V.V.; Analysis and/or Interpretation – E.G.,V.V.; Literature Search – E.G.; Writing Manuscript – E.G.; Critical Review – V.V., P.V.

Conflict of Interest: Medel, unrestricted research grant and travel grant paid to the hospital unrelated to this work. Cochlear, consultancy paid to the hospital unrelated to this work.

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