ORIGINAL ARTICLE

Middle ear impedance studies in elderly patients: implications on age-related hearing loss

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KEYWORDS
Acoustic impedance tests;
Pure-tone audiometry;
Aged;
Presbycusis;
Acoustic reflex

Abstract

Introduction: Controversies arise with respect to functioning of the middle ear over time.
Objective: To assess changes in middle ear impedance that may be related to aging, and/or if there was an association of these changes with those of the inner ear in the elderly patients.
Methods: Cross-sectional, comparative study of elderly patients managed in ear, nose and throat clinics. A structured questionnaire was administered to obtain clinical information. Pure tone audiometry, tympanometry, and acoustic reflexes were performed. Comparative analyses were performed to detect intergroup differences between clinico-audimetric findings and middle ear measures, viz. tympanograms and acoustic reflexes.
Results: One hundred and three elderly patients participated in the study; 52.4% were male, averagely 70.0 ± 6.3 years old, age-related hearing loss in 59.2%, abnormal tympanograms in 39.3%, absent acoustic reflex in 37.9%. There was no association between age and gender in patients with abnormal tympanograms and absent acoustic reflex. Significantly more patients with different forms and grades of age-related hearing loss had abnormal tympanometry and absent acoustic reflex.
Conclusion: Some abnormalities were observed in the impedance audimetric measures of elderly patients, which were significantly associated with parameters connected to age-related hearing loss.
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Introdução

Hearing involves a complex interplay and integration of several mechanisms, including conduction of sound waves from the environment through the external auditory canal, vibrations of the tympanic membrane, stimulation of the transformer mechanism in the middle ear, as well as the sensory hair cells of the cochlea the central neuronal connections with termination at the primary auditory cortex. The functions of some of these mechanisms are affected by aging and tend to manifest as hearing impairment, which is particularly common in the elderly.

A deficit in hearing acuity is the most common sensory disorder that has been associated with aging. In fact, studies have shown that approximately one-third of adults aged between 61 and 70 years, and over 80% of those older than 85 years have clinically obvious difficulty understanding speech and following conversations in the presence of background noise.1-2 On the average, hearing threshold increases by approximately 1 dB per year for subjects aged 60 years and above, with a tendency to further deterioration with increasing age.4 At audiometry, up to 35% of elderly subjects above 60 years had pure tone average threshold of 25 dB HL or more at frequencies between 0.5 and 4 kHz, which increased further to 50% in the age group between 70 and 80 years.5 While the reported prevalence of hearing loss among elderly subjects vary in different locations, it is an established fact that it increases with age.4

Traditionally, hearing loss is classified as conductive, sensory, neural, or mixed-type. Age-related changes in the inner ear and its central connections have been well documented among elderly subjects. These include loss of sensory hair cells of the cochlea consequent upon generalized degenerative processes, dysfunction of the stria vascularis (the main blood supply to the organ of Corti), and degeneration of the neurons of the cochlear nerve or its central connections.1 In the external ear, wax impaction in the external auditory meatus has been reported to be disproportionately more common in the elderly patients than in other groups of patients, causing conductive hearing loss.6 This is a consequence of the generalized degeneration of epithelia, including those of the microcilia, affecting the external auditory canal without an accompanying reduction in the rate of wax production. Other causes of conductive hearing loss are often related to the functioning of the middle ear.

Compared with other categories of patients, little attention has been paid to the conductive middle ear components in elderly patients. Controversies arise concerning the functioning of the middle ear as age advances. While some studies concluded that the conducting mechanisms of the middle ear remain normal and functional, or that they may play no serious role in the hearing impairment associated with aging,7-9 others observed some changes in the dynamic characteristics of the middle ear that may be related to aging.7-9 This might have resulted from different types of instruments used for assessing the middle ear functions. As part of the study on the epidemiology of hearing impairment among elderly patients, the author performed both pure-tone and impedance audiometries ( tympanometry) to assess the functions of the inner and middle ear, respectively.10 The observation of certain abnormal tympanometric tracings in some patients with normal audiograms and in patients with
supposedly purely sensorineural hearing loss (SNHL) stimulated this research. This study aimed to assess whether there were changes in the middle ear impedances that may be related to aging, and/or whether there were any associations of these changes with those of the inner ear in the elderly subjects. This is justifiable because hearing loss impacts the quality of life of elderly subjects.

**Methods**

**Study design**

This was a prospective (cross-sectional), comparative study of elderly patients followed-up at specialized ear, nose, and throat (ENT) clinics for a three-year period.

**Setting/study location**

This study was conducted at the ENT clinics of a tertiary referral hospital and of a private/missionary hospital. Ethics approval for this study was obtained from the Health Research and Ethics Committee, under approval number OOUTH/DA.326/T/197.

**Sampling criteria/technique**

The inclusion criteria were elderly patients aged 60 years and above, who had no clinical middle ear disease, attended one of the ENT clinics. Patients were consecutively recruited. The general nature, significance, requirements of the patients, including the fact that declining to participate in the study would not affect treatment, were explained to the patients. Consenting patients were included in the study. The categories of the patients that were excluded were: those who did not consent, history of recurrent ear discharges, and those with tympanic membrane perforations. Patients with wax impaction were treated before the continuation of the study protocols. Patients without complete investigations (both forms of audiometry – pure tone audiometry [PTA] and tympanometry), with asymmetric audiograms, or evidence of conductive or mixed hearing loss in their PTAs were subsequently excluded.

**Study period**


**Data sources and collection procedure/technique**

Data were generated using interviewer-administered questionnaires, divided into three sections. Section A comprised socio-demographic information. Section B consisted of the medical condition including questions on history of perceived hearing loss, duration of hearing impairment, and present or previous ear surgeries, among others.

Section C was documentation of the findings on physical examination, especially the status of the tympanic membranes, and records of the audiometric profiles of the patients, which included the PTA, tympanometry, and acoustic reflexes.

At PTA, air conduction and bone-conduction evaluations were performed in a commercial sound booth, using an Amplivox diagnostic audiometer model 240, with standard earphones enclosed in supra-aural ear cushions, and a standard bone-conduction oscillator and headband to evaluate air-bone gaps. Tympanometry was conducted by broadband middle ear power reflectance and measured using a calibrated, commercially available computer-controlled system (Interacoustics model MT 10.5N 156607) that incorporated a high-quality probe assembly to transduce stimuli and record acoustic responses from the ear canal. The acoustic reflex thresholds were tested with contralateral stapedial reflexes for frequencies of 500, 1000, 2000, and 4000 Hz; the thresholds were considered as normal when elicited between 75 and 110 dB HL.

Main outcome measure: patients were paired into different categories based on the PTA findings as Normal or Age-related hearing impairment-presbycusis). The tympanograms were classified according to Jerger types A, As, Ad, B, and C, with type A considered as normal, and any other tympanographic types as abnormal, while acoustic reflexes were classified as Present or Absent.

**Data analysis**

Descriptive analysis of the data was done and presented in tabular and graphical forms. Comparative analyses were performed to detect inter-group differences between the clinico-audiometric findings and different middle ear measures, viz. tympanograms and acoustic reflexes, by cross-tabulation with contingency tables. Categorical variables were presented as percentages and proportions and analyzed using Chi-square test, while continuous variables, presented as absolute values and means, were compared using Student’s t-test. The level of statistical significance was set at *p* < 0.05. Data analysis was performed using SPSS version 19.0 (Chicago, IL, United States).

**Results**

One hundred and three (103) elderly patients participated in the study, which comprised 52.4% males, (M:F = 1.1:1). The ages of the patients ranged between 61 and 96 years with a mean ± SD of 70.0 ± 6.3 years. The socio-demographic characteristics of the patients are shown in Table 1. Over half (59.2%) of the patients had audiometric evidences of ARHL, and the Schuknecht typology is represented in Fig. 1. The impedance audiometry findings based on tympanometric tracings according to Jerger's classification revealed that on average, 60.7% of the participants had normal (type A tympanograms), with a high concordance between the two ears. The acoustic reflexes were present in an average of 62.1% of the patients. The details of the impedance audiometric profile of the patients are shown in Table 2.
Age, gender, and PTA findings of the patients were comparatively analyzed against the tympanometric findings in Table 3. Based on the age distribution of the patients, they were subdivided into two groups, ≤70 and >70 years. There were no statistically significant differences in the tympanograms regarding age ($t = 1.498, p = 0.137$) and gender ($\chi^2 = 1.837, p = 0.175$) of the patients. There was a difference when the hearing status (PTA findings) was compared; significantly more patients with age-related hearing loss (ARHL) had abnormal tympanometric findings. These were also obvious when considering the different patterns of audiometric findings that were observed in patients with ARHL. Further analysis of the PTA of patients with ARHL, considering the degrees of hearing losses calculated as pure tone averages (PTAv) in dB HL at the low (0.25, 0.50, 1.0 kHz) and the high (2.0, 4.0, and 8.0 kHz) frequencies was performed.

Exploring the PTA in the better ear at the low (0.25–1.0 kHz) frequencies revealed a mean of 28.7 dB HL (SD = 18.0). Low frequency accentuation of the audiogram was taken as at least 40 dB HL for the PTA (WHO classification for moderate hearing loss) at the low frequencies. At the high (2.0–8.0 kHz) frequencies, computation of the PTA in the better ear, resulted in a mean of 45.4 dB HL (SD = 23.0). Estimate of the differences in the PTA in between the high tones and low tones in the better ears revealed a mean of 24.1 dB HL (SD = 10.1), thus a value of ≥25 dB HL difference was used as the criterion for a high tone preponderance of the audiogram.

The PTA in the low and high frequencies in the better ear and other parameters, namely low tone accentuation

<table>
<thead>
<tr>
<th>Variable</th>
<th>Right ear (%)</th>
<th>Left ear (%)</th>
<th>Average (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Tymanometry (Jerger’s type)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>A</td>
<td>60 (58.3)</td>
<td>65 (63.1)</td>
<td>62.5 (60.1)</td>
</tr>
<tr>
<td>B</td>
<td>6 (5.8)</td>
<td>7 (6.8)</td>
<td>6.5 (6.3)</td>
</tr>
<tr>
<td>C</td>
<td>14 (13.6)</td>
<td>9 (8.7)</td>
<td>11.5 (11.2)</td>
</tr>
<tr>
<td>AS</td>
<td>22 (21.4)</td>
<td>21 (20.4)</td>
<td>21.5 (20.9)</td>
</tr>
<tr>
<td>Ad</td>
<td>1 (1.0)</td>
<td>1 (1.0)</td>
<td>1 (1.0)</td>
</tr>
<tr>
<td><strong>Acoustic reflexes</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Present</td>
<td>65 (63.1)</td>
<td>63 (61.2)</td>
<td>64 (62.1)</td>
</tr>
<tr>
<td>Absent</td>
<td>38 (36.9)</td>
<td>40 (38.8)</td>
<td>39 (37.9)</td>
</tr>
</tbody>
</table>

![Figure 1](image_url) Distribution of PTA findings of the patients. Schuknecht’s typology only for patients with ARHL.
Middle ear impedance studies in elderly patients

Table 3  Relationship between clinico-audiometric and tympanographic findings.

<table>
<thead>
<tr>
<th>Clinico-audiometric parameter</th>
<th>Tympanographic findings</th>
<th>Normal</th>
<th>Abnormal</th>
<th>Statistic</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Age (mean)</strong></td>
<td></td>
<td>69.2</td>
<td>71.1</td>
<td>1.498</td>
<td>0.137</td>
</tr>
<tr>
<td><strong>Sex</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td></td>
<td>46.6%</td>
<td>60.0%</td>
<td>1.837</td>
<td>0.175</td>
</tr>
<tr>
<td>Female</td>
<td></td>
<td>53.4%</td>
<td>40.0%</td>
<td>1.837</td>
<td>0.175</td>
</tr>
<tr>
<td>ARHL (all cases)</td>
<td></td>
<td>46.6%</td>
<td>75.6%</td>
<td>8.827</td>
<td>0.003</td>
</tr>
<tr>
<td><strong>Schuknecht’s type in ARHL</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Type A</td>
<td></td>
<td>19.0%</td>
<td>6.7%</td>
<td>14.252</td>
<td>0.001</td>
</tr>
<tr>
<td>Type B</td>
<td></td>
<td>3.4%</td>
<td>20.0%</td>
<td>13.542</td>
<td>0.001</td>
</tr>
<tr>
<td>Type C</td>
<td></td>
<td>15.5%</td>
<td>28.9%</td>
<td>8.012</td>
<td>0.018</td>
</tr>
<tr>
<td>Type D</td>
<td></td>
<td>8.6%</td>
<td>20.0%</td>
<td>6.641</td>
<td>0.036</td>
</tr>
<tr>
<td><strong>PTAv in best ear</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Low frequency (0.25–1.0 kHz)</td>
<td></td>
<td>21.6</td>
<td>37.7</td>
<td>5.001</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>High frequency (2.0–8.0 kHz)</td>
<td></td>
<td>38.2</td>
<td>54.6</td>
<td>3.833</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Low tone accentuation</td>
<td></td>
<td>11.1%</td>
<td>64.7%</td>
<td>17.872</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>High tone preponderance</td>
<td></td>
<td>53.9%</td>
<td>29.4%</td>
<td>5.482</td>
<td>0.019</td>
</tr>
</tbody>
</table>

a Statistic, Student’s t-test.

and high tone preponderance, were compared with the tympanometric findings in patients with ARHL. All parameters presented statistically significant differences for tympanometric abnormalities, as shown in Table 3.

A similar comparative analysis was performed with the acoustic reflexes as the outcome variable. Similar to tympanometric findings, there were no associations between age of patients that had absent acoustic reflexes (t = 0.970, p = 0.334), and gender (χ² = 0.363, p = 0.549) in Table 4. Statistically significant differences were observed for patients with ARHL, those with type B Schuknecht audiometric pattern, the PTavs, and also in patients with low tone accentuation of their PTAs.

Discussion

This study has demonstrated that elderly patients had some functional anomalies in the middle ear impedances and acoustic reflexes. Impedance audiometric abnormalities

Table 4  Relationship between clinico-audiometric findings and acoustic reflexes.

<table>
<thead>
<tr>
<th>Clinico-audiometric parameter</th>
<th>Acoustic reflex</th>
<th>Normal</th>
<th>Abnormal</th>
<th>Statistic</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Age in years (Mean)</strong></td>
<td></td>
<td>69.5</td>
<td>70.8</td>
<td>0.970</td>
<td>0.334</td>
</tr>
<tr>
<td><strong>Sex</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td></td>
<td>54.8%</td>
<td>48.8%</td>
<td>0.363</td>
<td>0.549</td>
</tr>
<tr>
<td>Female</td>
<td></td>
<td>45.2%</td>
<td>51.2%</td>
<td>0.363</td>
<td>0.549</td>
</tr>
<tr>
<td>ARHL (all cases)</td>
<td></td>
<td>50.0%</td>
<td>73.2%</td>
<td>5.487</td>
<td>0.019</td>
</tr>
<tr>
<td><strong>Schuknecht’s type</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>A</td>
<td></td>
<td>12.9%</td>
<td>14.6%</td>
<td>4.961</td>
<td>0.085</td>
</tr>
<tr>
<td>B</td>
<td></td>
<td>4.8%</td>
<td>19.5%</td>
<td>10.106</td>
<td>0.006</td>
</tr>
<tr>
<td>C</td>
<td></td>
<td>17.7%</td>
<td>26.8%</td>
<td>2.937</td>
<td>0.230</td>
</tr>
<tr>
<td>D</td>
<td></td>
<td>14.5%</td>
<td>12.2%</td>
<td>0.154</td>
<td>0.925</td>
</tr>
<tr>
<td><strong>PTAv in best ear</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Low frequency (0.25–1.0 kHz)</td>
<td></td>
<td>24.1</td>
<td>35.9</td>
<td>3.326</td>
<td>0.001</td>
</tr>
<tr>
<td>High frequency (2.0–8.0 kHz)</td>
<td></td>
<td>39.3</td>
<td>54.5</td>
<td>3.448</td>
<td>0.001</td>
</tr>
<tr>
<td>Low tone accentuation</td>
<td></td>
<td>19.4%</td>
<td>63.3%</td>
<td>12.191</td>
<td>0.001</td>
</tr>
<tr>
<td>High tone preponderance</td>
<td></td>
<td>48.4%</td>
<td>36.7%</td>
<td>0.856</td>
<td>0.355</td>
</tr>
</tbody>
</table>

a Statistics, Student’s t-test.
were significantly higher in elderly patients with various forms and degrees of ARHL, being more pronounced in neural and strial types, and in low frequency accentuation of ARHL. Acoustic stapedial reflexes appeared to be less influenced by ARHL than tympanometry, and it may be a more reliable indicator of abnormal middle ear function.

Researchers assessing hearing and its impairment among elderly patients have focused disproportionately on ARHL relating to the sensorineural aspect of hearing, with apparent neglect of the conductive component. However, the present study revealed that an average of 39.3% of the elderly patients had abnormality in their tympanometric tracings, and average of 37.9% had absent acoustic reflexes. It cannot be conclusively ascertained whether these middle ear abnormalities were due to aging process, or mere coincidental findings. Nondahl et al.\textsuperscript{13} reported a small degree of middle-ear stiffening occurring over the years among older adults. An animal experiment also found structural changes in the middle ear of mouse that were attributable to aging.\textsuperscript{16}

There was no significant difference between the ages of elderly patients with normal or abnormal tympanograms and between those with and without acoustic reflexes. Galhede and Koefoed-Nielsen\textsuperscript{17} compared compliance and middle ear pressure measured by tympanometry between normal elderly subjects (mean age 77 years) and normal younger patients (mean age 29 years); they observed that middle ear compliance was not influenced by variation in age. Similarly, no association was found between the gender of the patients and middle ear mechanics analogous to findings of the Blue Mountains Hearing Study in Australia.\textsuperscript{18} These are at variance with reports concerning presbycusis, which were reported to be significantly associated with advancing age and also with the male gender.\textsuperscript{19}

The prevalence of anomalies observed in the middle ear mechanisms in this study was comparable to the reported prevalence of ARHL.\textsuperscript{20,21} This may suggest a simultaneous or concurrent effect in both the inner and the middle ear. The abnormal tympanometric findings of the patients revealed that the Jerger's type A tympanogram was the most common among the patients similar to that found among centenarians in China,\textsuperscript{20} providing an evidence of increased stiffness (reduced compliance) of the conducting mechanisms.\textsuperscript{15} This was followed by the type C tympanogram suggestive of eustachian tube dysfunction. Thus, it is hypothesized that common middle ear functional anomalies may be attributable to either of these two pathologies. Sometimes abnormalities occur in the tympanic membrane and in the bony ossicles, resulting in significant middle ear functional impairment.\textsuperscript{16} There is evidence that, with advancing age, the human tympanic membrane exhibits a loss of vascularization, a reduction in collagen structure, in elasticity, and greater rigidity in the middle fibrous layer.\textsuperscript{22} These structural changes would be expected to alter the compliance response of the middle ear. One belated investigation of air and bone conduction thresholds has observed middle-ear losses of as much as 12 dB in elderly patients.\textsuperscript{23}

The possibility that ARHL either initiates or aggravates abnormalities in the impedance characteristics of the middle ear should also be considered. The audiometric pattern of elderly patients with ARHL observed in the present study showed a preponderance of Schuknecht's type C, such as in other African populations,\textsuperscript{24} and distinct from the typical sloping pure tone audiogram common among whites.\textsuperscript{25} The finding that all Schuknecht's audiometric patterns in patients with ARHL were associated with tympanic abnormalities, suggested a link with the etiopathogenesis of these two entities in elderly patients. It is expected that subjects with abnormal tympanograms should manifest with hearing loss of conductive type. However, the finding of these tympanometric patterns also in patients with normal and sensorineural (ARHL) hearing loss should stimulate further research into middle ear impedance mechanisms.

Using Schuknecht's typology in patients with ARHL, two particular types of audiograms (B and C) theoretically had accentuation at the low frequencies. In this study, these two audiometric types comprised over half (33/61; 54.1%) of the audiometric types in patients with ARHL. Thus, the association of low tone accentuation of audiograms with abnormal tympanograms may derive from the disproportionate distribution of these two audiometric patterns in the ARHL patients. Eustachian tube compliance has been observed to change with aging,\textsuperscript{26} but whether this change is influenced more by neural or strial types of presbycusis remains to be ascertained. Contrary to reports of Feeney and Sanford,\textsuperscript{9} the present findings suggest an increase in middle-ear stiffness with specific types of ARHL. Thus, these impedance middle ear changes may be particularly common in the African population, and need further clarification.

It is noteworthy that there were discordant findings in some of the middle ear measures between the ears. These suggest that, despite the ears being exposed to almost the same conditions, the influences and the responses might not be exactly same. The possibility of confounding factors, such as osteoarthritis (which might affect ossicular joints of the ears unequally, producing type A tympanogram), may also be considered. Asymmetrical audiograms have also been reported in patients with ARHL.\textsuperscript{13,24}

Many experts consider 2.0 kHz as beginning of high frequency, although the definition varies.\textsuperscript{4,27,28} PT-Av at high frequencies and high tone preponderance HL were associated with abnormalities in tympanic findings in this study. Wiley et al.\textsuperscript{29} reported that, for younger age groups (50–69 years), threshold changes were higher for higher frequencies, while in older age groups (70–89 years), threshold changes were higher for lower frequencies. Interestingly, the age distribution of the present patients is in-between these two divisions. Causes of high-frequency hearing loss have a wide variability,\textsuperscript{21} and there is a possibility of coexistence of few of these in some of the present patients. Thus, it is possible that not enough patients with pure ARHL were studied. Conversely, low frequency hearing loss is not easy to identify, since it tends to be asymptomatic. In fact, lower frequency sounds do not have as much information as sounds in the higher frequencies.\textsuperscript{30} One of the few clues to a low-frequency hearing loss is that the person has difficulty hearing in groups or in a noisy place. It was reported that inertia of the middle ear is not an important contribution to the perception of bone conduction sounds for frequencies below 1.5 kHz, but appears to contribute at frequencies between 1.5 and 3.5 kHz.\textsuperscript{30} However, this statement may not apply to air-conducted sounds.
The pathway involved in the acoustic reflex is complex and can involve the ossicular chain, cochlea, auditory nerve, brain stem, facial nerve, and other components. The absence of acoustic reflex has been shown to effectively detect hearing losses exceeding 30 dB in adult subjects, although it may not be conclusive in identifying the source of the problem. Like impedance measures, parameters related to ARHL (namely Schneekht’s type B audiogram, PTAv, and low-tone accentuation) were significantly associated with absence of the acoustic reflexes in this study. However, the absence of the acoustic reflex appeared to be less influenced by parameters relating to ARHL, and it may possibly be a more reliable parameter in assessing the effect of ARHL on the functioning of the middle ear.

This study had some limitations. First is the lower sensitivity of the conventional tympanometer in assessing middle ear function compared with sweep frequency middle-ear analyzer. The fact that magnitude of the acoustic reflexes was not ascertained is also a limitation. Furthermore, the hospital-based nature of the study is prone to bias, as patients may not represent a normal population of the elderly. Despite these limitations, the study was able to demonstrate that the middle ear functioning of elderly patients may not be fully normal.

Conclusion

Some abnormalities were observed in impedance audiometric measures of elderly patients, which were significantly associated with parameters related to ARHL. This arouses suspicion of some middle ear changes that may be attributable to aging. It is imperative that elderly patients with hearing impairment have both their inner and middle ear assessed, in order to manage them optimally. Community-based, longitudinal studies are needed to further clarify these findings.

Conflicts of interest

The author declares no conflicts of interest.

References