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Sensorineural Hearing Loss in Cholesteatoma

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Objective: To determine whether middle ear cholesteatoma is associated with, sensorineural hearing loss, and whether patient age, cholesteatoma growth pattern, or, air bone gap size contribute to inner ear impairment.
Study Design: Cross-sectional comparative.
Setting: A tertiary hospital.
Patients: The subjects were 115 patients with middle ear cholesteatoma in one ear, and normal video-otoscopy in the contralateral ear (CLE).
Interventions: Otoendoscopy, pure-tone audiometry.
Main Outcome Measures: Bone conduction (BC) threshold differences between the normal CLE and the cholesteatoma ear. Comparisons of these differences between different cholesteatoma growth patterns. Correlation between the air bone gap size in the ear with cholesteatoma and the difference in bone conduction thresholds between both ears.
Results: The cholesteatoma ear was associated with greater BC thresholds than the CLE. With regard to different cholesteatoma growth patterns, the differences between associated BC thresholds were also significant in all groups at all frequencies, with the exception of the two routes of cholesteatoma group at 500 Hz. Comparing BC threshold differences, they were greater in the adult group at 500 Hz. The correlation between the air bone gap media in the ear with cholesteatoma and the difference in bone conduction thresholds between both ears was direct and moderate.
Conclusion: Cholesteatoma was associated with greater BC thresholds at all frequencies tested. The differences were independent of cholesteatoma growth patterns. As bigger the air bone gap in the ear with cholesteatoma, greater the inner ear damage. **Key Words:** Cholesteatoma—Hearing loss—Middle ear disease.

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Middle ear cholesteatoma is a destructive disease that can aggressively spread and erode through the limits of the middle ear cleft and surrounding structures. Hearing loss of varying types can accompany cholesteatoma, but it is typically conductive in nature, secondary to ossicular erosion or impairment of normal ossicular mobility (1).

The association between sensorioneural hearing loss (SNHL) and cholesteatoma is not well understood (2). Although erosion of the capsula otic, most commonly involving the lateral semicircular canal, could be considered a clear mechanism of SNHL in cholesteatoma (3), some authors have reported that labyrinthine fistula (LF), a sporadic phenomenon, had no influence on functional cochlear lesions in chronic otitis media (COM) in their investigations (2). However, when there is apparently no direct lesion into the inner ear produced by an existing cholesteatoma, the mechanisms responsible for sensorineural impairment and the magnitude of this damage are the source of even more debate.

The objectives of this study were to determine whether middle ear cholesteatoma is associated with SNHL, and to investigate whether cholesteatoma growth pattern, or air bone gap size contributes to inner ear impairment.

MATERIALS AND METHODS

This study included consecutive patients with cholesteatoma. Fiber-optic otoendoscopies were performed and recorded in both ears sequentially. Inclusion criterion was the presence of acquired cholesteatoma in one ear and normal video-otoscopy in the CLE. Exclusion criteria included history of any ear surgery and difficulty in cleaning or performing video-otoscopy.

All patients underwent pure-tone audiometry and air conduction (AC) thresholds; bone conduction (BC) thresholds and air bone gaps (ABG) were determined. Narrow band masking noise was applied when needed. In young children, play-conditioned audiomety with spraural earphone was performed.

The findings of video-otoscopy were analyzed and cholesteatomas were classified into one of the following (4):

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1) posterior epitympanic, 2) posterior mesotympanic, 3) two routes (attical and mesotympanic), 4) indeterminate, and 5) anterior epitympanic. Cholesteatomas were also classified according to the presence of inflammation (purulent secretion and granulation tissue).

The hospital's Research Ethics Committee approved this study (protocol number 14918). All participating patients, or their parents or guardians where the participant was a child, provided written informed consent before their inclusion in the study.

To compare inflammation among the cholesteatomas we used χ^2 test. To compare BC thresholds we used Mann–Whitney and Wilcoxon tests. To compare the sizes of the BC differences among the audiometric frequencies, we used the Friedman test and the multiple comparison by Student's t distribution. To correlate ABG with the bone conduction difference between the two ears, we used the 500, 1000, 2000, 3000, and 4000 Hz threshold average and applied the Person correlation test. All tests were two-tailed, and the level of significance was set at $p \leq 0.05$.

RESULTS

One hundred fifteen patients were included. The characteristics of the total sample are shown in Table 1. All the patients had used topical antibiotics with neomycin for otorrhea.

Prevalence of inflammation was greater in undetermined cholesteatomas (94.4%) than in posterior epitympanics (57.1%), posterior mesotympanics (66.7%) and two routes (50.0%) ($p = 0.03$). We did not find differences in the cochlear damage between cholesteatomas with and without inflammation at all frequencies ($p = 0.23$ at 500 Hz; $p = 0.65$ at 1000 Hz; $p = 0.77$ at 2000 Hz; $p = 0.19$ at 3000 Hz, and $p = 0.14$ at 4000 Hz).

Preoperative CT scan or surgical data were not available in 32 (27.8%) patients. In 70 (84.3%), the presence of labyrinth LF was analyzed via surgical data, and in 13 (15.7%) it was analyzed via CT scan. Fistula was found in 5 of these 83 patients (6%). In 4 it was on the lateral semicircular canal.

At all frequencies studied, the presence of cholesteatoma in the middle ear was associated with greater BC thresholds than in the CLE ($p < 0.001$ at 500, 1000, 2000, 3000, and 4000 Hz) (Fig. 1).

TABLE 1. *Description of the patients included in the study*

Age (years old)	
Median, standard deviation (minimum and maximum)	32.40, 20.29 (3–81)
No. of males (prevalence)	56 (48.7%)
No. of children (prevalence)	44 (38.3%)
No. of cholesteatoma growth pattern (prevalence)	
Anterior epitympanic	6 (5.2%)
Posterior epitympanic	37 (32.2%)
Posterior mesotympanic	40 (34.8%)
Two routes	11 (9.6%)
Undetermined	21 (18.3%)
Inflammation	76 (65.7%)

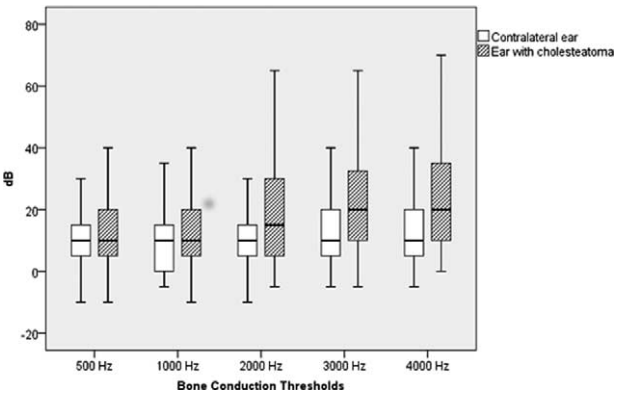

FIG. 1. Boxplot comparing the bone conduction thresholds between the ear with cholesteatoma and the normal contralateral. Median (black horizontal line inside the box), interquartile range (box superior limit [75th percentile]), and box inferior limit (25th percentile).

Comparing the sizes of BC differences at the different audiometric frequencies, there were significant differences among them ($p < 0.001$). The median differences were 5 dB at 500, 1000, and 4000 Hz, and 10 dB at 2000 and 3000 Hz. Multiple comparisons testing revealed that the BC differences between the cholesteatoma ear and the CLE were greater at 2000 and 3000 Hz than at 500 Hz ($p < 0.05$). No significant differences were evident among the other frequencies.

When we grouped the patients according to the cholesteatoma growth pattern, the differences between the BC thresholds were also significant in all groups and frequencies, with the exception of the two routes of cholesteatoma group at 500 Hz (Table 2).

When we compared the BC differences between posterior epitympanic and posterior mesotympanic cholesteatomas, we did not find any significant differences at all between any of the frequencies ($p = 0.64$ at 500 Hz, $p = 0.91$ at 1000 Hz, $p = 0.51$ at 2000 Hz, $p = 0.98$ at 3000 Hz, and $p = 0.34$ at 4000 Hz) (Fig. 2).

Correlation between the air bone gap average in the ear with cholesteatoma and difference of bone conduction thresholds average between the ear with cholesteatoma and the normal contralateral was $R = 0.64$ ($p = 0.0001$, Fig. 3).

DISCUSSION

Cholesteatoma is well known to be the most aggressive type of COM (3). The authors reported an LF frequency of 16.7%, mostly identified during surgery. We found a smaller frequency of fistula, although 27% of our sample had not been operated on at the time of data collection. Jesic et al. (3) did not find a correlation between the presence of LF and SNHL in patients with fistulas detected during surgery. However, in two patients with CT-visible labyrinthine destruction, whose audiograms showed moderate and severe SNHL, a significant influence of such LF on SNHL was found. These observations could

TABLE 2. *Comparison of bone conduction thresholds between the ear with cholesteatoma and the contralateral ear in the different cholesteatoma growth patterns (Mann–Whitney test)*

BC Frequency	Ear With Cholesteatoma Media (SD); Median (IR)	Contralateral Ear Media (SD); Median (IR)	*p* Value
500 Hz			
Posterior epitympanic (n = 39)	17.31 (14.55); 15.00 (5–20)	11.18 (11.47); 10.00 (0–15)	<0.001
Posterior mesotympanic (n = 39)	12.69 (15.34); 05.00 (0–20)	08.21 (10.67); 05.00 (0–10)	0.008
Two routes (n = 11)	14.55 (21.15); 05.00 (0–25)	09.09 (8.31); 05.00 (5–15)	0.680
Indeterminated (n = 22)	18.41 (15.84); 12.50 (8.75–31.25)	09.77 (8.50); 10.00 (3.75–15)	0.003
1000 HZ			
Posterior epitympanic (n = 39)	16.67 (17.14); 10.00 (5–20)	09.61 (12.21); 07.50 (0–15)	<0.001
Posterior mesotympanic (n = 39)	16.15 (18.93); 10.00 (5–20)	08.85 (11.95); 05.00 (0–10)	<0.001
Two routes (n = 11)	19.09 (19.47); 15.00 (5–25)	09.09 (08.89); 10.00 (0–10)	0.041
Indeterminated (n = 22)	19.09 (19.91); 10.00 (5–35)	10.23 (08.79); 10.00 (5–15)	0.025
2000 Hz			
Posterior epitympanic (n = 39)	20.77 (17.11); 20.00 (10–25)	11.97 (12.81); 10.00 (3.75–15)	<0.001
Posterior mesotympanic (n = 39)	19.10 (18.49); 15.00 (5–30)	11.28 (15.20); 05.00 (5–15)	<0.001
Two routes (n = 11)	20.45 (19.80); 15.00 (5–30)	07.27 (06.84); 10.00 (0–10)	0.011
Indeterminated (n = 22)	25.68 (21.89); 15.00 (10–46.25)	11.82 (12.96); 10.00 (5–16.25)	0.001
3000 HZ			
Posterior epitympanic (n = 39)	24.05 (20.13); 20.00 (10–25)	15.81 (14.93); 10.00 (7.5–20)	<0.001
Posterior mesotympanic (n = 39)	22.63 (17.92); 15.00 (10–30)	16.32 (22.62); 10.00 (5–21.25)	<0.001
Two routes (n = 11)	26.50 (22.61); 20.00 (8.75–45)	10.00 (12.47); 05.00 (0–21.25)	0.008
Indeterminated (n = 22)	28.64 (22.31); 20.00 (13.75–51.25)	14.09 (17.01); 12.50 (0–21.25)	<0.001
4000 Hz			
Posterior epitympanic (n = 39)	23.59 (20.93); 20.00 (10–25)	18.16 (17.10); 15.00 (10–20)	0.002
Posterior mesotympanic (n = 39)	21.84 (19.29); 17.50 (5–35)	14.74 (22.09); 10.00 (5–15)	<0.001
Two routes (n = 11)	23.64 (23.56); 20.00 (5–40)	10.00 (16.88); 00.00 (0–20)	0.025
Indeterminated (n = 22)	30.45 (24.29); 20.00 (15–60)	16.82 (18.22); 10.00 (5–30)	0.022

mean that only large fistulas that can be easily identified on CT can lead to a greater sensorineural impairment. Thus, LF is just one of several mechanisms by which cholesteatoma can cause damage to the inner ear.

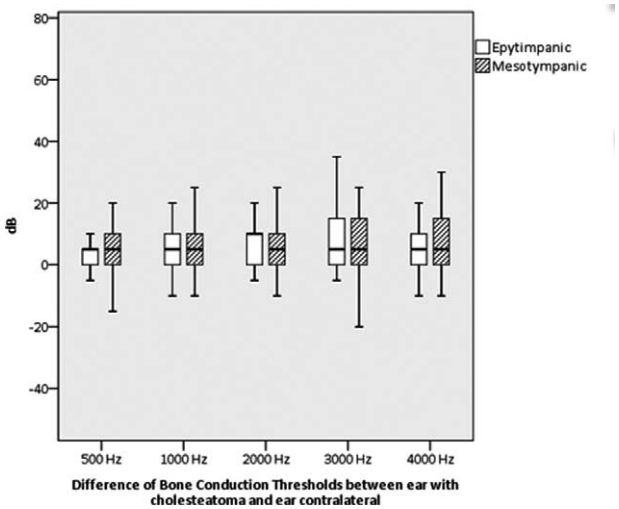

FIG. 2. Boxplot comparing the difference of bone conduction thresholds between the ear with posterior epitympanic and posterior mesotympanic cholesteatomas and the normal contralateral. Median (black horizontal line inside the box), interquartile range (box superior limit [75th percentile]), and box inferior limit (25th percentile).

The influence of inflammatory factors, free radicals, and bacterial toxins on cochlear function has been well described (5,6). Paparella et al. (7) hypothesized that cochlear dysfunction associated with COM in the absence of direct invasion of the otic capsule was caused by penetration of inflammatory cells and mediators, via the round window membrane. Eisenman and Parisier (1)

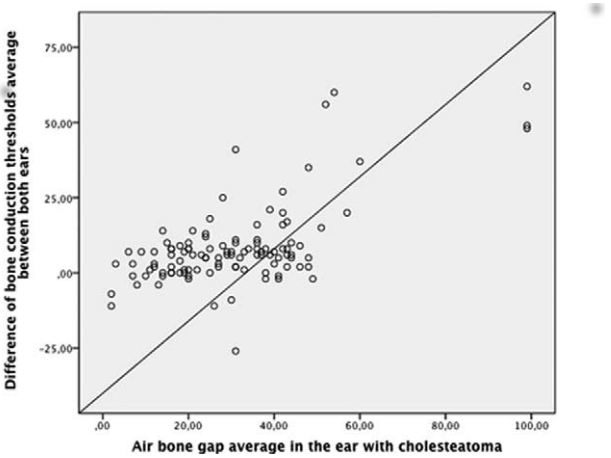

FIG. 3. Scatter of correlation between the air bone gap average in the ear with cholesteatoma and difference of bone conduction thresholds average between the ear with cholesteatoma and the normal contralateral.

reported an interaural difference at 4000 Hz. They argued that if sensorineural dysfunction is a result of the passage of inflammatory mediators across the round window membrane, one might expect increased thresholds at higher frequencies. Our results suggest that damage at 2000 and 3000 Hz is greater than that at 500 Hz. However, the greatest effect was not observed at 4000 Hz in our study.

Cholesteatoma, frequently associated with longstanding middle ear inflammation and assumed to produce toxic and lytic enzymes from the active epithelium, has been suggested by some to pose a higher risk of the development of SNHL, independently of direct invasion of the inner ear (1,8,9). In our previous study (10), we demonstrated a significant difference in SNHL between patients with and without cholesteatoma, but only at 500 Hz. Jesic et al. (3), however, found that a predictive factor for SNHL appearance is COM itself, independent of pathology. Redaelli de Zinis et al. (2) also did not detect an association between cholesteatoma and increasing BC thresholds.

We observed significant differences between the cholesteatoma ear and the CLE for all cholesteatoma growth patterns. Thus, inner ear impairment can occur irrespective of the location or propagation route of the cholesteatoma or inflammation degree. Another factor that can contribute to sensorineural damage is the duration of the disease (2). Jesic et al. (3) did not detect a correlation between the duration of cholesteatoma and SNHL. The objectivity of the estimation of disease duration is questionable because it is mainly based on anamnestic data and subjective symptoms. For that reason, we did not analyze this factor in our study. In addition, we removed all patients who had undergone ear surgery. All the patients made use, at some point, of topical antibiotics to control otorrhea, including formulas containing aminoglycosides because they are cheaper. The implication of this use in the sensorineural loss, however, especially in patients of much secretion and inflamed middle ear, seem minimal, as shown in previous studies (11–13).

Although Eisenman and Parisier (1) reported an interaural difference of only 5 dB, we observed medians of 5 dB at 500, 1000, and 4000 Hz, but of 10 dB at 2000 and 3000 Hz. Some authors argue that although these differences are statistically significant, they may not be clinically relevant. Notably, however, the 5 and 10 dB differences referred to herein are medians, so in fact there were several patients in the study with greater degrees of impairment. We think that understanding the sensorineural damage associated with cholesteatoma nowadays, where there are several kinds of prostheses and bone-anchored hearing aids specifically indicated for patients with COM, is very valuable. This knowledge may assist the development or improvement of new technologies, and may be of even more benefit with regard to BC than our demonstration that SNHL may be present in most patients with cholesteatoma, and that this damage can be clinically relevant in several patients.

CONCLUSION

Cholesteatoma was associated with greater BC thresholds at all frequencies tested, when compared with the normal CLE. These BC differences were observed independently of cholesteatoma growth pattern or inflammation degree. As bigger the ABG in the ear with cholesteatoma, greater the inner ear damage.

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