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Volume of the epitympanum and blockage of the tympanic isthmus in chronic otitis media: a human temporal bone study

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Introduction

The anatomy of tympanic compartments is crucial for understanding and treating chronic middle ear infections. From an anatomical and ventilation point of view, the middle ear is divided into two compartments by the epitympanic diaphragm, consisting of the incus, the malleus, and their folds. The epitympanic diaphragm is described as the floor of the epitympanum, which is the dividing structure from the mesotympanum [1, 2, 3]. Recently, Palva and his colleagues described the tympanic isthmus (TI) as the main pathway for mastoid and epitympanic ventilation. According to this theory, blockage of the TI may lead to inadequate ventilation of the mastoid and epitympanum [4].

The aeration pathway from the Eustachian tube leads directly to the mesotympanic and hypotympanic space, whereas the epitympanum is away from the direct air stream [4]. A previous study demonstrated that the area of TI was related to the degree of pneumatization

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of human temporal bones (HTBs) [5]; however, to our knowledge, there have been no studies of the relationship of the area of the TI and the volume of the epitympanum. In a previous study of HTBs with and without chronic otitis media (COM), the narrowest area of the TI was smaller than in HTBs with COM [5]. Several studies have reported blockage of the TI with some pathologic changes such as cholesteatoma, tympanosclerosis, swollen mucosa, and mucoid secretions [3, 6]. However, the relationship of the TI and the volume of the epitympanum have not been studied.

Diamant proposed that the extent of pneumatization is genetically determined; small middle ear cleft predisposes to chronic or acute otitis media [7–9], while some porcine studies have shown that chronic middle ear infection caused suppressed pneumatization of the middle ear, decreasing volume [5, 10]. Even though there are differing views on the relationship between the volume of the middle ear cleft and COM [5, 7, 8, 10, 11], it is well accepted that a small middle ear cleft, including antrum and mastoid, are often associated with COM and cholesteatoma [11, 12]. Because mastoid cells are directly connected to the epitympanum, there is always an interaction between the mastoid air cell system and the epitympanum. It might be expected that epitympanic volume in COM would be smaller than the volume in HTBs without COM, however, to our knowledge, this has not been previously studied.

For this study, we defined the epitympanum as the space, which is surrounded by the lateral attic bone, the labyrinthine capsule, a straight line from anterior tympanic spine to cochleariform process, and the aditus antrum. The TI was defined as the space surrounded by the tensor tympani tendon, the medial portion of the posterior incudal ligament, the attic bone, and the body and short process of the incus and the head of the malleus. In this study, we compared the volume of the bony boundaries of the epitympanum and the area of the TI in HTBs with and without COM having epitympanic involvement to determine if there was any difference in the bony volume of the epitympanum and/or the area of the TI in COM.

We also investigated whether there was a correlation between the epitympanic bony volume and the bony and aerated area of the TI, the main aeration/drainage pathway for the epitympanic cavity.

Materials and Methods

All specimens used for this study were from the HTB collection of the Otopathology Laboratory of the University of Minnesota.

In the present study, we selected HTBs with COM. We defined COM as an inflammatory condition of the middle ear cleft containing intractable pathological changes such as cholesterol granuloma, granulation tissue, fibrocystic structures, fibrosis, or tympanosclerosis. Excluded were subjects who had a history of otological surgery, tumor metastasis, cholesteatoma, bony erosion, and those with processing artifacts, since all of these may contribute to changes of bony volume of the middle ear.

HTBs from children 4 months to 15 years of age with at least one of the chronic intractable pathologies in the epitympanum described above were included in our study. Our control

group was comprised of age and sex matched cases from HTBs that were free from COM, abnormal pathological findings, or anomalies.

HTBs were removed, decalcified, embedded in celloidin, and sectioned at 20 μm. Every tenth section was stained with hematoxylin and eosin and mounted on glass slides. The slides were examined under a light microscope. Stained slides were scanned with a high-resolution slide scanner (PathScan Enabler IV, Meyer Instruments, Houston, TX).

1.Epitympanum

In order to segment the areas, we focused on the following bony landmarks of the epitympanum on horizontal sections of histopathological slides: 1) Landmark a: origin of the anterior tympanic spine of the lateral attic bone, 2) Landmark b: posterior point of the cochleariform process, 3) Landmark c: the most anterior point of the head of the malleus, 4) Landmark d: lateral side of the aditus antrum, 5) Landmark e: medial side of the aditus antrum, and 6) Landmark f: the most posterior point of the incus body/short process (Figure 1).

For our study, we defined the limits of the epitympanum as follows: 1) lateral, the lateral attic bone; 2) medial, the labyrinthine capsule; 3) front, a straight line from Landmark a to Landmark b; and 4) posterior, a straight line from Landmark e to Landmark f.

We chose the most superior level of the epitympanum where the medial tip of the incus, in articular surface in the incudomalleal joint, appears anterior to the lateral tip of the incus. Where the incus body disappears was chosen as the most inferior level of the epitympanum. All slides within that area were examined. The interval between the adjacent slides was generally 200μm.

The epitympanum was divided into 5 different compartments: 1) Anterior compartment (A): the triangular space with vertices a, b, and c; 2) Posterior compartment (P): the triangular space with vertices d, e, and f; 3) Lateral compartment (L): the space surrounded by the line connecting a and c, the lateral side of the malleus head and the incus body, the line connecting d and f, and the medial side of lateral attic bone; 4) Medial compartment (M): the space surrounded by the line connecting b and c, the medial side of labyrinthine capsule, the line connecting e and f, and the medial side of the malleus head and the incus body; and 5) Malleus-Incus compartment (MI): the malleus head and the incus body (Figure 1). Measurements included only the boundaries, exclusive of any soft tissue such as ligaments, membranes, and folds or exudates.

The scanned slide images were launched to the three-dimensional (3D) reconstruction software (AMIRA®), aligned, and the Anterior area, Posterior area, Lateral area, Medial area, and area of Malleus-Incus were outlined and labeled as different materials (Figure 1). After segmentation, the 3D model was generated (Figure 2). Measurements of the bony volumes of each compartment were taken.

The total bony volume of the epitympanum was calculated by the sum total of the volume of each compartment. Comparisons of the COM and control groups for each compartment or each value were made.

2. Tympanic isthmus (TI)

According to Palva [13], anatomical boundaries of the TI were defined as the tensor tympani tendon anteriorly, the medial portion of the posterior incudal ligament posteriorly, the attic bone medially, and the body and short process of the incus and the head of the malleus laterally (Figure 3). All slides from the lower limit to the upper limit of the tensor tympani tendon were examined. Within the boundaries described above, only the aerated space, excluding exudates, fibrous tissues, or granulation tissues, were outlined as the aerated TI (Figure 4).

Based on the definition of the medial compartment described above, the area per section of the medial compartment was obtained as the area of bony TI. In the section, below the bottom of the incus body, the medial limit of the bony TI was defined as the line connecting the middle of the posterior side of the head of the malleus and the middle of the anterior side of the long process of the incus and the middle of the facial recess. Inflamed soft tissue and exudates that were seen within the bony boundaries of the bony TI were not taken into consideration (Figure 3). All slides from the lower limit to the upper limit of the tensor tympani tendon were examined. The area of the aerated TI and bony TI were outlined, and measurements of their areas per each slide were obtained using AMIRA®. We chose the narrowest area in each case. Comparisons of the narrowest area of the aerated TI or the bony TI between COM and control groups were made.

3. The correlation between the epitympanic bony volume and the area of TI

We also investigated the correlation between the bony volume of the total epitympanum and the narrowest area of the aerated or bony TI within each group.

For statistical analysis, JMP version 10 (SAS, North Carolina) was used. Due to the small sample size, a non-parametric test, Wilcoxon rank sum test (Mann-Whitney's U test), was employed to compare the volume or area between the two groups, and Spearman's rank correlation coefficient was employed in comparing the volume of epitympanum with the areas of TI. For statistical power analysis, G*Power 3 (Faul, Erdfelder, Lang&Buchner, 2007) was used.

Results

There were 21 HTBs meeting our inclusion criteria, and 11 HTBs from 9 patients remaining after application of the exclusion criteria. Of the 9 patients, 4 had unilateral COM, and 5 had bilateral COM. The ages ranged from 1 to 15 years (4, 5.09±4.10) (median, average± SD), and there were 6 males and 5 females. The control group consisted of 11 HTBs from 9 patients, 6 males and 5 females. The ages ranged from 0 to 15 years (4, 5.73±4.43) (median, average± SD).

1. Epitympanum

The results of the bony volumes are shown in Table 1. In the control group, the mean volume of total epitympanum was 46.41 mm^3 (SD 5.53). In the COM group, the mean bony volume of total epitympanum was 42.40 mm^3 (SD 7.21). In the COM group, the volume of

every compartment except the anterior compartment and the bony volume of total epitympanum were smaller than in the control group. Particularly in the posterior compartment, the malleus-incus compartment, and the total volume of the epitympanum, the effect sizes ranged from medium to large ($d>0.5$). There were, however, no statistically significant differences between the two groups in any compartment ($p>0.01$).

2. Tympanic isthmus (TI)

The results of the areas of TI are shown in Table 2. The average area of the narrowest aerated TI was 9.80±3.53 mm^2 in controls, and 6.06±2.27 mm^2 in COM (average±SD). The average area of the narrowest bony TI was 9.85±3.31 mm^2 in controls, and 9.88±1.80 mm^2 in COM. The narrowest area of the aerated TI in COM was statistically smaller than that in the control group ($p<0.01$, $d=1.26$). The area of the narrowest bony TI in COM did not differ from that in the control group.

3. The correlation between the epitympanic bony volume and the area of TI

There was no significant relationship between the area of the narrowest aerated TI and total epitympanic volume among groups ($p>0.01$) (Figure 5). In the control group, there was no significant relationship between the area of the narrowest bony TI and total epitympanic bony volume ($p>0.01$, $\rho=0.045$). In the COM group, however, there was a significant negative correlation between the area of the narrowest bony TI and total bony volume of the epitympanym ($p<0.001$, $\rho=-0.855$) (Figure 6).

Discussion

Volumetric findings of the epitympanum in this study should provide insight into the etiopathogenesis of epitympanic pathologies. Ikui stated that total volume of the tympanic cavity increased in proportion to increasing pneumatization in the bone surrounding the cavity [14]. It has been proposed that enlargement of the epitympanum after birth, which is greater than that of the mesotympanum, may be due to the fact that the epitympanum is connected directly with the mastoid, which develops significantly after birth [14, 15].

It has been suggested that recurrent episodes of otitis media during the developmental stages of the temporal bone causes decreased pneumatization, predisposing the middle ear to otitis media [11, 16]. In our study limited to the epitympanum, all compartments except the anterior compartment in COM group were smaller than in controls, though these findings were not significant. However the effect sizes of the volumes of the posterior compartment, the malleus-incus compartment, and the total of all compartments are greater than medium size. Furthermore, the sample size of this study was small so that statistical power was not strong enough. This finding does not deny the relationship between the decreased epitympanic bony volume and COM.

Obstruction of the TI is a very common finding in various types of middle ear disease, and that causes a disturbance in air-diffusion within the temporal bone pneumatic system [17]. Dysventilation of the tympanic cavity due to the blockage of or a narrowed ventilation/drainage route has been suggested to predispose the middle ear to COM [18]. Swollen mucosa and tympanosclerotic deposits can obstruct the TI, resulting in accumulation of

exudates above the level of the epitympanic diaphragm [3, 17]. Ishii reported that there was a good correlation between the narrowest area of the TI and the degree of pneumatization of the mastoid air cells in nonpathologic HTBs, but there was no correlation between them in pathologic HTBs [5].

In our study, there was no difference in the size of the area of the bony TI between the two groups. This suggests that congenital or developmental stenosis of the TI is not likely to be a direct cause of COM. On the other hand, the area of the aerated TI was smaller in COM than that in the control group. Therefore, partial or total obstruction of the TI due to inflammation may create a tendency for the development of COM.

It is known that HTB processing, especially due to fixation, can cause 10–20% shrinkage of soft tissues. However, the shrinkage effect of fixative solutions commonly causes separation of the soft tissues from the borders of the bony structures. We usually see that the shrinkage artifact may create a space in between the soft tissue or effusion and the borders of the pneumatized spaces of the HTBs. This finding strengthens our finding of soft tissue blockage in the TI in COM. In addition, because the study includes both cases with COM and controls, it has been assumed that 10% shrinkage may occur equally in both groups, so shrinkage can be ignored in our analysis.

No change in the bony epitympanic volume, but decreased area of the aerated TI may indicate that aeration of the epitympanum is associated with COM with epitympanic pathology.

Conclusion

We found no significant relationship between the epitympanic bony volume and COM with epitympanic pathology, or between the area of the narrowest aerated TI and epitympanic bony volume. The area of the narrowest aerated TI in the COM group was significantly smaller than in the control group. Though our sample size was small, our results suggest that congenital stenosis of the TI is not a likely cause of COM, but obstruction of TI due to soft tissue or exudate may be associated with COM with epitympanic pathology.

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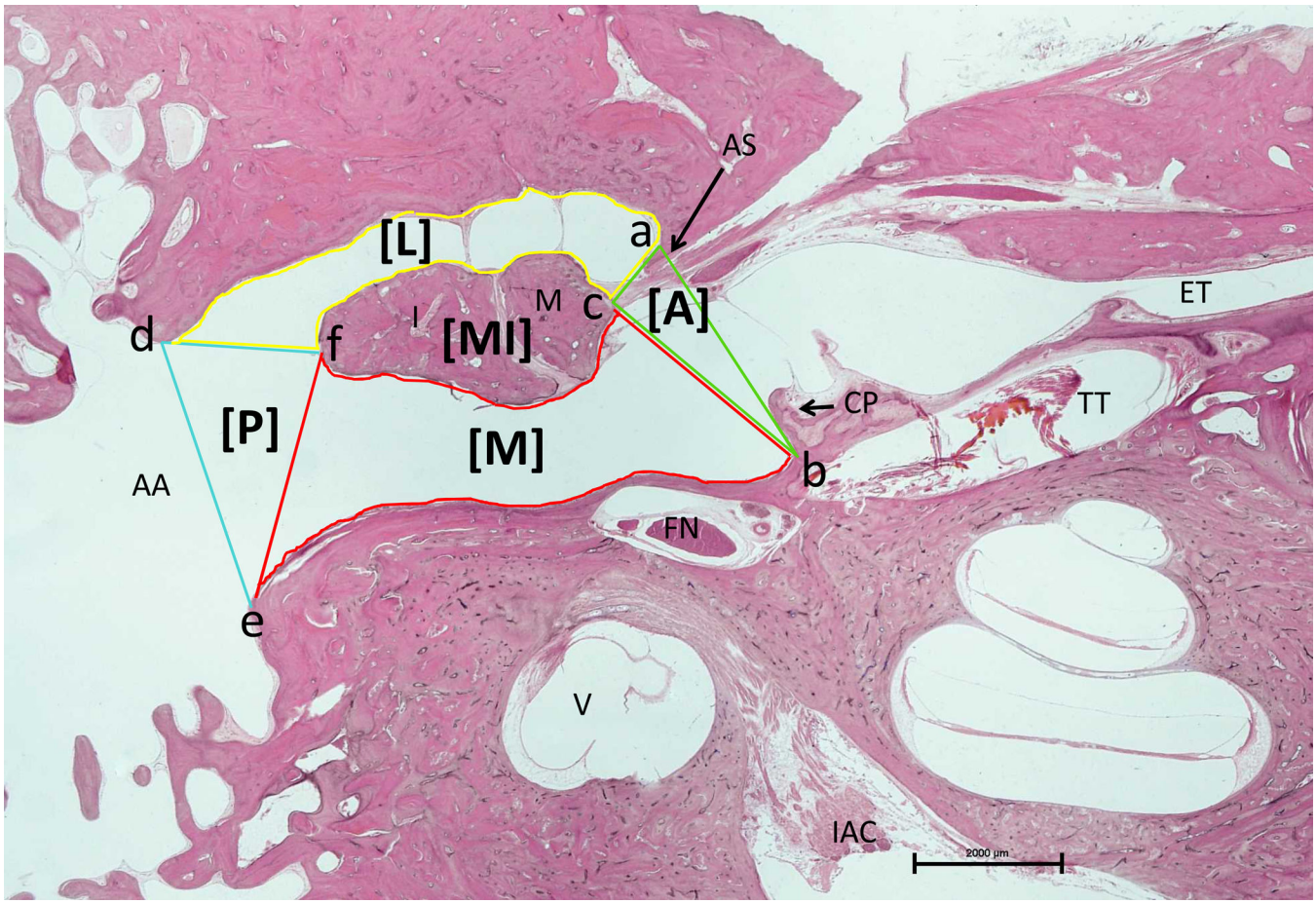

Figure 1.

A horizontal human temporal bone section that shows epitympanic compartments from a patient without chronic otitis media (hematoxylin-eosin, ×20). a = origin of the anterior tympanic spine of the lateral attic bone; b = posterior point of the cochleariform process; c = the most anterior point of the head of the malleus; d = lateral side of the aditus antrum; e = medial side of the aditus antrum; f = the most posterior point of the incus; [A] (Anterior compartment) = the triangular space with vertices a, b, and c; [M] (Medial compartment) = the space with vertices b, c, e, and f; [P] (Posterior compartment)= the triangular space with vertices d, e, and f; [L] (Lateral compartment) = the space with vertices a, c, d, and f; [MI] (Malleus-Incus compartment) = the malleus head and the incus body; AA = aditus antrum; I = incus; M = malleus; AS = anterior tympanic spine; V = vestibule; FN = facial nerve; CP = cochleariform process; TT = tensor tympani muscle; ET = eustachian tube; and IAC = internal auditory canal.

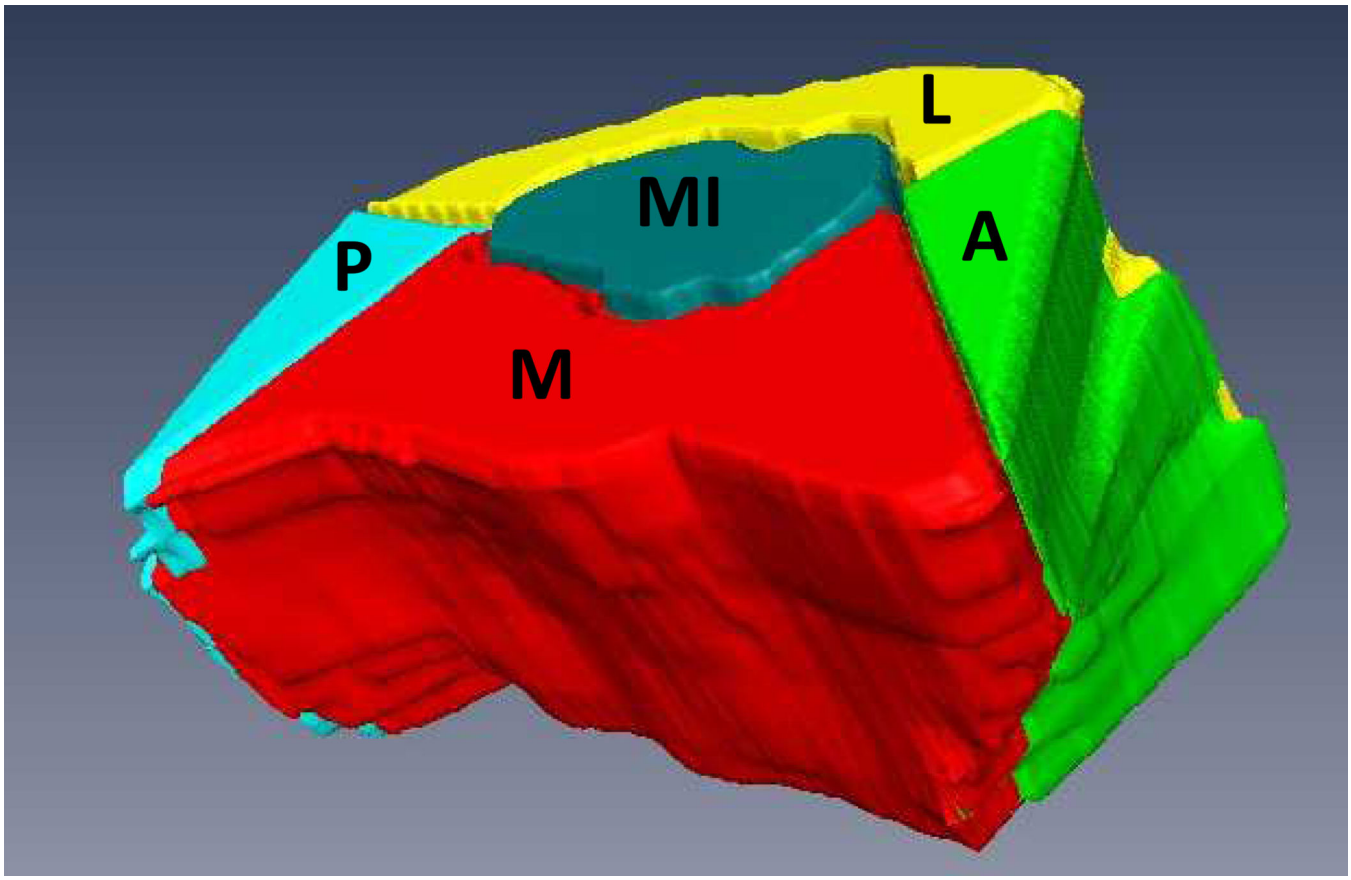

Figure 2.

3D reconstruction model of epitympanic compartments in a human temporal bone (hematoxylin-eosin, ×20). A = Anterior compartment; P = Posterior compartment; L = Lateral compartment; M = Medial compartment; and MI = Malleus-Incus compartment.

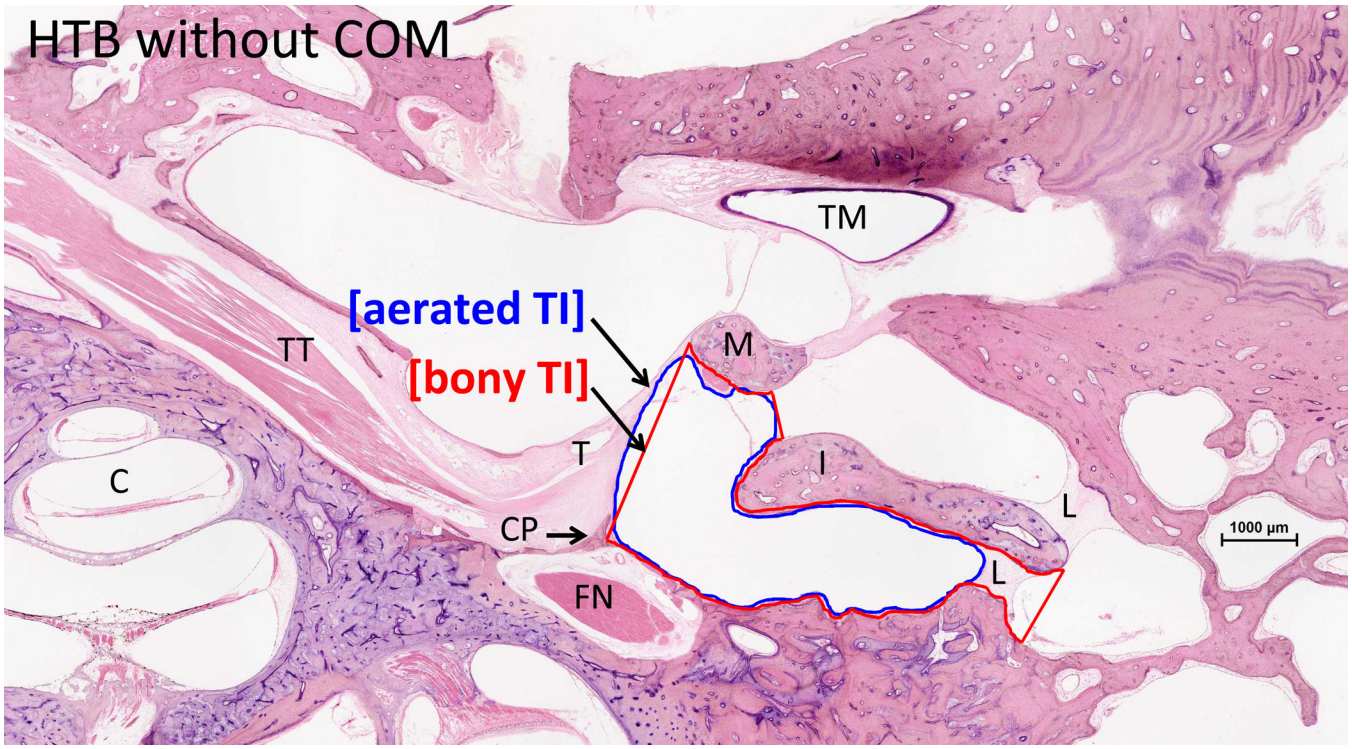

Figure 3.

A human temporal bone section without chronic otitis media (hematoxylin-eosin, ×20). The area surrounded by the blue line indicates the area of the aerated tympanic isthmus. The area surrounded by the red line indicates the area of the bony tympanic isthmus. TM = tympanic membrane; M = malleus; I = incus; L = posterior incudal ligament; T = tensor tympani tendon; CP = cochleariform process; FN = facial nerve; C = cochlea; and TT = tensor tympani muscle.

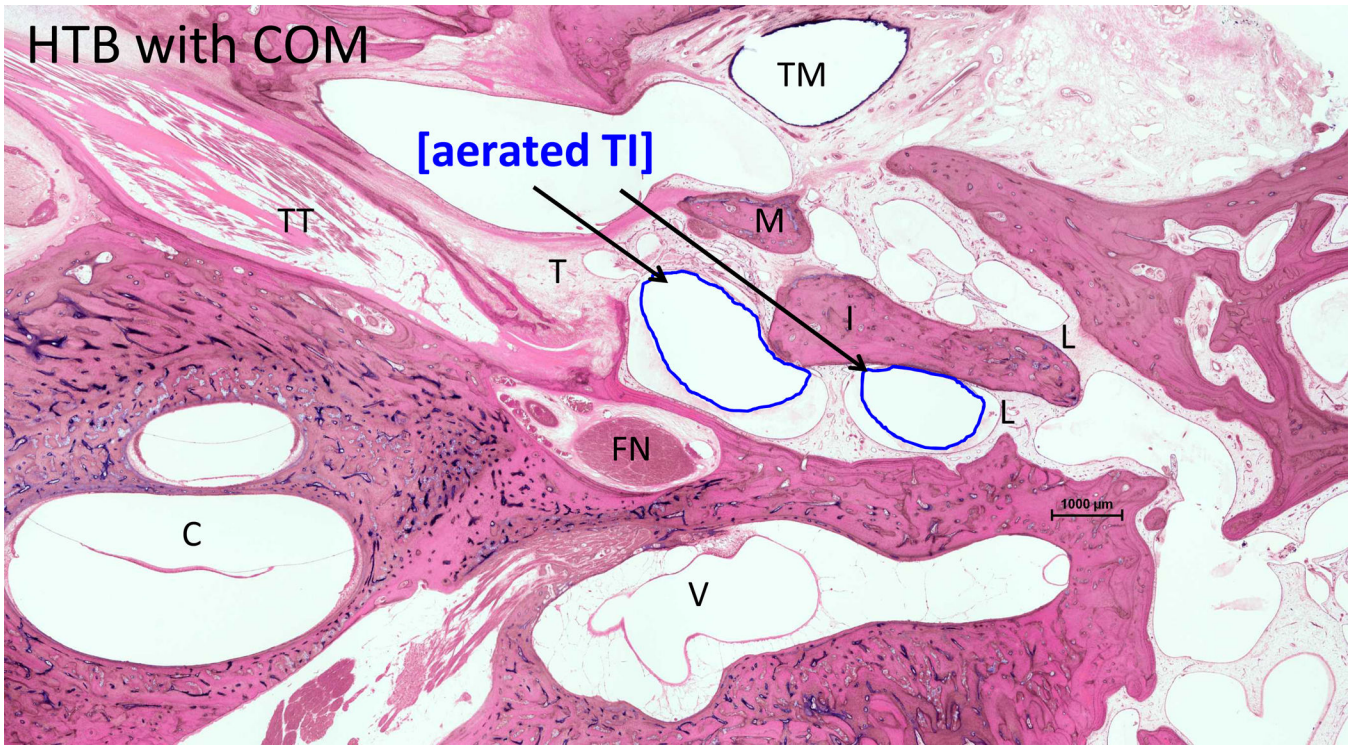

Figure 4.

A human temporal bone section with chronic otitis media (hematoxylin-eosin, ×20). The area surrounded by the blue line indicates the area of the aerated TI. TM = tympanic membrane; M = malleus; I = incus; L = posterior incudal ligament; T = tensor tympani tendon; FN = facial nerve; TT = tensor tympani muscle; C = cochlea; and V = vestibule.

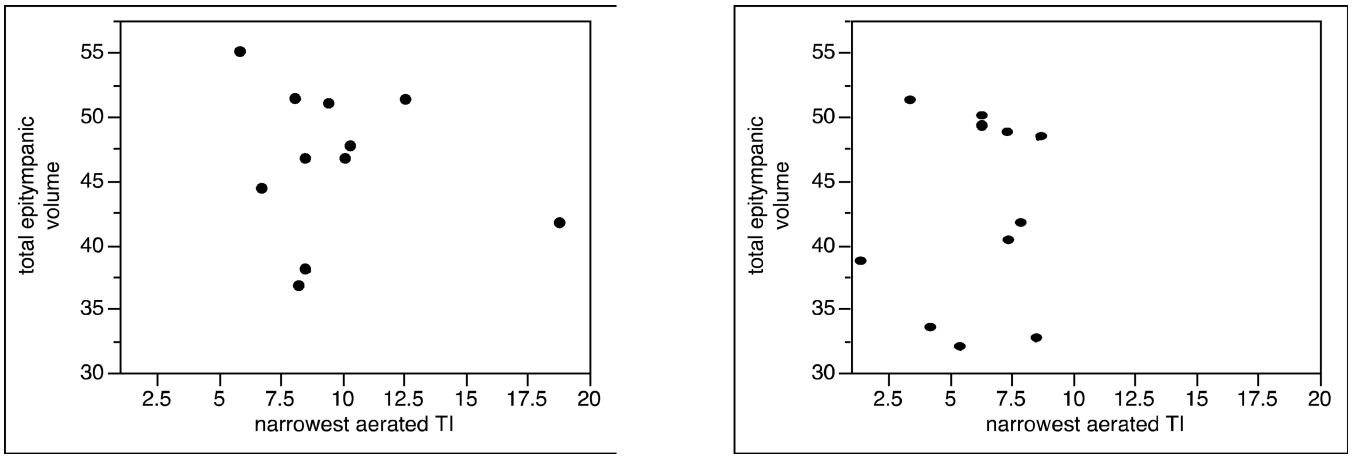

Figure 5.

Relationship between the narrowest aerated TI area (mm^2) and total epitympanic volume (mm^3). Left, control group, n=11,ρ=−0.055, P> 0.01; Right, COM group, n=11,ρ=0.091, P> 0.01.

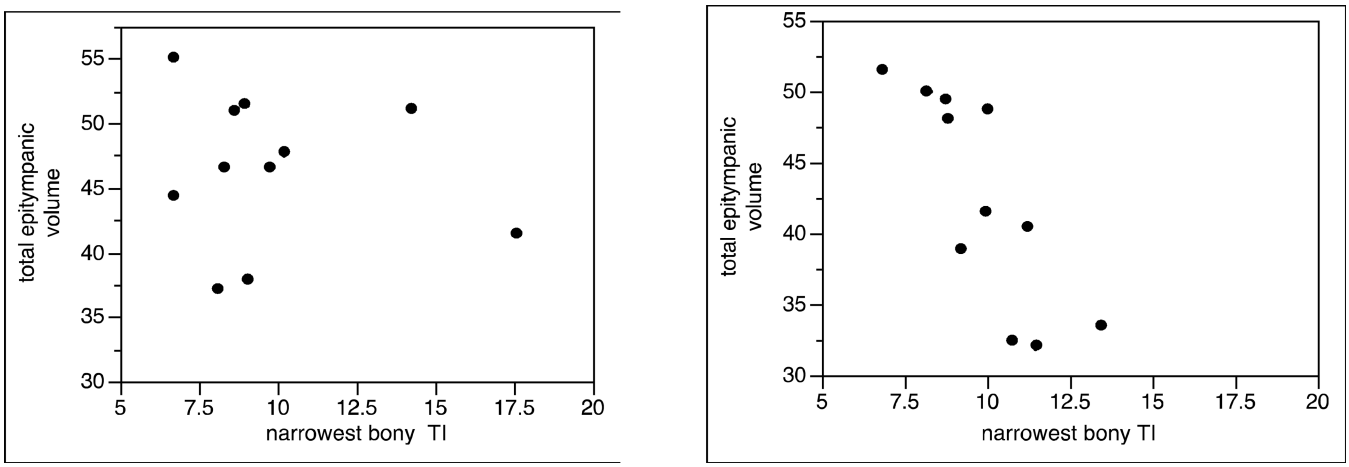

Figure 6.

Relationship between the narrowest bony TI area (mm^2) and total epitympanic volume (mm^3). Left, control group, n=11,ρ=0.046, P> 0.01; Right, COM group, n=11,ρ=−0.85, P< 0.001*.

Table 1

Volume of the epitympanum

Comparison of the bony volume of epitympanic compartments and the total epitympanum (total) in mm^3 between the control group and chronic otitis media group. Represented by average± 1SD.

	Compartment	Control (N=11)	COM (N=11)	p	Effect size (d)
Volume (mm^3)	Anterior	2.47 ± 0.64	2.81 ± 0.83	0.32	0.46
	Posterior	3.56 ± 1.08	2.69 ± 0.97	0.15	0.85
	Lateral	12.34 ± 2.93	11.15 ± 4.25	0.36	0.33
	Medial	17.20 ± 2.37	16.16 ± 2.92	0.36	0.39
	Malleus-Incus	10.85 ± 1.44	9.59 ± 1.35	0.12	0.90
	Total	46.41 ± 5.53	42.40 ± 7.21	0.32	0.62

Table 2

Area of the tympanic isthmus

Comparison of the area of the narrowest aerated/ bony tympanic isthmus in mm^2 between the control group and chronic otitis media group. Represented by average± 1SD.

		Control (N=11)	COM (N=11)	p	Effect size (d)
The narrowest area (mm^2)	Aerated tympanic isthmus	9.80±3.53	6.06±2.27	<0.01*	1.26
	Bony tympanic isthmus	9.85±3.31	9.88±1.80	0.39	0.01

*P< 0.01 compared with the control group.