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Cochlear and vestibular volumes in inner ear malformations

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Abstract

Objective: A gold standard for quantitatively diagnosing inner ear malformations (IEM) and a consensus on normative measurements are lacking. Reference ranges and cut-off values of inner ear dimensions may add in distinguishing IEM types. This study evaluates the volumes of the cochlea and vestibular system in different types of IEM.

Study Design: Retrospective cohort.

Setting: Tertiary academic center.

Patients: High-resolution CT scans of 115 temporal bones (70 with IEM; [cochlear hypoplasia (CH; n=19), incomplete partition type I and III (IP; n=16), IP type II with an enlarged vestibular aqueduct (Mondini malformation [MM]; n=16), enlarged vestibular aqueduct syndrome (EVAS; n=19), and 45 controls.

Interventions: Volumetry by software-based, semi-automatic segmentation and 3D reconstruction.

Main Outcome Measures: Differences in volumes among IEM and between IEM types and controls; inter-rater-reliability (IRR).

Results: Compared to controls (mean volume:78.0mm^3), only CH showed a significantly different cochlear volume (mean volume 30.2mm^3, $p<0.0001$) among all types of IEM. A cut-off value of 60mm^3 separated 100% of CH cases from controls. Compared to controls, significantly larger vestibular system volumes were found in MM (mean difference 22.9mm^3, $p=0.009$) and IP (mean difference 24.1mm^3, $p=0.005$). In contrast, CH showed a significantly smaller vestibular system volume (mean difference 41.1mm^3, $p<0.0001$). A good IRR was found for all three-dimensional measurements (ICC=0.86–0.91).

Conclusion: Quantitative reference values for IEM obtained in this study were in line with existing qualitative diagnostic characteristics. A cut-off value of <60mm^3 may indicate an abnormally small cochlea. Normal reference values for volumes of the cochlea and vestibular system may aid in diagnosing IEM.

Keywords: Cochlear malformation, Inner ear malformation, diagnosis, volume, 3D segmentation

Introduction

Inner ear malformations (IEM) represent a heterogenous group of anatomical anomalies that are associated with sensorineural hearing loss, vertigo or both [1–3]. The true overall prevalence of IEM is difficult to determine because not all IEMs are detected on sectional imaging due to technical limitations [4]. Sectional imaging is the clinical standard for the evaluation of temporal bone structures in vivo [5–8]. Different classification systems for IEM have been developed. Jackler et *al*. first classified IEM types in 1987 based on the arrested development theory which interprets every IEM type as a result of a developmental arrest at a specific embryonal stage during inner ear morphogenesis [9]. This theory was further developed by Sennaroglu and Saatci, and a differentiation of incomplete partition types was added [10]. This classification currently represents the most accepted categorization of IEM. Newer studies have demonstrated that not every type of IEM may be diagnosed with the existing classification systems and have presented another approach, which includes the severity of the malformation in the grading system [11]. Yet, the types of IEM are still characterized by qualitative characteristics determined solely by visual inspection of radiological images [4,8,12]. This poses several difficulties to the radiological diagnosis of IEMs corroborated by a recent study, which found that only one third of IEM cases were directly diagnosed by simple visual inspection [4]. However, as in several other radiological diagnoses, where reference values exist that help to distinguish normal from abnormal, reference values for measurements of inner ear structures might be helpful in distinguishing between a normal and malformed cochlea. Correct diagnosis of the correct type of IEMs can contextualize the patient’s symptoms, establish a likely prognosis and determine appropriate treatment [13,14]. Despite a high number of detailed descriptions on the anatomical particularities of different IEMs, a gold standard for *quantitatively* diagnosing IEM is lacking and there is currently no consensus on normal measurements of inner ear structures to aid in distinguishing IEM types. Attempts to add quantitative radiographic measurements of inner ear structures to improve diagnosis are sparse and not widely accepted [15,16]. Only a few attempts to characterize IEMs through measurements have been made (e.g. in diagnosing an enlarged vestibular aqueduct)[17–19]. In mild or ambiguous cases of IEM, radiographic measurements may be a crucial diagnostic feature that distinguishes, not only a normal inner ear from an ear exhibiting an IEM, but may also help in differentiating distinct types of IEM from each other. However, currently existing parameters for measuring temporal bone structures are determined in a certain plane of sectional imaging that is chosen individually by each examiner, which significantly contributes to inter-observer variability [16,20,21].

One proposed attempt to reduce inter-observer differences in radiologic measurements of inner ear structures is the use of segmentation and three-dimensional reconstruction [20–22]. Therefore, investigating the association of two-dimensional and three-dimensional measurements of inner ear structures may yield information on novel diagnostic parameters. The current study is based on the hypothesis that normative measurements of inner ear structures may help to identify IEM and to assess possible treatment options. This study aimed to i) establish normative metric and volumetric ranges and values for healthy and malformed inner ear structures ii) to evaluate whether the development of cut-offs is possible to distinguish between different malformation types and iii) to compare differences in the inter-observer-agreement in three-dimensional volumetric measurements and two-dimensional measurements of IEM.

Methods

The study protocol was made according to the Helsinki declaration and its amendments and was approved by the local ethics committee (No. 21-7358-BR). In this retrospective multi-center study, 70 high-resolution CT (HRCT) temporal bone datasets from patients with IEM were analyzed and compared to HRCT datasets of 45 patients with no inner ear pathology. Slice thickness varied between 0.625 mm and 1 mm. Within the group of IEM, 19 cases of enlarged vestibular aqueduct syndrome (EVAS), 19 cases of cochlear hypoplasia (CH), 16 cases of incomplete partition (IP) type I (IPI) and type III (IPIII) and 16 cases of IP type II (IPII) with an enlarged vestibular aqueduct (Mondini malformation = MM). All CT datasets were anonymized prior to image analyses.

Image analysis

The A-value (diameter) and B-value (width) of the cochlear basal turn were assessed from CT datasets in the oblique coronal view. The H-value corresponds to the height of the cochlea, i.e. the distance between the apex and the base of the cochlea [20].

CT datasets were reconstructed using 3D slicer (https://www.slicer.org/, version 4.13.0, Massachusetts, USA [23]). Segmentation of the inner ear was performed using threshold analysis (threshold range: -1024 to 700 Hounsfield units) and a three-dimensional model of the inner ear was reconstructed as previously described[22] (Figure 1A–C). Volumes were calculated using the segment statistics module and the segmentation module of the 3D slicer software. IEM were diagnosed according to the Sennaroglu and Saatci classification [10,24] by a senior neuroradiologist with significant expertise in temporal bone radiology. In inconclusive cases, the INCAV criteria were added [11]. All measurements were performed by two independent examiners with at least one year experience in the diagnosis of temporal bone imaging. Both investigators were blinded to the measurements of the other investigator.

Statistical analysis

Statistical analyses were performed using Prism (version 8, GraphPad Software, La Jolla, CA, USA). The significance level was set to $p < 0.05$. To compare differences among groups, a one-way analysis of variance (ANOVA) was used. Tukey's test was used to correct for multiple comparisons. Correlations were assessed using Pearson's correlation. A Person's correlation coefficient of <0.3 was interpreted as an indicator of a weak correlation, 0.3–0.59 of a fair correlation, 0.6–0.79 of a moderate correlation, and 0.8–0.99 of a very strong correlation [25,26]. The inter-rater reliability (IRR) was determined by calculating the intra-class correlation coefficient (ICC). The reference range for cochlear and vestibular volume was calculated from the control group as two standard deviations below the mean to two standard deviations above the mean.

Receiver operating characteristic (ROC) curves were determined to estimated sensitivity and specificity. The optimal cut-off value was selected where Youden's index, i.e. sensitivity + specificity – 1, reached its maximum.

Results

Two-dimensional *measurements*

A one-way ANOVA revealed significant differences in the *A-value*, *B-value* as well as the *H-value*. Post-hoc analysis showed significant differences between the A-value of CH and the A-value of every other group ($p < 0.0001$, Figure 2A). The same applied to the B-value ($p < 0.0001$, Figure 2B) and the H-value ($p < 0.0001$). Furthermore, the H-value significantly differed between the control group and both IP (mean difference 0.6 mm, $p < 0.0001$) and MM (mean difference 0.4 mm, $p = 0.002$). Moreover, the H-value of IP was significantly different from EVAS (mean difference 0.5 mm, $p = 0.005$; Figure 2C).

Volume

A three-dimensional model of the bony labyrinth of the inner ear was successfully reconstructed in every case. The values for individual volumes among the different IEM are shown in Table 1. A one-way ANOVA revealed significant differences in the cochlear volume (5 groups, $n = 115$, $p < 0.0001$) and the volume of the vestibular system (5 groups, $n = 115$, $p < 0.0001$) between different groups of IEM.

Concerning the cochlear volume (Vo-C), post-hoc analysis showed significant differences between $Vo\text{-}C_{CH}$ and $Vo\text{-}C_{control}$ (mean difference 47.80 mm^3; 95% confidence interval [95%CI] 33.0–62.6 mm^3; $p < 0.0001$), between $Vo\text{-}C_{CH}$ and $Vo\text{-}C_{MM}$ (mean difference 47.4 mm^3, 95%CI 29.0–65.8 mm^3, $p < 0.0001$), between $Vo\text{-}C_{CH}$ and $Vo\text{-}C_{EVAS}$ (mean difference 52.2 mm^3, 95%CI 34.6–69.8 mm^3, $p < 0.0001$) as well as between Vo-C_{CH} and Vo-C_{IP} (mean difference 61.5 mm^3, 95%CI 43.1–79.9 mm^3, $p < 0.0001$; Figure 3A).

Concerning the volume of the vestibular organ (Vo-V) post-hoc analysis showed significant differences between Vo-V_{CH} and Vo-$V_{control}$ (mean difference 41.1 mm^3; 95%CI 23.4–58.7 mm^3; $p < 0.0001$), between Vo-V_{CH} and Vo-V_{MM} (mean difference 63.9 mm^3, 95%CI 42.0–85.8 mm^3, $p < 0.0001$), between Vo-V_{CH} and Vo-V_{EVAS} (mean difference 52.4 mm^3, 95%CI 31.5–73.4 mm^3, $p < 0.0001$) as well as between Vo-V_{CH} and Vo-V_{IP} (mean difference 65.2 mm^3, 95%CI 43.2–87.1 mm^3, $p < 0.0001$; Figure 3B).

Correlation volume and 2-dimensional measurements

The cochlear volume correlated strongly to the A-value ($r = 0.80$, Figure 2D) and the B-value ($r = 0.85$, Figure 2E) and moderately to the H-value ($r = 0.75$, Figure 2F). The best correlation was found between the cochlear volume and the B-value ($r = 0.85$).

A good to excellent inter-rater reliability was found for all the A-value measurements (ICC = 0.86) as well as for the B-value measurements (ICC = 0.96) and the H-value measurements (ICC = 0.86). Comparatively, the inter-rater reliability for the three-dimensional measurements were good to excellent for the cochlea (ICC = 0.91) and the vestibular system (ICC = 0.86).

Based on a multiple regression model from these data, a cochlear volume can be estimated from the A-, B- and H-value as follows:

$$Cochlear\ volume = 4.4 \cdot A\text{-}value + 12.2 \cdot B\text{-}value + 13.2 \cdot H\text{-}value - 102.9$$

Correlation cochlear volume and volume of the vestibular system

The cochlear volume correlated moderately to the volume of the vestibular system in the control group ($r = 0.69$, $p < 0.0001$, Figure 4E) as well as in EVAS ($r = 0.78$, $p < 0.0001$, Figure 4D). A moderate negative correlation was found in CH ($r = -0.79$, $p < 0.0001$, Figure 4A). The cochlear volume correlated fairly to the volume of the vestibular system in MM ($r = 0.50$, $p = 0.04$, Figure 4C). No correlation was found between cochlear volume and the volume of the vestibular system in IP (Figure 4B).

Reference ranges and cut-off values for inner ear volumes

Based on the normal control group, normal volume range for the bony labyrinth were estimated to 59 mm^3 – 97 mm^3 for the cochlea and to 71 mm^3 – 146 mm^3 for the vestibular system. A cochlear volume of < 58.3 mm^3 differentiated CH from a normal cochlea with a specificity of 100.0 % (95%CI 83.2%–100.0%) and a sensitivity of 100.0% (95%CI 92.1%–100.0%). A vestibular system volume of < 95.8 mm^3 differentiated CH from a normal vestibular system with a specificity of 100.0% (95%CI 83.2%–100.0%) and a sensitivity of 82.2% (95%CI 68.7%–90.7%). A cut-off value in vestibular system volume of < 69.0 mm^3 was 100% (95%CI 92.1%–100.0%) specific for CH with a sensitivity of 36.8% (95%CI 19.2%–59.0%).

Discussion

This study assessed volumes of separate regions of the bony labyrinth, i.e. cochlea and vestibular system in different IEM and in normal controls. Further, the volumes of the cochlea and the vestibular system were correlated to each other, and two-dimensional measurements of the cochlea were correlated to cochlear volume. Significant differences in all volumes were found among the different types of IEM and between IEM and controls. Specifically in CH, we found that not only the cochlear volume, but also the volume of the vestibular system is reduced compared to the other types of IEM. CH showed a strong negative correlation between cochlear volume and the volume of the vestibular system. Regarding possible quantitative, cut-off values for diagnosing IEM, two-dimensional measurement data of IEM exhibited a considerable overlap with the reference values of the control group (Figure 2A and 2C). In contrast, three-dimensional measurement data showed less overlap (Figure 3A), so that diagnostic cut-off values may be easier to define for volumes than for two-dimensional measurements. Thus, considering two-dimensional images alone may complicate the diagnosis of the correct IEM.

The most widely accepted classification systems of IEM were introduced by Jackler and Sennaroglu. Neither of these well-known classification systems utilized three-dimensional reconstruction and neither measured inner ear volumes. Only a few studies report volumetric data on the normal human cochlea. These results are comparable to the control group presented in the present study [27,28]. Comparable normative data on IEM is lacking. Previous studies have provided valuable methods for qualitative radiologic diagnosis of IEM [16,21,22,29–31]. However, particularly CH may be difficult to diagnose, as it is difficult to assess when applying the existing classifications [32]. A specific pitfall is CH type IV, since it resembles a normal cochlea in the basal turn (Figure 1D–F), but with hypoplastic (smaller diameters and volume) middle and apical turns located anterior and medially [24]. This is particularly challenging before cochlear implantation, because the insertion of a cochlear implant electrode can be difficult due to the narrow space in the temporal bone and the reduced cochlea volume. This study provides evidence for both small cochlea and small vestibule in CH cases, which may explain why diagnosis of CH at first glance from clinical imaging might be challenging since the cochlear proportions resemble a normal cochlea. Based on the present preliminary data, a volume below approximately 60 mm^3 may differentiate CH from a normal cochlea. Concerning the vestibular system, such a cut-off may be less evident. Based on our data, values < 70 mm^3 suggests CH, although a considerable overlap in vestibular system volumes was found between CH and controls. The normative A-values and B-values reported in this study are in agreement with the existing literature[33].

The present study is limited by the small sample size of IEMs. However, given the rarity of IEM, the sample can still be considered representative and is well-suited to provide an approximation of reference values. Another limitation is that 3D-slicer is not approved as medical diagnostic device. Lastly, the three-dimensional analysis is time-consuming. For these reasons, the method has not yet found its way into clinical routine.

Conclusion

Quantitative reference values of cochlear and vestibular volume obtained in IEM were in line with existing qualitative diagnostic characteristics. Volumetric assessment using three-dimensional segmentation avoids measurement variability that arises from two-dimensional measurements based on orientation and position of any particular slice or section. Normal reference values for volumes of the cochlea and vestibular system may aid to diagnosing IEM. Notably, a cut-off value of < 60 mm^3 may indicate an abnormally small cochlea.

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Tables

Table 1. Descriptive statistics of inner ear volumes in controls and different types of inner ear malformations.

Figure legends

Figure 1. Exemplary inner ear segmentation and three-dimensional volume reconstruction in a normal temporal bone (A–C) and in a case of cochlear hypoplasia (D–F). **A–C** In this normal temporal bone, the cochlea exhibits an A-value of 10.2 mm and a volume of 84.1 mm^3. **D–F** In this exemplary case of cochlear hypoplasia, the cochlea has an A-value of 8.2 mm and a volume of 37.2 mm^3. Magenta, cochlear space; yellow, vestibular space. Co, cochlea (basal turn); EAC, external auditory canal; Inc, incus. LSC, lateral semicircular canal; Ma, mastoid; Mal, malleus. Scale bars: 5mm. Black cube shows orientation in space (I, inferior; P, posterior; R, right).

Figure 2. Two- and three-dimensional inner ear measurements in controls and different types of inner ear malformations. **A–C** Scattered bar plot showing A-value (A), B-value (B), and H-value (C) in controls and different types of inner ear malformations. Box indicates mean, whiskers indicated standard deviation. **D–F** Correlation between cochlear volume and A-value (G), B-value (H), and H-value (I). Solid black line represents linear regression line, dashed grey lines represent 95% prediction intervals. r, Pearson's correlation coefficient. Color of single dots corresponds to groups in A–F. CH, cochlear hypoplasia; IP, incomplete partition; MM, Mondini malformation; EVAS, enlarged vestibular aqueduct syndrome.

Figure 3. Scattered bar plot showing cochlear volume (A) as well as volume of the vestibular system (B) in controls and different types of inner ear malformations. Box indicates mean, whiskers indicated standard deviation. Green dotted lines indicate normal mean value ± two standard deviations.

Figure 4. Correlation between cochlear volume and volume of the vestibular system of IEM and controls. Cochlear hypoplasia (A). Incomplete partition (B), Mondini malformation (C), Enlarged vestibular aqueduct syndrome (D) and controls (E). Solid black line represents linear

regression line, dashed grey lines represent 95% prediction intervals. r, Pearson's correlation coefficient.

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