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Review

Investigating Additional Cochlear Parameters: A follow-up systematic review and meta-analysis

Deven P. Curtis [a,*], Anthony N. Baumann [a], Natasha Salmen [a], Anita Jeyakumar [a,b]

[a] Northeast Ohio Medical University, Rootstown, OH, USA
[b] Bon Secours Mercy Health, Youngstown, OH, USA

ABSTRACT

Objectives: The movement towards personalization of cochlear implantation has continued to generate interest about variabilities in cochlear size. In a recent meta-analysis, Atalay et al. (2022) examined organ of corti length, cochlear lateral wall, and "A" value and found that most covariates, other than congenital sensorineural hearing loss, did not impact cochlear size via these measurements. However, no meta-analysis exists on how patient-specific variables could impact other cochlear size measurements, such as cochlear height (CH), and "B" value (defined as the distance between opposite lateral walls and perpendicular to "A" value). The purpose of this systematic review and meta-analysis is to examine how patient-specific variables impact additional cochlear size measurements to assist clinical decision-making.

Databases reviewed: A systematic review for cochlear size measurements using PRISMA methodology was performed using PubMed, CINAHL, and MEDLINE from database inception to October 1st, 2022.

Methods: Search terms used included English, cochlea, size, histology, anatomy, and human. Inclusion criteria were measurements for human cochlea, full-text articles, and articles in English. Primary measurements were "B" value and CH, as these measurements differ from the recent meta-analysis on this topic. Cochlear duct length (CDL) was also included. A random-effects continuous model for meta-analysis was performed. Measurements were stratified by gender (male/female) and disease type (sensorineural hearing loss (SNHL)/conductive hearing loss (CHL)).

Results: A total of 7 articles met final inclusion criteria from a total of 674 articles received on initial search, resulting in 2263 total human cochleae. There was a statistical difference between male CDL ($n = 681$ cochlea) compared to female CDL ($n = 657$) from four articles ($p < 0.001$; Cohen's d effect size (ES):0.421; 95% confidence intervals (CI): 0.171, 0.671). The frequency weighted mean for male CDL was 33.5 mm ± 1.8 mm and the frequency weighted mean for female CDL was 32.4 mm ± 1.5 mm with an unstandardized mean difference of 0.854 mm. There was no statistical difference between male "B" value ($n = 329$) and female "B" value ($n = 349$) for cochlea from two studies ($p = 0.184$; Cohen's d ES: 0.410; 95% CI: 0.194, 1.014). The frequency weighted mean for male "B" value was 6.5 mm ± 0.1 mm and the frequency weighted mean for female "B" value was 6.4 mm ± 0.1 mm with an unstandardized mean difference of 0.126 mm. There was no statistical difference between CH for SNHL ($n = 282$) and CHL ($n = 275$) from two studies ($p = 0.486$; ES: 0.085; 95% CI: 0.323, 0.153, F ig. 3). The frequency weighted mean for SNHL CH was 4.6 mm ± 0.8 mm and the frequency weighted mean for CHL CH was 4.3 mm ± 0.8 mm with an unstandardized mean difference of 0.032 mm.

Conclusion: Male CDL is statistically larger than female CDL. There is no statistically significant association between gender or hearing loss type and "B" value or CH. The effect size for all comparisons is small, indicating little practical significance between any existing differences. The results of this study provide two additional cochlear metrics and indicate similar findings to the study by Atalay and colleagues as patient-specific characteristics appear to have no statistically significantly impact on cochlear size.

1. Introduction

Unlike most organs, the human cochlea is fully formed during gestation and reaches adult size by birth (Pelliccia et al., 2014; Pappas et al., 1990; Nemzek et al., 1996; Jackler et al., 1987). Apart from the marked early maturity relative to other organs, the cochlea also exhibits remarkably little interpersonal size variation compared to other structures, such the temporal bone (The postnatal growth of the, 1994; Koch et al., 2017). Pioneering scientists and physicians dating back to Retzius in the 1880s and Hardy in the 1930s began measuring the cochlea first directly and then indirectly to explain anatomy and investigate function (Koch et al., 2017; Hardy, 1938).

Due primarily to the invention of the cochlear implant, modern cochlear-size research is most often done with the aim of improving patient outcomes and informing future treatments (Ketterer et al., 2018; Roche and Hansen, 2015). The modalities used in determining such

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* Corresponding author. 3434 Atterbury St, Cuyahoga Falls, OH, USA.
E-mail address: curtis@neomed.edu (D.P. Curtis).

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measurements vary widely with the most common methods being computed tomography (CT)—including high resolution, cone beam, and, recently, ultra-high resolution—to less common methods such as plastic casts or fixed-distance photography (Koch et al., 2017; Dimopoulos and Muren, 1990; Atalay et al., 2022; Heutink et al., 2020).

One area of current discord within the literature is the debate of whether there exists sufficient interpersonal cochlear size variation to warrant routine pre-operative cochlear measurements and subsequent personalized cochlear implant electrodes (Ketterer et al., 2018; Meng et al., 2016; Van Der et al., 2014; Kuthubutheen et al., 2019; Helpard et al., 2020). Furthermore, it is unknown which patient-specific characteristics might influence the degree of size variation. While dozens of individual studies have addressed these questions directly or indirectly, the results have been largely equivocal with some, such as Braga et al. (2019) or Alanazi et al. (2018), concluding that cochlear size varies with gender or race while others such as Vu et al. (2019) indicate that there are no known associations between size variation and demographic traits (Braga et al., 2019; Alanazi and Alzhrani, 2018; Vu et al., 2019).

In 2022, Atalay et al., provided the most sweeping response to these questions to date, conducting a large review and meta-analysis which initially evaluated over 4000 publications and ultimately included over 4700 cochleae (Atalay et al., 2022). Atalay et al. reported on three measurements: the organ of corti, lateral wall, and “A” value (defined as the distance from the round window, through the modiolus, to the opposite wall) and found no statistically significant relationship to any covariate including gender, age, or disease state. Since the cochlea is a complex geometrical structure other measurements such as cochlear height (CH) and “B” value have been developed to allow for proper assessment of morphology. To the authors knowledge, no existing meta-analysis has examined CH or “B” value, (see Figs. 1 and 2). CH, in particular, has been recently highlighted as a clinically consequential measurement which influences the final position of the electrode array in cochlear implant (CI) surgery (Ketterer et al., 2018).

2. Purpose

The purpose of this systematic review and meta-analysis is to examine measurements beyond those considered by Atalay et al. (2022), namely CH, and “B” value. Cochlear duct length (CDL) is also assessed as a tangential finding.

3. Methods

The study was IRB exempt.

3.1. Study design

The study is a systematic review and meta-analysis examining the association of patient-specific variables on CH and “B” value. The primary search was conducted using PubMed, CINAHL, and MEDLINE from database inception until October 1st, 2022. This study follows the guidelines of the latest Preferred Reporting Items for Systematic Review and Meta-Analyses (PRISMA). This study was not registered on PROSPERO prior to completion.

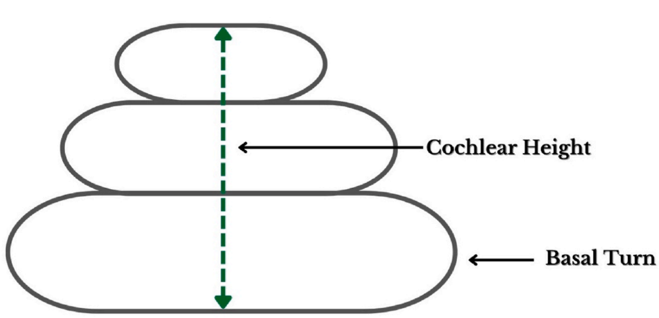

Fig. 1. The cochlear spiral with illustration of cochlear height.

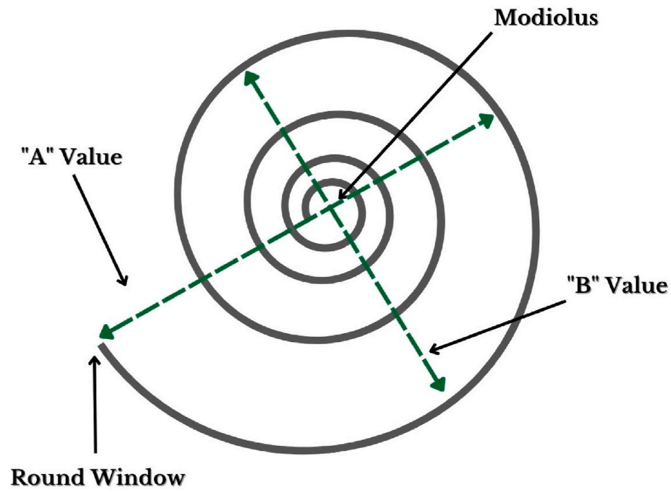

Fig. 2. The cochlear spiral with illustration of “B” value as reported in this study and “A” value for reference.

3.2. Eligibility criteria

Included articles were available in full text, written in English, involving human cochleae, which provided mean numerical measurements and standard deviations for relevant cochlear parameters. Review articles and case reports were excluded. Articles were also excluded if they did not provide analyzable numerical measurements (numbers only in line plots), or if they failed to group patients according to demographic characteristics (gender or hearing loss type) and provide measurements for variables of interest (CH, “B” Value, and CDL).

3.3. Study definitions

For the purposes of this study, CH refers to the distance from the lowest portion of the base of the basal turn to the peak of the cochlear spiral (Fig. 1). While “A” value is not reported in the present study, it is a common measurement taken histologically or via imaging and is described in the text and illustrated in Fig. 2 as a reference for explaining “B” Value. “A” Value, (defined as the distance from the round window, through the modiolus to the opposite lateral wall) is a measurement initially proposed in the 2006 article from Escude et al., and is widely used within the literature (Escudé et al., 2006). “B” value is traditionally described in reference to “A” value as a measurement taken in the same plane, also through the modiolus, but perpendicular to “A” value as illustrated in Fig. 2.

3.4. Article screening

After initial search, all articles were screened by two researchers for manual removal of all duplicate articles. Resultant articles were then screened by title and abstract for relevance followed by full text retrieval and detailed screening according to eligibility criteria to arrive at the final article count.

3.5. Data extraction

Primary measurements included “B” value, CDL, and CH as these measurements differ from the recent meta-analysis by Atalay et al. on this topic (Atalay et al., 2022). Other data extracted included first author, year of publication, number of cochleae, patient gender, patient disease state (sensorineural hearing loss (SNHL)/conductive hearing loss (CHL)) where available, and mean with standard deviation of the three primary measurements of interest.

3.6. Statistical analysis

The Statistical Package for the Social Sciences (SPSS) version 29.0 statistical software was used for analysis for this study. Descriptive statistics and frequency weighted means were used to pool the data for simple description. For meta-analysis, a random-effects continuous model was used for the three primary measurements with Cohen's d (standardized mean difference) used for effect size for statistical significance. A random-effects model was used due to different raters, different study locations, and possible differences in exact measurement technique throughout each study. Due to low total number of included articles in final selection, funnel plots were not generated to assess for bias across articles. Bias was assessed within the individual included articles using the methodological index for non-randomized studies (Minors) scale as described in Table 1 (Slim et al., 2003). Unstandardized mean difference was used only for determining the actual difference in relevant units between groups and was not used to determine statistical significance. Statistical significance was set at 0.05 for this study.

4. Results

4.1. Search results

A total of 7 articles met final inclusion criteria from a total of 674 articles received on initial search (Ketterer et al., 2018; Heutink et al., 2020; Meng et al., 2016; Alanazi and Alzhrani, 2018; Teissier et al., 2010; Stefanescu and Motoi, 2018; Mori and Chang, 2012). See Fig. 3 below for a visual depiction of the inclusion process for this study.

4.2. Sample size information

A total of 2263 human cochleae were examined with some cochleae being used for multiple different comparisons. A total of 1338 cochleae were used for male and female comparisons for CDL, 678 cochleae were used for male and female comparisons for "B" value, and 557 cochleae were used for SNHL and CDL comparisons for CH. Imaging modalities used for individual studies included CT, high-resolution CT, cone-beam CT, and ultra-high-resolution CT.

4.3. Male to female cochlear duct length comparisons

There was a statistically significant difference between male CDL compared to female CDL from four articles with a small overall ES ($p < 0.001$; Cohen's d ES:0.421; 95% CI: 0.171, 0.671; Fig. 4). The frequency weighted mean for male CDL ($n = 681$) was 33.5 mm ± 1.8 mm and the frequency weighted mean for female CDL ($n = 657$) was 32.4 mm ± 1.5 mm with an unstandardized mean difference of 0.854 mm.

Table 1
Individual study risk of bias results per Minors scale in which a higher score corresponds with lower risk of bias with the highest possible score for non-comparative studies being 16.

First Author (Study Year)	MINORS Score
Meng et al. (2016)	16
Alanazi (2018)	13
Huetink (2020)	16
Stefanescu (2018)	16
Ketterer et al. (2018)	15
Teissier et al. (2010)	15
Mori (2012)	16

4.4. Male to female "B" value comparisons

This study found that there was no statistical difference between male "B" value ($n = 329$) and female "B" value ($n = 349$) for cochleae from two studies ($p = 0.184$; Cohen's d ES: 0.410; 95% CI: 0.194, 1.014; Fig. 5). The frequency weighted mean for male "B" value was 6.5 mm ± 0.1 mm and the frequency weighted mean for female "B" value was 6.4 mm ± 0.1 mm. The unstandardized mean difference between male "B" value and female "B" value was 0.126 mm.

4.5. Hearing loss type cochlear height comparisons

This study found that there was no statistical difference between SNHL CH and CHL CH for cochleae between two studies ($p = 0.486$; Cohen's d ES: 0.085; 95% CI: 0.323, 0.153, Fig. 6). The frequency weighted mean for SNHL CH ($n = 282$) was 4.6 mm ± 0.8 mm and the frequency weighted mean for CHL CH ($n = 275$) was 4.3 mm ± 0.8 mm. The unstandardized mean difference between SNHL and CHL CH was −0.032 mm.

5. Discussion

Our understanding of interpersonal anatomical cochlear differences is evolving—likely in part due to the increasing reporting on cochlear size as well as the increasingly routine use of CT imaging in the clinical setting (Meng et al., 2016; Teissier et al., 2010; Dhanasingh, 2019). The advent of customized cochlear implants, too, is likely both a cause and effect of these studies and advancements (Pietsch et al., 2022). The results from the present study are in concordance with many recent studies in concluding that there are indeed interpersonal variations in cochlear dimensions (Braga et al., 2019; Alanazi and Alzhrani, 2018; Gee et al., 2021). And while we know more than ever before about the normative dimensions and interpersonal variability of the human cochlea, the information we have from these various studies is often in conflict, and some dimensions are still poorly substantiated (Pelliccia et al., 2014; Atalay et al., 2022; Meng et al., 2016; Kuthubutheen et al., 2019; Escudé et al., 2006; Dhanasingh, 2019).

Many primary studies from the past two decades, for instance, indicate that gender is associated with variations in cochlear measurements, generally indicating that males have one or more cochlear dimensions different than females, usually being larger (Meng et al., 2016; Braga et al., 2019; Alanazi and Alzhrani, 2018; Vu et al., 2019; Escudé et al., 2006). Yet, Atalay et al. (2022), who drew upon many of those very studies, determined that no statistically significant differences exist between cochlear size and gender. Our analysis agrees with the findings of Atalay et al. in that we provide an additional two meta-analytically analyzed measurements, CH and "B" value, which have not been previously analyzed, both of which show no significant relationship between interpersonal cochlear size variations and gender or hearing loss type.

Since our findings show no association between type of hearing loss and CH, it may be that CH is less affected by SSNHL than other measures like CDL, which has been previously found to have a statistically significantly relationship with SSNHL (Atalay et al., 2022). Like many of the previous studies, but unlike Atalay et al., we found that the association between CDL and gender was statistically significant (Atalay et al., 2022; Meng et al., 2016; Braga et al., 2019; Alanazi and Alzhrani, 2018; Vu et al., 2019; Escudé et al., 2006). However, when the effect size is calculated and considered, the clinical significance of this finding among our data may be small. As of this review, any existing differences between male and female cochlear measurements are due to unknown mechanisms and the data is mixed both among small trials and large reviews as to whether such differences are statistically significant. Further research needs to be done to better quantify and determine the significance and cause of any existing gender-associated differences. Our study finds gender-related size differences in CDL and thus may

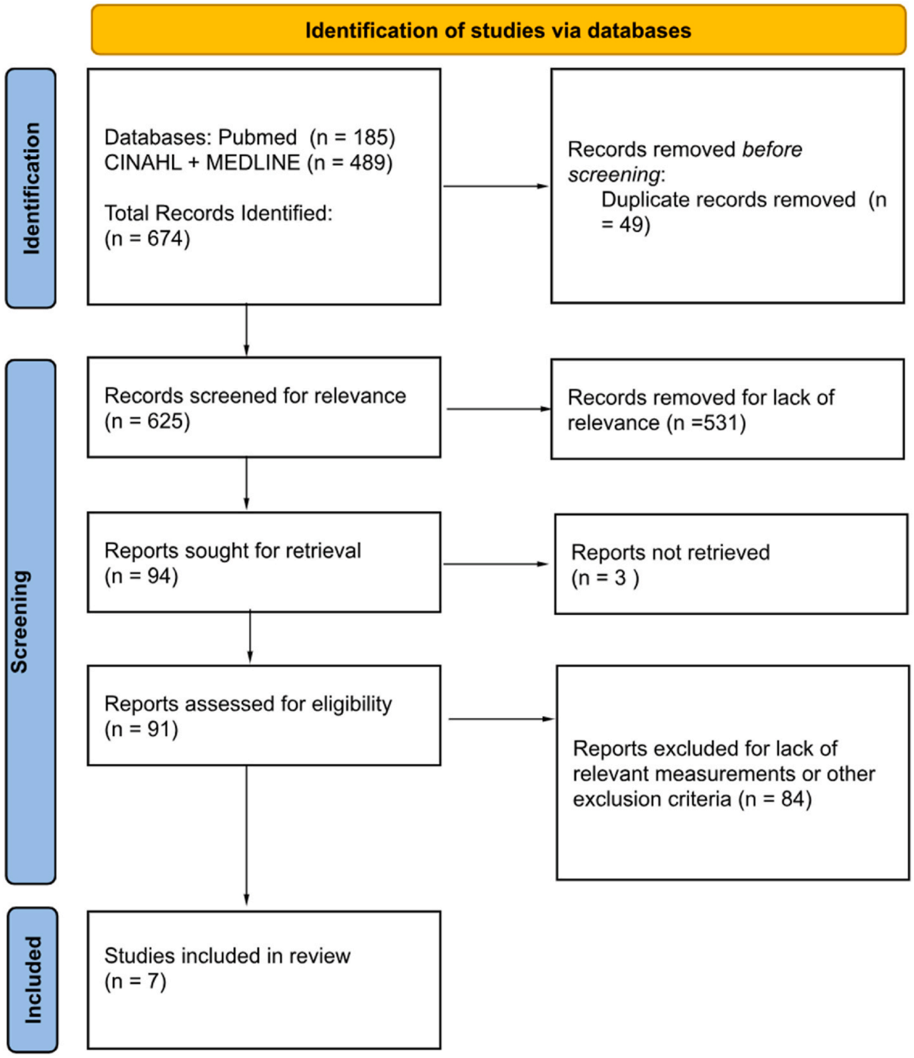

Fig. 3. 2020 PRISMA statement describing records identified, screened, and included during the selection process for this systematic review and meta-analysis.

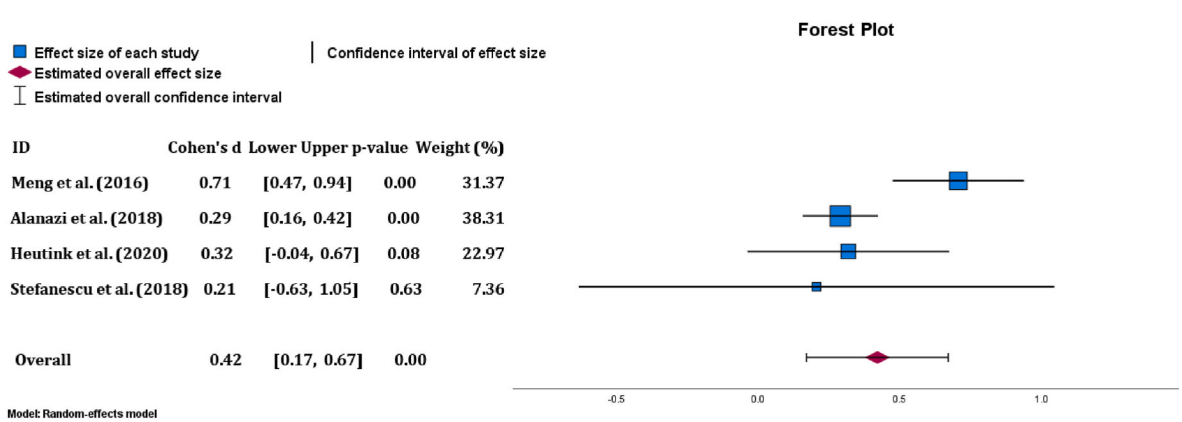

Fig. 4. Forest plot comparing male to female cochlear duct length (Heutink et al., 2020; Meng et al., 2016; Alanazi and Alzhrani, 2018; Stefanescu and Motoi, 2018).

cautiously suggest that pre-operative CT measurements prior to CI surgery may be a helpful consideration for personalization, although more research is needed on this topic.

While CT is now routinely used in CI surgery—preoperatively to rule out cochlear malformation, and postoperatively to rule out dislocation—there is little indication within the literature that these imaging modalities are used for to take patient-specific cochlear measurements (Widmann et al., 2020). This lack of treatment tailoring is likely a reflection of the traditional "one-size-fits-all" model which likely stems from our understanding that the cochlea is fully formed at birth with minimal evidence of change in size over time (Pelliccia et al., 2014; Pappas et al., 1990; Jackler et al., 1987; Mori and Chang, 2012). This

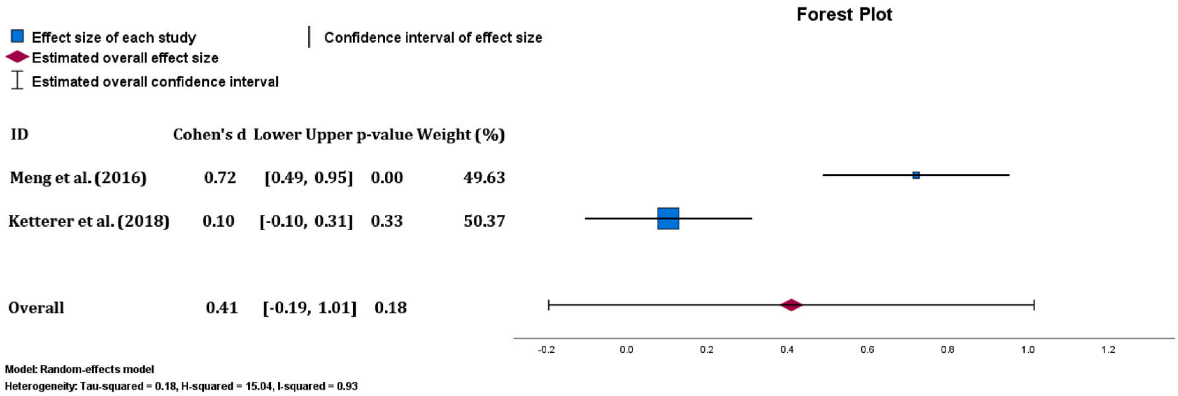

Fig. 5. Forest plot showing male to female “B” value comparisons (Ketterer et al., 2018; Meng et al., 2016).

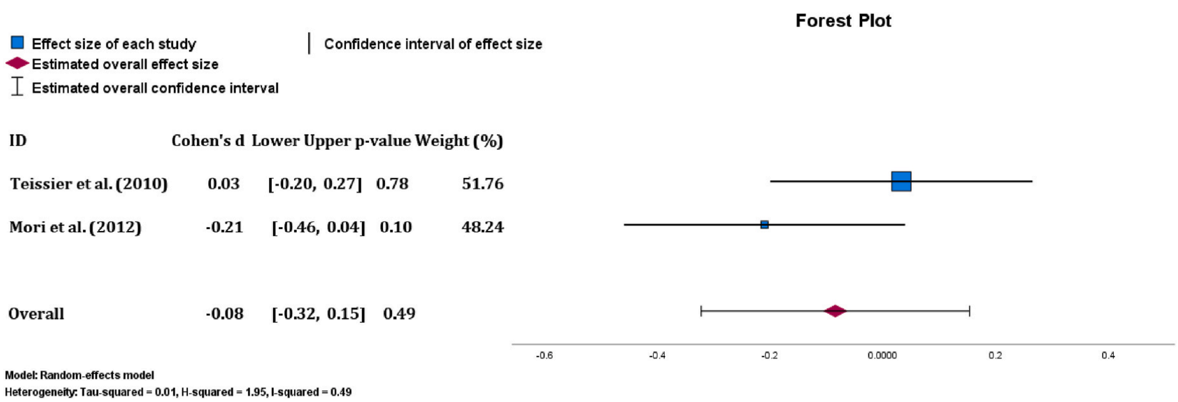

Fig. 6. Forest plot showing sensorineural hearing loss to conductive hearing loss for cochlear height (Teissier et al., 2010; Mori and Chang, 2012).

traditional model is being both challenged and reaffirmed by emerging literature, and our findings contribute to this larger picture by suggesting another subset of measurements which appear to be independent of patient demographic traits.

Since cochlear size—particularly the CH—is becoming a “defining factor” of choice of electrode in CI surgery the findings of this study may also have clinical implications. Specifically, a short cochlear height may be associated with tight turning of the cochlear spiral, potentially affecting the insertion of the CI electrode. Similarly, “B” value is a measurement with clinical significance; the shape of the basal turn has also been shown to influence the ease of insertion of the electrode, and “A” and “B” ratio suggest the shape of the cochlear basal turn (Khurayzi et al., 2021). Our results indicate that hearing loss type (CHL and SSNHL) and gender have no statistically significant association with interpersonal variations of CH or “B” value, which may indicate that the studies within the literature which have found associations between cochlear parameters and gender may be less applicable to CH and “B” value or may need a larger sample to make more definitive conclusions.

5.1. Limitations

While Atalay et al. included the length of the organ of corti and lateral wall, both of which are measures of the CDL, we still elected to report CDL in our study as a tangential data point to further validate or challenge previous findings. The results of our smaller sample size ran contrary to those of the larger sample size examined by Atalay et al., which further points to the likely clinically insignificant association between CDL and gender evidenced by the small effect size.

To lower bias, this meta-analysis only utilized cochlear measurement comparisons within the same study which resulted in an inherently smaller sample size. This limitation results in conclusions being drawn based on comparisons between only two different studies in some cases. Ideally, a larger number of studies would be involved to back meaningful conclusions about the impact of patient demographics on cochlear size. To the author’s knowledge, however, the pooled sample size of cochleae presented here represents the largest number of cochleae ever examined for the “B” value and CH and patient-specific characteristics in the literature, thus despite inherent limitations, these findings provide insights not previously available for either the hearing loss or general population.

6. Conclusion

Male CDL is statistically significantly larger than female CDL, but likely fails to reach any clinical significance. There is no statistically significant association between gender, or hearing loss type and “B” value or CH. The effect size for all comparisons is small, indicating little practical significance between any existing differences. The results of this study provide two additional cochlear metrics and indicate similar findings to the study by Atalay et al. (2022) as patient-specific demographic characteristics appear to have no significant statistical impact on cochlear size.

Disclosures

All listed authors declare they have no disclosures to make.

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