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Journal of Otology 12 (2017) 74–79

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Disagreement in middle ear volume estimation between tympanometry and three-dimensional volume reconstruction in the context of tympanic membrane perforation

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Received 5 March 2017; revised 29 March 2017; accepted 5 April 2017

Abstract

Introduction: Middle ear volume (MEV) is a clinically relevant parameter across middle ear diseases. MEV values between these techniques have never before been tested for agreement in ears with perforated tympanic membranes (TMs).
Methods: Middle ears were identified from 36 patients ranging 18–89 years of age with TM perforations who underwent tympanometry and temporal bone computed tomography (CT) between 2005 and 2015. MEVs calculated by both tympanometry and three-dimensional volume reconstruction (3DVR) were analyzed for agreement using Bland Altman plots. The differences between tympanometric and 3DVR MEV values for each given middle ear were characterized across MEV quartiles (1 = smallest; 4 = largest) and across increasing states of middle ear disease using Kruskal–Wallis and Wilcoxon testing with Bonferroni correction.
Results: Bland Altman plots demonstrated significant disagreement between MEV measurement techniques. Differences between tympanometric (T) and 3DVR MEV values were significantly greater with increasing average (i.e. (T+3DVR)/2)) MEV per linear regression ($p < 0.0001$). Significance was demonstrated between fourth and first average MEV quartiles ($p = 0.0024$), fourth and second quartiles ($p = 0.0024$), third and first quartiles ($p = 0.0048$), and third and second quartiles ($p = 0.048$). Absolute MEV difference was not significantly different across varying states of middle ear disease ($p = 0.44$).
Conclusion: Statistically and clinically significant disagreement was demonstrated between tympanometric and 3DVR MEV values. Studies that vary in MEV estimation techniques may be expected to demonstrate significantly different results. These preliminary results suggest that clinicians should endeavor to seek further confirmation when interpreting high tympanometric MEV values.

Keywords: Middle ear volume; Tympanometry; Three-dimensional volume reconstruction; Tympanic membrane perforation

1. Introduction

Middle ear volume (MEV), defined as the continuous volume occupied by the tympanic cavity and mastoid air cells, has been characterized in the setting of various middle ear pathologies using both tympanometry and three-dimensional volume reconstruction (3DVR). Determining MEV size by tympanometry has proved clinically useful in various settings. Clinical indications for tympanometry include screening for

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Peer review under responsibility of PLA General Hospital Department of Otolaryngology Head and Neck Surgery.

http://dx.doi.org/10.1016/j.joto.2017.04.001

middle ear disease as well as determining the presence of tympanic membrane (TM) perforation following an indeterminate otologic exam. Using tympanometry, greater MEV was shown to directly relate to Eustachian tubal function and successful closure of dry, central TM perforations (Holmquist, 1970; Neel et al., 1977). Secretory middle ear pathologies were subsequently shown to recur more commonly in ears with smaller MEVs (Sederberg-Olsen et al., 1983). More recently, using tympanometry, smaller MEV has been correlated to conductive hearing loss secondary to TM perforation (Voss et al., 2001; Mehta et al., 2006; Voss et al., 2007).

3DVR of computed tomography (CT) scans has since emerged as a gold standard for MEV estimation for studies of middle ear anatomy. The correlation of MEV to TM perforation-induced conductive hearing loss, first identified by studies using tympanometry, has been expanded by those using 3DVR (Park et al., 2015). Novel applications for MEV have also emerged, such as determining surgical candidacy in patients with aural atresia (Osborn et al., 2011).

Statistical agreement in MEV between widely available tympanometry and precise 3DVR techniques has never been assessed in the context of tympanic membrane (TM) perforation. Characterizing agreement in MEV values between tympanometry and 3DVR is the primary objective of this study, secondarily determining whether agreement is influenced by middle ear disease states or sizes. It is hypothesized that MEV will differ between tympanometry and 3DVR for middle ears with TM perforations. Characterizing the agreement between MEV techniques will address limitations in the current literature surrounding MEV, and will provide context for clinicians who face the challenge of incorporating MEV estimations in their assessment of middle ear disease.

2. Methods

2.1. Subjects

This is a retrospective study approved by the Duke University Health System Institutional Review Board (IRB). A search was conducted of Duke University Medical Center medical records for all patients ranging from 18 to 89 years of age with perforated tympanic membranes (TMs) who underwent tympanometry up to one month prior to a standard-of-care temporal bone computed tomography (CT) between October 15th, 2005 and October 15th, 2015. One patient with inadequate CT resolution was excluded. 36 qualifying patients met study criteria.

2.2. Three dimensional volume reconstruction

Images of temporal bone CT scans were imported from the electronic health record into the medical imaging software, Avizo™ (FEI Visualization Sciences Group, Burlington, MA) for creation of three-dimensional (3D) models of the middle ear. All CT scans were de-identified in Avizo™ prior to any 3D model construction or further analysis. Imaging parameters included a section thickness of 0.6 mm, 512 × 512 matrix, rotation time of 1 s, and exposure time of 1825 ms. Patients were in the head first-supine position with 0 gantry tilt. Digital imaging and communications in medicine (DICOM) images had 512 rows, 631 columns, and a pixel spacing of 0.176 by 0.176 mm. Middle ear volume (MEV) was defined as the continuous, non-opacified airspaces of the middle ear cavity and mastoid air cells of the temporal bone.

A single investigator performed all 3DVR calculations blinded to tympanometric MEV values. To identify MEV on 3DVR, the TM was located using a previously validated approach (Patki et al., 2016) as the most lateral sagittal image where the temporal bone demonstrated a continuous circumference around the airspace, which denoted the boundary between the external auditory canal and middle ear (Fig. 1). MEV was defined as all continuous airspaces medial to the TM, including the tympanic cavity and mastoid airspaces. When directly measuring MEV, a cutoff of −2000 to −609 Hounsfield units was used to standardize opacification.

2.3. Disease cohorts

Middle ears were grouped into disease cohorts to account for the potential effects of impaired TM and ossicular function on calculated MEV values. TM perforation may be associated with cholesteatoma or not. When present, cholesteatoma may erode the ossicular chain. Therefore, grouping by “perforated” middle ears (P; n = 8) with TM perforations and without cholesteatoma or ossicular dysfunction, middle ears (PC; n = 7) with TM perforations and cholesteatoma but without ossicular dysfunction, and middle ears (PCO; n = 21) with TM perforations, cholesteatoma, and ossicular dysfunction provided an approximate categorization by severity of middle ear disease.

2.4. Analysis of agreement

MEV difference was defined as the tympanometric MEV value (MEV_T) minus the 3DVR MEV value (MEV_{3DVR}), and average MEV was defined as the sum of MEV_T and MEV_{3DVR} divided by 2. Linear regression of absolute MEV difference against average MEV values was performed to provide statistical context to subsequent Altman Bland plots. Per (Bland and Altman, 1986), MEV difference was plotted with 1.96 standard deviation boundaries with respect to average MEV. The line of equality (MEV difference = 0) and clinically acceptable thresholds for agreement were provided for comparison. Because prior studies have analyzed MEV as quartiles to mitigate errors in MEV measurement rather than as a continuous variable (Mehta et al., 2006; Park et al., 2015), the clinically acceptable threshold for MEV difference was set *a priori* at ±1.27 mL because this value was the averaged difference from the median to the inner-quartile boundaries for average MEV of the sample set.

A second Bland and Altman plot was constructed for all MEV values using a correction factor that accounts for external auditory canal (EAC) volume. Primary analysis did not include this correction factor because the majority of

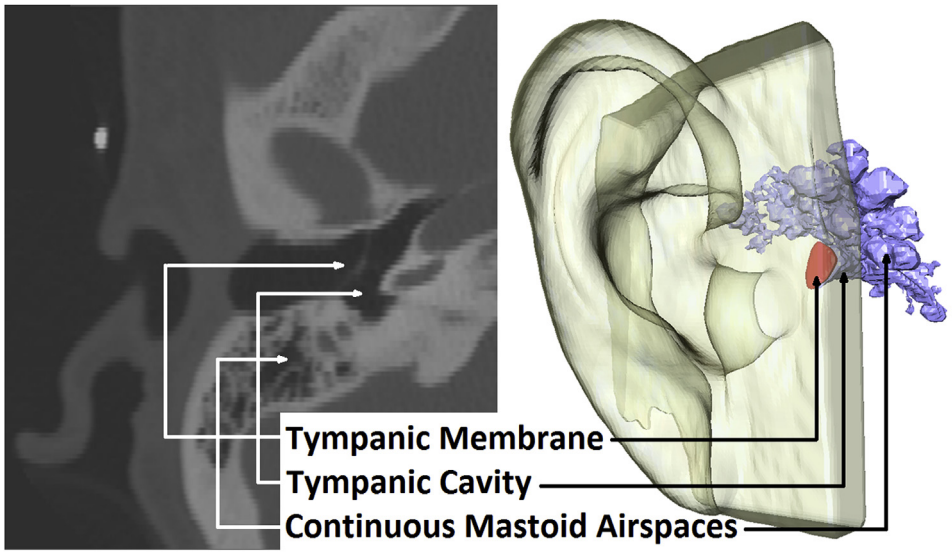

Fig. 1. Middle ear volume was determined using a standardized three-dimensional volume reconstruction approach that involved locating the tympanic membrane on temporal bone CT scans.

tympanometric studies of MEV and related clinical environments do not apply such corrections. Tympanometric MEVs of contralateral non-diseased middle ears with intact TMs (n = 29) were averaged to estimate ipsilateral EAC volume. This value, as a correction factor, was subtracted from each primary tympanometric MEV, which allowed determination of middle ear and mastoid volume only. To account for the resulting effect on MEV difference and MEV average, the *a priori* threshold for clinically significant difference in this corrected dataset was set at ±1.83 mL.

Subsequent analysis across disease cohorts and MEV quartiles was performed using the Kruskal–Wallis test and Wilcoxon Rank-Sums testing with Bonferroni correction. All statistical analysis was performed using SAS statistical software package JMP (Cary, NC).

3. Results

Middle ear volume (MEV) values are provided for the 36 analyzed patients (Table 1), 77.1% of whom were female, with an average age of 51.9 ± 18.9 years. Using linear regression modeling, we found that the absolute MEV difference (i.e. $MEV_T - MEV_{3DVR}$) was significantly larger as the average MEV (i.e. $[MEV_T + MEV_{3DVR}]/2$) increased ($R^2 = 0.529$; $p < 0.001$) (Fig. 2). Expressing MEV difference values as a Bland Altman plot demonstrated disagreement between tympanometric and 3DVR MEV values (Fig. 3A). Specifically, the ±1.96 standard deviation (SD) boundaries for (T−3DVR) MEV difference of 7.39 and −6.45 mL were much wider than the *a priori* clinical thresholds for agreement of ±1.27 mL. Moreover, the overall mean MEV difference, 1.49 mL, was outside the agreement threshold, as was every individual middle ear with an average MEV of 2.43 mL or greater.

Contralateral MEV was 1.06 ± 0.41 mL across the 29 subjects with available tympanometric MEVs for contralateral middle ears without TM perforation. This second Bland Altman plot, correcting tympanometric MEV by subtracting contralateral MEV from each tympanometric MEV value, demonstrated disagreement albeit to a lesser degree (Fig. 3B). Although the 1.96 standard deviation boundaries for MEV difference, 6.41 and −5.45 mL, were still outside of the clinically significant threshold of ±1.83 mL, the average MEV difference of 0.48 was within the clinical threshold, unlike that of the uncorrected Bland Altman plot. 21 of 36 (58%) middle ears were within the clinical threshold for agreement after subtracting the contralateral MEV correction factor, as compared to 12 of 36 (33%) in the uncorrected dataset.

Secondary analyses by middle ear size and disease state were performed without using a tympanometric correction factor to more accurately address the comparison between previous studies using tympanometry versus those using

Table 1
Middle ear volume (mL) by tympanometry and 3-dimensional volume reconstruction.

Cohort	Tymp	3DVR	Cohort	Tymp	3DVR	Cohort	Tymp	3DVR
P	4.60	0.98	PC	7.00	3.70	PCO	0.80	0.52
P	0.90	4.01	PC	1.80	0.40	PCO	7.00	0.77
P	1.90	0.08	PC	0.80	0.52	PCO	1.40	0.55
P	2.00	0.28	PCO	1.40	3.31	PCO	1.90	0.98
P	7.00	1.03	PCO	1.90	6.41	PCO	2.90	1.95
P	4.20	8.13	PCO	3.40	1.93	PCO	0.80	0.45
P	5.70	1.40	PCO	0.90	0.51	PCO	2.90	1.36
P	1.70	1.92	PCO	7.00	0.00	PCO	1.10	0.81
PC	7.00	0.00	PCO	1.90	0.19	PCO	1.20	0.39
PC	4.50	2.29	PCO	7.00	0.06	PCO	1.80	0.36
PC	7.10	3.69	PCO	7.20	3.56	PCO	1.80	0.09
PC	1.58	0.65	PCO	3.80	8.85	PCO	0.76	0.71

Cohorts were defined as [P] middle ears with TM perforations, without cholesteatoma or ossicular dysfunction (n = 8), [PC] with TM perforations and cholesteatoma without ossicular dysfunction (n = 21), and [PCO] with TM perforations, cholesteatoma, and ossicular dysfunction (n = 12).
Abbreviations: Tymp = tympanometry, 3DVR = Three-dimensional volume reconstruction.

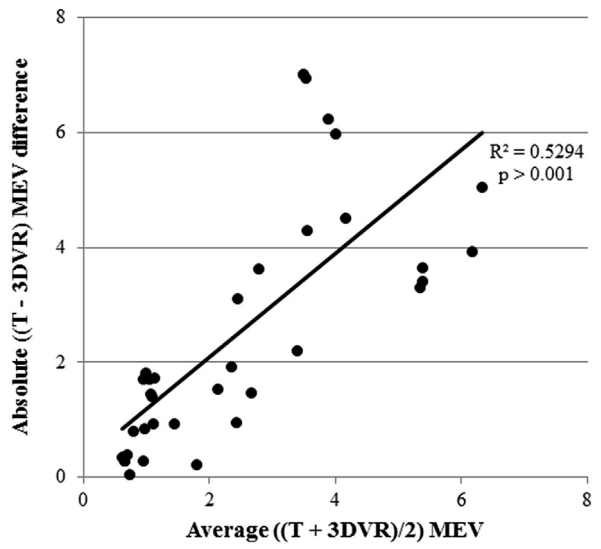

Fig. 2. Bivariate fit of absolute difference between middle ear volume (MEV) techniques to average MEV between techniques is shown.

3DVR. No statistical significance in absolute MEV difference was demonstrated across middle ear disease cohorts per Kruskal–Wallis testing ($p = 0.44$; Fig. 4A). Mean absolute MEV differences decreased with increasing degrees of middle ear disease.

Absolute MEV difference averaged 0.50 ± 0.55 mL in quartile 1, 1.30 ± 0.52 mL in quartile 2, 3.80 ± 2.51 mL in quartile 3, and 4.48 ± 1.07 mL in quartile 4. Kruskal–Wallis testing was significant ($p < 0.001$) for MEV differences across average MEV quartiles (Fig. 4B). Absolute MEV difference was significantly greater in the fourth than the first quartile ($p = 0.0024$), fourth than the second quartile ($p = 0.0024$), third than the first quartile ($p = 0.0048$), and third than the second quartile ($p = 0.048$).

4. Discussion

Larger MEV differences corresponded to larger average MEV values, while MEV difference was consistently high across middle ears with TM perforations with and without cholesteatoma and ossicular erosion, although no differences were noted across the three disease cohorts. These preliminary observations may suggest that (1) when relying on MEV to make clinical decisions, providers should seek further confirmation when interpreting higher MEV measurements; and that (2) middle ear disease should not influence provider confidence in tympanometric MEV.

These data should be placed in their proper clinical context: MEV should be interpreted with regard to the corresponding tympanogram and exam findings. Type B tympanograms, indicative of middle ear pathology, provide one such example. MEV is clinically applied in the context of type B tympanograms to distinguish between middle ear pathologies with "low," (i.e. impacted cerumen) "normal," (middle ear effusion) or "high" MEVs (TM perforation or impacted ear tubes) (Katz et al., 2002). Where clear visualization of the TM proves difficult on exam, MEV helps distinguish between pathologies. Although type B tympanograms have been demonstrated to have high specificity (0.91) and good specificity (0.79) (Watters et al., 1997), these statistics come from a report that did not include adults, perforated TMs, or address specific instances where MEV was required to interpret other findings. In contrast, our data were collected specifically in adults with perforated TMs and middle ear disease—clinical situations where MEV values may directly influence clinical management. Thus, these data may suggest that clinicians relying on MEV should note that MEV values, especially "normal" to "high" values, might not be an accurate means of diagnosing middle ear disease in the absence of a clear visualization of the TM on exam.

Historically, accuracy of tympanometry has been difficult to assess in the context of middle ear disease. The accuracy of

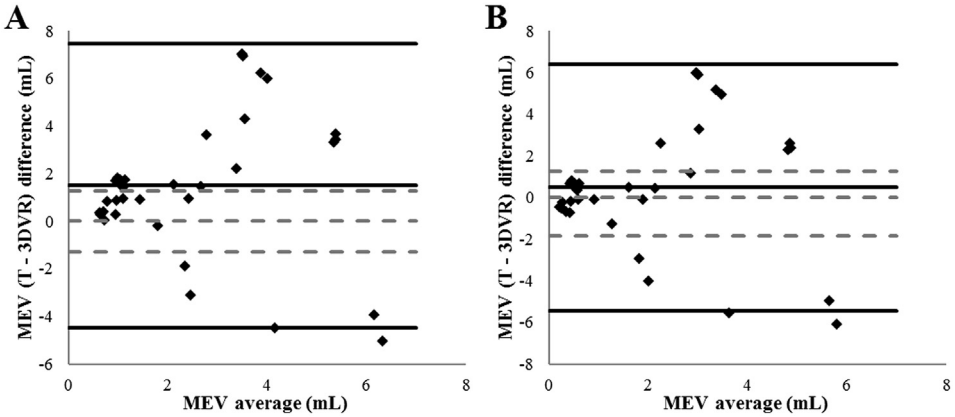

Fig. 3. Bland and Altman plots for agreement in middle ear volume (MEV) estimation between tympanometric and three-dimensional volume reconstruction (A) before applying a correction factor and (B) afterward. Average MEV difference and ±1.96 SD are shown as solid black lines, while the line of equality with clinically acceptable differences (75th to 25th percentiles of MEV average) are shown as dashed gray lines.

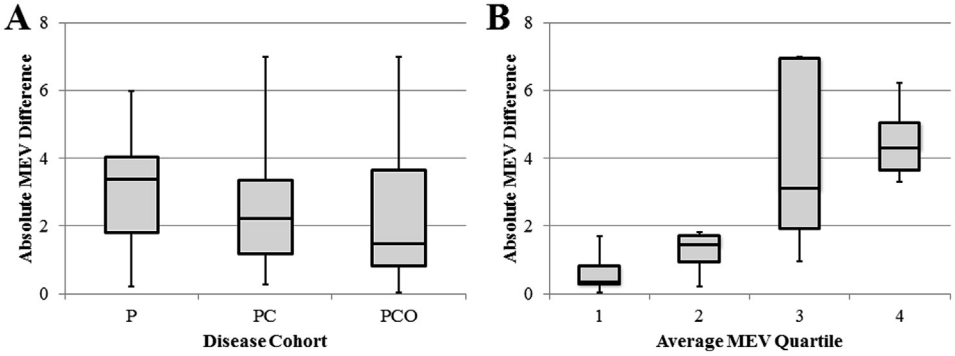

Fig. 4. A. Box-and-whisker plots are shown for absolute (T-3DVR) MEV difference for disease cohorts. Cohorts consist of [P] middle ears with TM perforations, without cholesteatoma or ossicular dysfunction (n = 8), [PC] with TM perforations and cholesteatoma without ossicular dysfunction (n = 21), and [PCO] with TM perforations, cholesteatoma, and ossicular dysfunction (n = 12). B. Absolute (T-3DVR) difference between estimation techniques is shown between estimation techniques for quartiles of average MEV, shown from smallest (1) to largest (4).

tympanometry MEV has been validated in middle ears with dry TM perforations by comparison to an aspiration technique using Boyle's law (Lindeman and Holmquist, 1982). However, altering the tympanic membrane or ossicles is known to affect the accuracy of tympanometry (Feldman, 1974; Molvaer et al., 1978; Buckinghamy et al., 1980; Lindeman and Holmquist, 1981; Shanks and Lilly, 1981; Osguthorpe, 1986; Rock, 1991; Gaihede, 2000). Secretory middle ear pathologies have been shown to influence middle ear pressure and volume measurements (Gaihede, 2000). To address these limitations, a growing number of studies have characterized and applied 3DVR MEV estimation across a wide variety of pathophysiologic contexts in which tympanometric MEV estimates were previously used (Osborn et al., 2011; Park et al., 2015; Byun et al., 2016). Our findings of disagreement should be considered across studies that differ in their MEV estimation technique.

The disagreement present between tympanometry and three-dimensional volume reconstruction (3DVR) techniques for MEV estimation in subjects with TM perforation can be further characterized. Bland and Altman plots (Fig. 3) reveal that this lack of agreement cannot be attributed simply to bias; that is, one technique did not consistently overestimate the other as seen in a prior comparative study of MEV techniques in secretory otitis media (Ahn et al., 2008). We observed a large number of values for MEV difference (i.e. $MEV_T - MEV_{3DVR}$) outside both the upper and lower boundaries of the clinically acceptable threshold. The violation of the clinically acceptable threshold demonstrates that observed MEV values varied between techniques by more than the MEV inter-quartile difference. Thus, previous efforts to limit MEV estimation error by converting continuous MEV values to quartile distributions may not have adequately addressed measurement error (Mehta et al., 2006).

5. Study limitations

Selection bias is present in the retrospective patient population where both tympanometric testing and a temporal bone CT scan is available, particularly because such CT scans are often not obtained. While 3DVR MEV estimates were standardized using a previously validated protocol (Patki et al., 2016), pair-wise analysis of tympanometric MEV values collected in rapid succession would help distinguish between accuracy and precision. Repeated pre-operative tympanometric MEV estimates were not available to measure precision for this sample of patients. The categorization of increasing disease states, though indicated due to limited sample sizes, is an imperfect assessment of true middle ear disease.

6. Summary

Clinically significant agreement was not observed between MEV estimates obtained by tympanometry and three-dimensional volume reconstruction. This lack of agreement was most pronounced at the higher average middle volumes typical of TM perforations, and persistent yet not appreciably different across varying severities of middle ear disease. Based on these preliminary findings, clinicians and investigators should exercise caution when interpreting high tympanometric MEVs and across studies with different MEV estimation techniques.

Funding

Research reported in this article was supported by the National Institutes of Health under Award Numbers 5T32DC013018-03 and TL1TR001116. The content is solely the responsibility of the authors and does not necessarily represent the official views of the National Institutes of Health.

Conflicts of interest

All authors declare no competing interests.

Author disclosure statement

Research reported in this article was supported by the National Institute on Deafness and Other Communication Disorders of the National Institutes of Health under Award

Number 5T32DC013018-03 and by the National Center for Advancing Translational Sciences of the National Institutes of Health under Award Number TL1TR001116. The content is solely the responsibility of the authors and does not necessarily represent the official views of the National Institutes of Health.

Ethical approval

This article does not contain any studies with human participants or animals performed by any of the authors.

Acknowledgments

The authors gratefully acknowledge Dr. Greg Samsa and Dr. Heather Whitson for support with statistical design.

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