ALTERATIONS OF VESTIBULAR FUNCTION IN COCHLEAR IMPLANTATION

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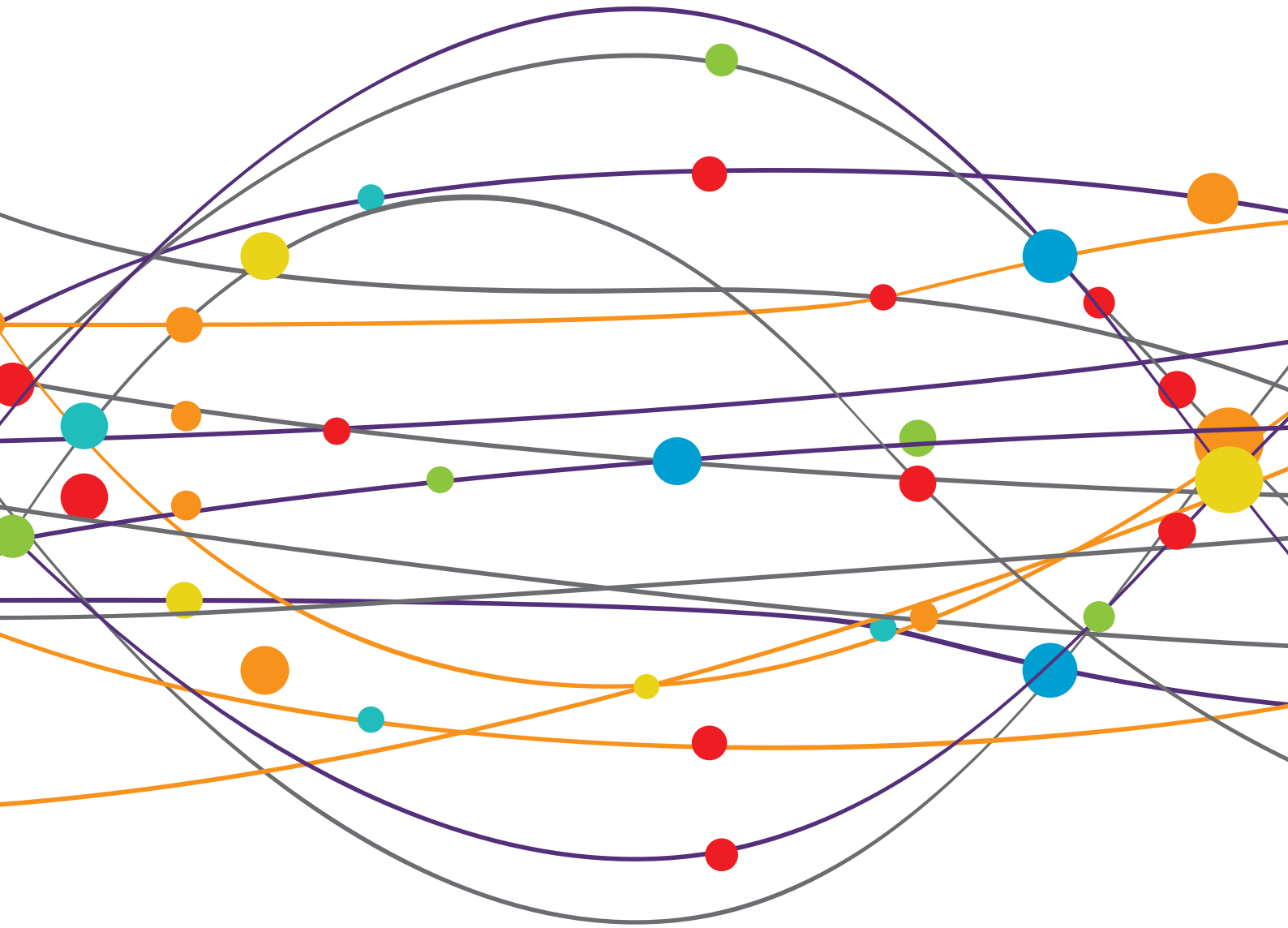

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ALTERATIONS OF VESTIBULAR FUNCTION IN COCHLEAR IMPLANTATION

Topic Editors:
Louis Murray Hofmeyr, Stellenbosch University, South Africa
Anandhan E. Dhanasingh, MED-EL (Austria), Austria
Ingo Todt, Bielefeld University, Germany

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EDITORIAL
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Editorial: Alterations of Vestibular Function in Cochlear Implantation

Anandhan Dhanasingh[1]*, *Ingo Todt*[2]* and *Louis Hofmeyr*[3]*

[1] MED-EL (Austria), Innsbruck, Austria, [2] Department of Otolaryngology, Head and Neck Suregry, Bielefeld Clinic, Bielefeld, Germany, [3] Stellenbosch University, Stellenbosch, South Africa

Keywords: vestibular function, vestibular testing, cochlear implantation, round window and cochleostomy electrode insertion, vestibular testing in children

Editorial on the Research Topic

Alterations of Vestibular Function in Cochlear Implantation

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Edited by:
Michael Strupp, Ludwig Maximilian University of Munich, Germany

Reviewed by:
Nils Guinand, Geneva University Hospitals (HUG), Switzerland
Guyot Jean-Philippe, University of Geneva, Switzerland

***Correspondence:**
Anandhan Dhanasingh
anandhan.dhanasingh@medel.com
Ingo Todt
todt@gmx.net
Louis Hofmeyr
louishofmeyr@icloud.com

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Cochlear implantation is a widely accepted treatment option in restoring hearing in subjects of all age groups with profound or partial sensorineural hearing loss. The cochlear implant (CI) electrode array is placed inside the scala-tympani (ST) to electrically stimulate the neural elements, which is linked to the auditory pathway reaching the cortex to complete the hearing restoration process. The ST is filled with a sodium-rich fluid called perilymph, which is highly conductive and facilitates the spread of electrical impulses coming out of the electrode array to inside the ST and possibly other neighboring structures. The scala media (SM) is a small compartment seen right above the ST, separated by the basilar membrane (BM), as seen in the mid-modiolar section, and is filled with potassium rich endolymph. The SM is connected directly to the vestibular portion of the inner ear and any disturbance to the BM and SM during the CI electrode insertion process can disturb the vestibular function. The SM and the BM could be disturbed by the surgical approach of electrode array insertion (round window membrane vs. promontory drilling of cochleostomy) and/or the stiffness along with the length of the CI electrode array that goes inside the ST. Evaluation of the vestibular function involves sensitive testing methods that is often challenging in children. Any disturbance to vestibular function following the CI surgery could negatively affect the patients by causing symptoms of dizziness, feeling off-balance, disorientation, or falling or stumbling and in their overall quality of life (QoL). Therefore, it was the initiative of the editors to set-up this special issue entitled "Alterations of vestibular function in cochlear implantation" inviting researchers to submit their clinical findings along this topic.

This editorial summarizes the key findings of the manuscripts submitted by researchers in response to the invitation, which underwent peer-review process and published successfully. Tsukada and Usami reported a reduced risk of damage to vestibular function using the round window approach in CI surgery with flexible lateral wall electrode arrays in contrast to promontory drilling of a bony cochleostomy and using pre-curved electrode array types. Their findings were supported by Koyama et al. who had similar outcomes in a pediatric population. They went on further to report that even using the extended round window approach of electrode array insertion could affect the vestibular function negatively as evaluated by cVEMP (caloric vestibular evoked myogenic potential). cVEMP is used to assess the patient's balance function by evaluating their saccular function. Wang et al. reported that children with enlarged vestibular aqueduct (EVA) are more likely to have preserved saccular and utricular functions after CI surgery than children with "normal" ear anatomy due to less pressure-related damage to those structures as a result of the EVA. It is generally assumed that the length of the electrode array that is inserted inside the cochlea could also affect the vestibular function. Weinmann et al. reported that the reduced probability of vertigo

when using flexible electrodes was not clearly observed nor of negative influence of the electrode insertion length. Rasmussen et al. made an interesting report on the vestibular dysfunction reaching a plateau 4-months post-operatively after which there was no further deterioration or improvement in vestibular function. The long-term effect of the biological stressors on the degradation of vestibular function is still to be understood and therefore long-term follow-ups are necessary to validate the findings of Rasmussen et al. Guan et al. reported no difference in vestibular dysfunction in unilateral and sequentially implanted bilateral subjects following CI. The video head impulse test (v-HIT) is a quick, non-invasive, and relatively cheap test to evaluate vestibular function compared to the caloric test. The other key reason to consider using v-HIT is its ability to test in high-frequency range which is effective enough in testing the body and gaze stabilization. Bassaletti et al. evaluated the effectiveness of using v-HIT to select CI-candidates that require caloric testing before cochlear implantation. Vestibular implants (VI) are currently under research to understand the safety and effectiveness of VI in restoring the vestibular function in patients with conditions like bilateral vestibulopathy and Meniere's disease. Montesdeoca et al. reported that the electrically evoked cVEMPs can be present after cochlear and vestibular stimulation. They claim that by measuring the cVEMP following the direct electrical stimulation of the vestibular portion with VI, the vestibular elements can be stimulated safely. Sonsa-Duranowska et al. showed that hearing preservation techniques in cochlear implantation are connected with vestibular protection, but the risk of vestibular damage is never eliminated completely. QoL in older adults with a history of loss of balance and in patients with a history of Menière's disease after cochlear implantation is an interesting topic. Rogers citing existing literature, reported that the risk of falling in older adults after CI is high and urges proper testing methodology to assess their vestibular function before and after the CI surgery. Lassaletta et al. reported that the hearing results and QoL benefits perceived by CI candidates with Menière's disease is similar to regular CI candidates. They further reported that patients who undergo simultaneous CI and labyrinthectomy may experience worse QoL. Li et al. have nicely photographed the vestibular space and the nerves associated with the vestibular organ using micro-computer tomography (μCT) and high radiation synchrotron phase-contrast images. They report that drilling of a cochleostomy may disturb vestibular organ function by injuring the endolymphatic space and disrupting fluid barriers. The saccule is at particular risk due to its proximity with the surgical area and may explain immediate and long-term post-operative vertigo. Round window insertion may be less traumatic to the inner ear; however, it may affect the vestibular receptors. Their claims are nicely supported by the reports of other researchers mentioned above.

Overall, testing the vestibular function periodically for many years following CI surgeries would help the CI community to learn more about the effect of CI surgery and other factors on the alteration of vestibular function. As editors of all these articles, we would like to encourage the readers to take their time to read these articles and to update their knowledge on these topics.

AUTHOR CONTRIBUTIONS

All authors listed have made a substantial, direct and intellectual contribution to the work, and approved it for publication.

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ORIGINAL RESEARCH
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Vestibular Organ and Cochlear Implantation–A Synchrotron and Micro-CT Study

Hao Li[1], *Nadine Schart-Moren*[1,2], *Gunesh Rajan*[3,4], *Jeremy Shaw*[5], *Seyed Alireza Rohani*[6], *Francesca Atturo*[7], *Hanif M. Ladak*[6,8†], *Helge Rask-Andersen*[1*†] *and Sumit Agrawal*[6,8†]

[1] *Department of Surgical Sciences, Otorhinolaryngology and Head and Neck Surgery, Uppsala University, Uppsala, Sweden,* [2] *Section of Otolaryngology, Head and Neck Surgery, Uppsala University Hospital, Uppsala, Sweden,* [3] *Department of Otolaryngology, Head & Neck Surgery, Luzerner Kantonsspital, Lucerne, Switzerland,* [4] *Department of Otolaryngology, Head & Neck Surgery, Division of Surgery, Medical School, University of Western Australia, Perth, WA, Australia,* [5] *Centre for Microscopy, Characterization and Analysis, Perth, WA, Australia,* [6] *Department of Otolaryngology-Head and Neck Surgery, Western University, London, ON, Canada,* [7] *Department of Otolaryngology, University of Sapienza, Rome, Italy,* [8] *Department of Medical Biophysics and Department of Electrical and Computer Engineering, Western University, London, ON, Canada*

Background: Reports vary on the incidence of vestibular dysfunction and dizziness in patients following cochlear implantation (CI). Disequilibrium may be caused by surgery at the cochlear base, leading to functional disturbances of the vestibular receptors and endolymphatic duct system (EDS) which are located nearby. Here, we analyzed the three-dimensional (3D) anatomy of this region, aiming to optimize surgical approaches to limit damage to the vestibular organ.

Material and Methods: A total of 22 fresh-frozen human temporal bones underwent synchrotron radiation phase-contrast imaging (SR-PCI). One temporal bone underwent micro-computed tomography (micro-CT) after fixation and staining with Lugol's iodine solution (I_2KI) to increase tissue contrast. We used volume-rendering software to create 3D reconstructions and tissue segmentation that allowed precise assessment of anatomical relationships and topography. Macerated human ears belonging to the Uppsala collection were also used. Drilling and insertion of CI electrodes was performed with metric analyses of different trajectories.

Results and Conclusions: SR-PCI and micro-CT imaging demonstrated the complex 3D anatomy of the basal region of the human cochlea, vestibular apparatus, and EDS. Drilling of a cochleostomy may disturb vestibular organ function by injuring the endolymphatic space and disrupting fluid barriers. The saccule is at particular risk due to its proximity to the surgical area and may explain immediate and long-term post-operative vertigo. Round window insertion may be less traumatic to the inner ear, however it may affect the vestibular receptors.

Keywords: human, synchrotron, micro-CT, vestibular organ, cochlear implant

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Edited by:
Louis Murray Hofmeyr,
Stellenbosch University, South Africa

Reviewed by:
Wilhelm Wimmer,
University of Bern, Switzerland
Stefan Weber,
University of Bern, Switzerland

***Correspondence:**
Helge Rask-Andersen
helge.rask-andersen@surgsci.uu.se
orcid.org/0000-0002-2552-5001

†These authors share senior authorship

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INTRODUCTION

There are various reports on the incidence of vestibular dysfunction and vertigo following cochlear implantation (CI) in adults and children. Although CI is considered to be safe, the traumatic action of electrode insertion into the cochlea risks impairing vestibular function. Seriously incapacitating vertigo is rare, and there is usually complete resolution (1). Different factors have been ascribed

as possible causes, such as labyrinthine status before CI surgery or concurrent inner ear disease. Older patients and patients with preoperative dizziness may be more prone to vestibular injury, and this may occasionally be associated with tinnitus and fluctuating hearing loss (2–5). Dizziness may be experienced directly after surgery or with delayed onset (6). In some instances, endolymphatic hydrops (EH) may be suspected (7). Therefore, vestibular impairment can be influenced by surgical impact, patient age, and cause of deafness.

The human ear contains five end-organs, each of which can be affected by surgery at the cochlear base or by electrode insertion itself. Postmortem histopathological studies of the temporal bones of CI recipients have reported significant structural changes in end-organs, including the saccule, the utricle, and the semicircular canals (8, 9). Injury of cochlear and vestibular tissue may lead to the mixing of fluids and the alteration of otolith membranes and receptor cells. CI may damage the lateral cochlear wall disturbing endolymph homeostasis leading to cochlear hydrops. CI may also obstruct endolymph flow between the cochlea and the saccule by blocking the reunion duct (RD) or cochlear duct causing cochlear hydrops and collapse of the saccule (9). Long-term changes may occur from inflammation, fibrosis, and ossification (8). There is a particular risk of damage to the saccule, which is located in the spherical recess close to the base of the cochlea and round window (RW). Moreover, the main cochlear vein is located in the floor of the scala tympani (ST) near the final position of the CI electrode.

Non-invasive, high-resolution synchrotron radiation and 3D imaging of temporal bone specimens have earlier been performed (10). To improve soft tissue contrast, chemical staining was also introduced to visualize the hearing organ and nerve elements using absorption based synchrotron imaging (11, 12). This necessitates opening of the windows of the inner ear with risk for artifact generation. In lieu of staining, synchrotron radiation phase-contrast imaging (SR-PCI) can be used to increase visualization of soft tissues. This technique exploits x-ray intensity variations to produce edge contrast thereby improving soft tissue visualization. At the same time, SR-PCI conserves visualization of bone while avoiding the artifacts introduced with staining, sectioning, and decalcification used in histopathology (13–15). Elfarnawany et al. first performed SR-PCI on intact human cochleae to obtain 3D reconstructions of cochlear soft tissues (16). The high-resolution scans obtained through this technique were capable of revealing cytoarchitecture similar to histology (17, 18). Subsequent groups have applied the SR-PCI technique to other parts of the temporal bone, including the middle ear and ossicles (19, 20). Recently, Anschuetz et al. demonstrated synchrotron radiation imaging of the human auditory ossicles at the sub-micron level (21).

The present study aimed to three-dimensionally analyze the intricate anatomy of the surgical region to optimize atraumatic approaches in CI to limit the surgical impact on the vestibular apparatus and associated neural pathways. A total of 22 fresh human temporal bones underwent SR-PCI and one fresh bone underwent micro-computed tomography (micro-CT) after fixation and staining with Lugol's iodine solution (I_2KI) to increase tissue contrast. In addition, we analyzed the archival temporal bone collection in Uppsala described in earlier investigations (22, 23). Different cochleostomies (COs) were made with metric analyses. Volume-rendering software was then used to create three dimensional (3D) reconstructions allowing tissue segmentation and detailed assessment of anatomical relationships, metric analyses, and topography. It was found that the RW surgical approach may be preferred to limit the risk for vestibular dysfunction and vertigo after CI, assuming there are no anatomical restrictions preventing this approach.

MATERIALS AND METHODS

Ethical Statements

Human Temporal Bones

Twenty-two adult human cadaveric cochleae were used in this study. Specimens were obtained with permission from the body bequeathal program at Western University, London, Ontario, Canada, in accordance with the Anatomy Act of Ontario and Western's Committee for Cadaveric Use in Research (approval no. 06092020). Ethics approval for the micro-CT project was obtained from the University of Western Australia (UWA, RA/4/1/5210), and the human temporal bones were provided by the Department of Anatomy at UWA.

The adult cadaveric temporal bones were fresh-frozen and then fixed in 3.7% formaldehyde and 1% glutaraldehyde in phosphate buffer for 5 days. The bones were thawed and cut to a sample (40 mm diameter, 60 mm length) from each temporal bone. All samples were cut from the middle ear toward the inner ear. The tissue was rinsed and dehydrated in a graded ethanol series. No staining, sectioning, or decalcification was performed on the specimens.

SR-PCI and Imaging Technique

The SR-PCI technique used in the present investigation was recently described by Elfarnawany et al. (16) and Koch et al. (13). Each sample was scanned using SR-PCI combined with CT at the Bio-Medical Imaging and Therapy (BMIT) 05ID-2 beamline at the Canadian Light Source, Inc. (CLSI) in Saskatoon, SK, Canada. The imaging field of view was set to 4,000 × 950 pixels corresponding to 36.0 × 8.6 mm, and 3,000 projections over a 180° rotation were acquired per CT scan. CT reconstruction was performed, and the 3D image volume had an isotropic voxel size of 9 μm. The acquisition time to capture all projections per view was ∼30 min. For 3D segmentations of the cochlear anatomy, structures were traced and color-labeled manually on each SR-PCI CT slice (approximately 1,400 slices per sample).

Abbreviations: ACO, Anterior cochleostomy; AICO, Anterior-inferior cochleostomy; BM, Basilar membrane; CA, Cochlear aqueduct; CI, Cochlear implantation; CO, Cochleostomy; Dice-CT, Diffusible iodine-based contrast-enhanced computed tomography; EH, Endolymphatic hydrops; IAC, Internal acoustic canal; ICO, Inferior cochleostomy; ICV, Inferior cochlear vein; I_2KI, Lugol's iodine solution; LSSC, Lateral semicircular canal; LVAS, Large vestibular aqueduct syndrome; Micro-CT, Micro-computed tomography; OSL, Osseous spiral lamina; OW, Oval window; PSSC, Posterior semicircular canal; RD, Reunion duct; RM, Reissner's membrane; RW, Round window; SG, Spiral ganglion; SL, Spiral ligament; SR-PCI, Synchrotron radiation phase-contrast imaging; ST, Scala tympani; VEMPS, Vestibular-evoked myogenic potentials; vHIT, Video head impulse test; VOR, Vestibule-ocular reflex.

The open source medical imaging software, 3D Slicer version 4.10 (24), was used to create detailed 3D representations of the basilar membrane (BM), spiral ganglion (SG), and connective dendrites between these structures, which allowed for accurate delineation when compared with traditional two-dimensional (2D) slices. Measurements were made in 22 temporal bones by two independent observers. Distances from the utricle macula, posterior semicircular canal ampulla, saccule macula, and saccule membrane to the middle of the RW were assessed.

Micro-CT

Micro-CT was used to analyze the 3D anatomy of the nerves in the internal acoustic meatus. We used a diffusible iodine-based technique to enhance contrast of soft tissues for diffusible iodine-based contrast-enhanced computed tomography (dice-CT) (25). Increased time penetration of Lugol's iodine (aqueous I_2KI, 1% I_2, 2% KI) offers possibilities to visualize between and within soft tissue structures (25). The temporal bone was fixed in a modified Karnovsky's fixative solution of 2.5% glutaraldehyde, 1% paraformaldehyde, 4% sucrose, and 1% dimethyl sulfoxide in 0.13 M of Sorensen's phosphate buffer. Soft tissue contrast was achieved by staining the sample for 14 days, as described by Culling et al. (26). X-ray micro-CT was conducted using a Versa 520 XRM (Zeiss, Pleasanton, CA, USA) running Scout and Scan software (v11.1.5707.17179). Scans were conducted at a voltage of 80 kV and 87 μA, using the LE4 filter under 0.4× optical magnification and a camera binning of 2. Source and detector positions were adjusted to deliver an isotropic voxel size of 23 μm. A total of 2,501 projections were collected over 360°, each with an exposure time of 1 s. Raw projection data were reconstructed using XM Reconstructor software (v10.7.3679.13921; Zeiss) following a standard center shift and beam hardening (0.1) correction. The standard 0.7 kernel size recon filter setting was also used.

Uppsala Temporal Bone Collection

We used the archival human temporal bones from autopsies and 324 plastic and silicone molds described in earlier publications (22, 23). The collection was established during the 1970s and 1980s at the Department of Diagnostic Radiology and Otolaryngology at Uppsala University Hospital (27, 28). All bones and molds underwent micro-CT as described earlier (23). The topographic anatomy of the "hook" region with relationships between the oval window (OW), RW, osseous spiral lamina (OSL), and spiral ligament (SL) were examined and photographed as described earlier by Atturo et al. (29). Different sized cochleae were analyzed and conventional anterior (ACOs), antero-inferior (AICOs), and inferior COs were made, including the enlarged RW approach (30, 31). The proximity of various COs to the vestibular organ was studied, both from "inside" and "outside" the labyrinth.

RESULTS

SR-PCI and micro-CT with contrast enhancement reproduced both the soft and bony tissue of the human cadaver labyrinth. A notable 3D reproduction of the membranous labyrinth in a left human temporal bone is shown in **Figure 1**. The cochlear and

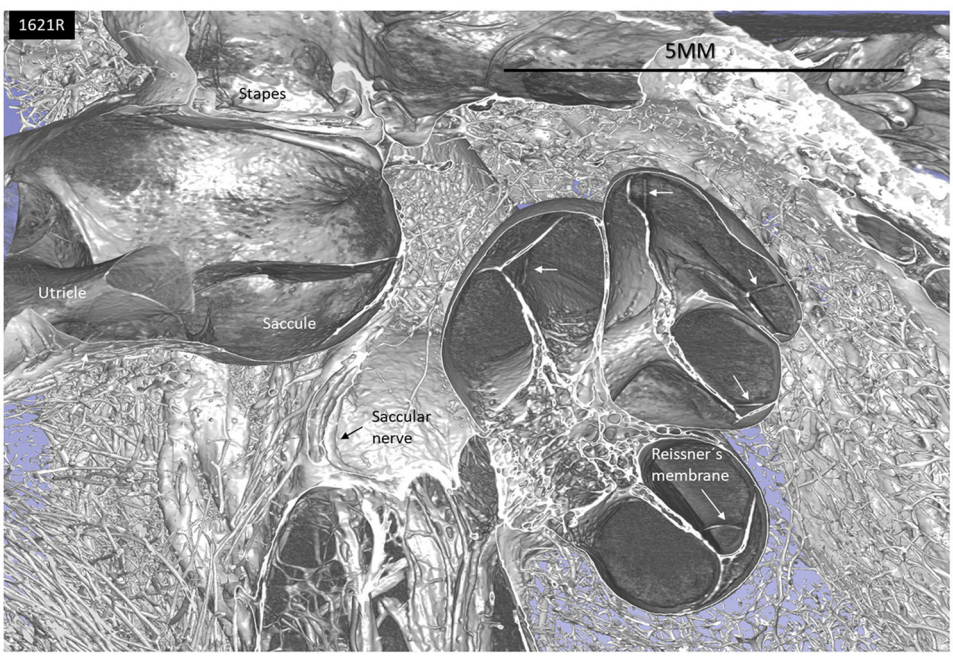

FIGURE 1 | SR-PCI and 3D reconstruction of a left human inner ear (superior view) using 3D slicer (version 4.10; www.slicer.org). The cochlea, utricle, saccule, and saccular nerve are seen with cranial nerves in the fundus of the IAC.

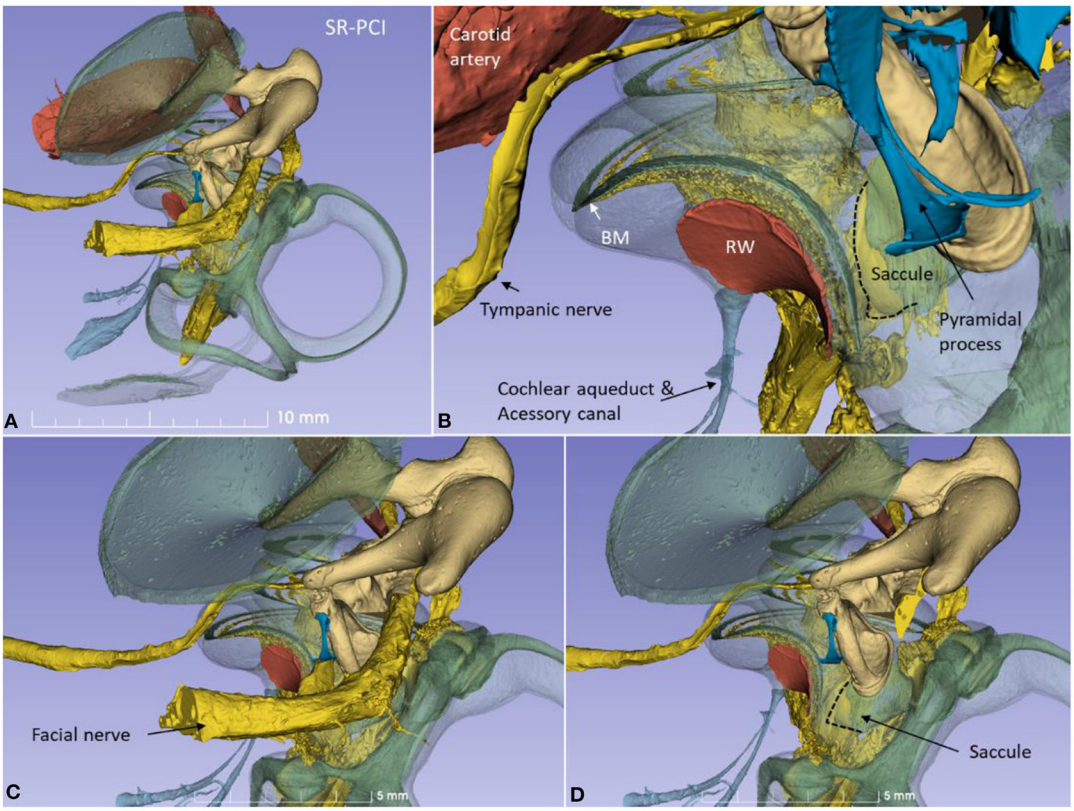

FIGURE 2 | (A) SR-PCI 3D modeling of a left human temporal bone with a surgical view through the facial recess. **(B)** The relationship between the RW and the saccule is seen. The cochlear aqueduct (CA) and a second accessory canal are seen. **(C,D)** show the facial recess anatomy with **(C)** and without **(D)** the facial nerve.

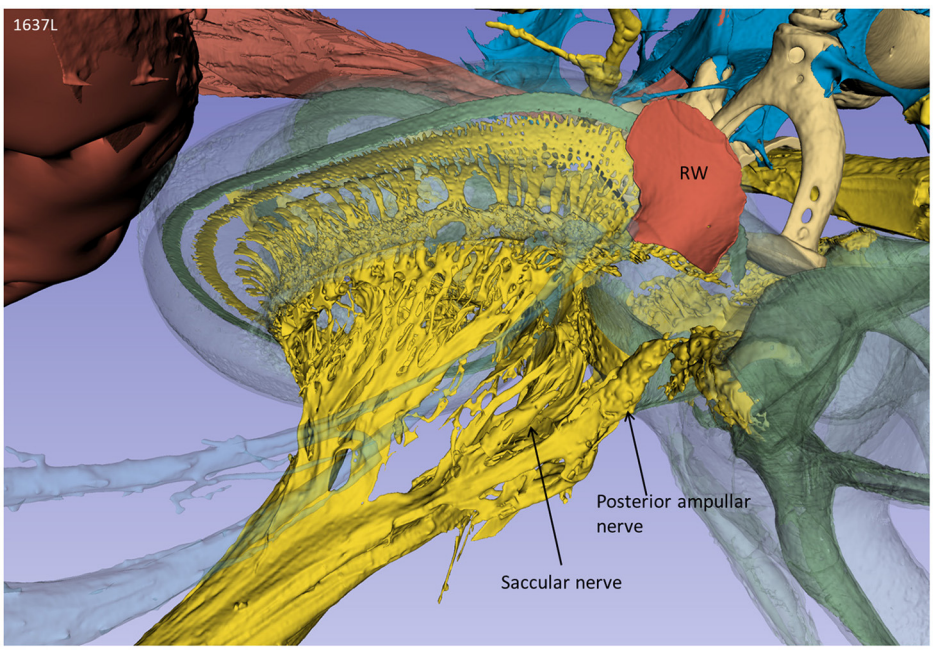

FIGURE 3 | A posterior-inferior view of the specimen shown in **Figure 2**. The relationships between the RW and the posterior ampulla and saccular nerves are shown. The distance between the middle of the RW and the middle part of the posterior ampulla was 2.6 mm.

vestibular nerves and their branches could be followed from the internal acoustic canal (IAC) to the peripheral organs.

The 3D modeling shows the surgical anatomy through the facial recess (**Figure 2**). The anatomical details of the cochlear base are visualized together with the saccule and utricle. Removal of the facial nerve demonstrates the close relationship between the cochlea and the saccule.

From an inferior angle, the relationship between the RW and the saccular and posterior ampulla nerves is shown (**Figure 3**).

Lateral sectioning at the cochlear base of a left ear demonstrates the relationship between the saccule and utricle and the ST in more detail (**Figure 4**). Electrode insertion near the posterior corner of the RW and at an acute angle may jeopardize the OSL with consequences of entering the vestibule. The RD lies on the superior edge of the SL and connects the scala media and saccule. The RD is challenged if the bony lamina is perforated. The mean distance between the mid-portion of the RW and the saccule was 2.66 mm ($SD = 0.35$ mm) and between the RW and the saccule macula was 3.21 mm ($SD = 0.29$ mm). The mean distance between the RW and the utricle macula was 3.79 mm ($SD = 0.32$ mm) (**Supplementary Table 1**).

The saccular wall consists of both a thick and a thin part. The two parts are separated by a thickening in the membrane. The thin part faces the middle ear, while the thick part reinforces the saccule against the spherical recess. The thin part was difficult to reproduce three-dimensionally and gave the impression of an imperfection in the wall.

The macerated human ears revealed extensive anatomic variations of the basal or "hook" region of the cochlea. Drilling and insertion of a CI electrode via an anterior or anterior-inferior CO invariably damaged cochlear structures. Membrane rupture may lead to a mixture of fluids, and bone dust potentially contaminates the vestibule with risk for damage to the vestibular receptors. The soft tissue suspending the BM along the rim of the RW varied among individuals, and even an inferiorly located CO occasionally damaged cochlear tissues. A larger distance between the OW and RW seemed to diminish the risk for mechanical trauma to the SL at inferior CO drilling. Smaller cochleae increased the risk of injuring the SL by leading to a direct trajectory to the saccule. A RW inserted electrode is visualized in **Figure 5**, from "inside" the labyrinth. Distances from the utricle macula, saccule macula, and saccule membrane to the middle of the RW were measured in all 22 temporal bones and are shown in a box plot. The distances from different COs to the utricular and saccular macular nerve foramina were also assessed (**Figures 6**, **7**).

A virtual CI surgery using the RW approach in a 3D reconstructed human temporal bone from a micro-CT is demonstrated in **Figures 8**, **9**. The position of the saccule is seen after the bony capsule was made transparent (**Figures 8A,B**). The

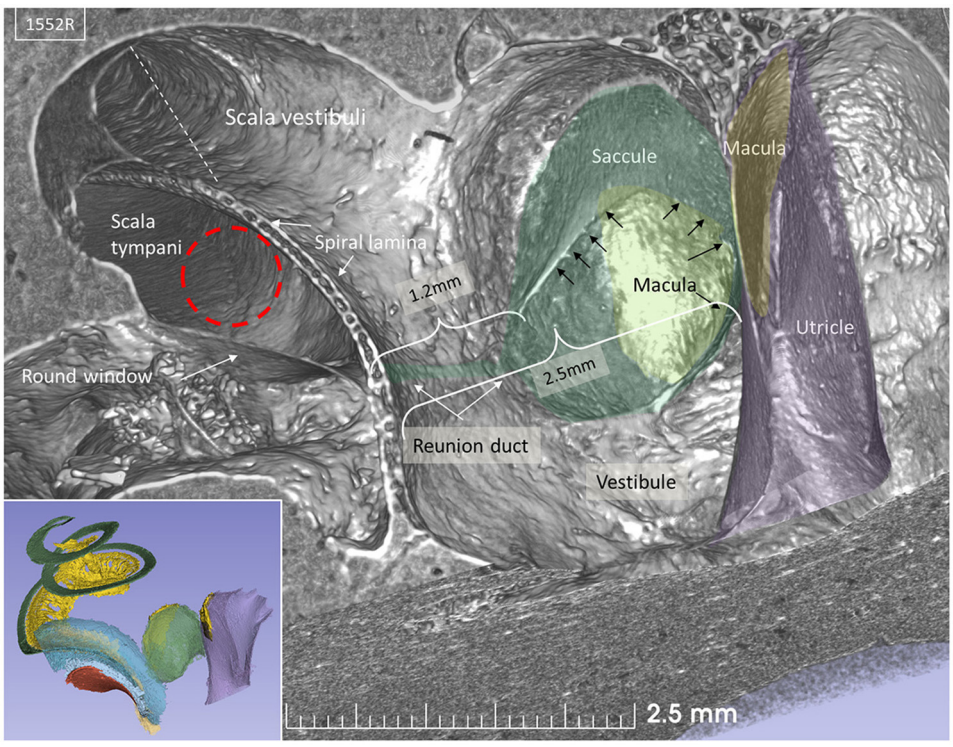

FIGURE 4 | SR-PCI section at the level of the RW and vestibule (lateral view). The RW and the position of a virtual electrode (dashed red line) are shown. The saccule lies in the spherical recess in the medial bony wall of the vestibule. It consists of a thicker and thinner part limited by thicker bands (arrows). The macula is stained yellow. The position of the RD is shown. Inset shows the modeled 3D anatomy with the saccule, RW (red), and spiral ligament of the cochlear base (blue). The broken line represents Reissner's membrane.

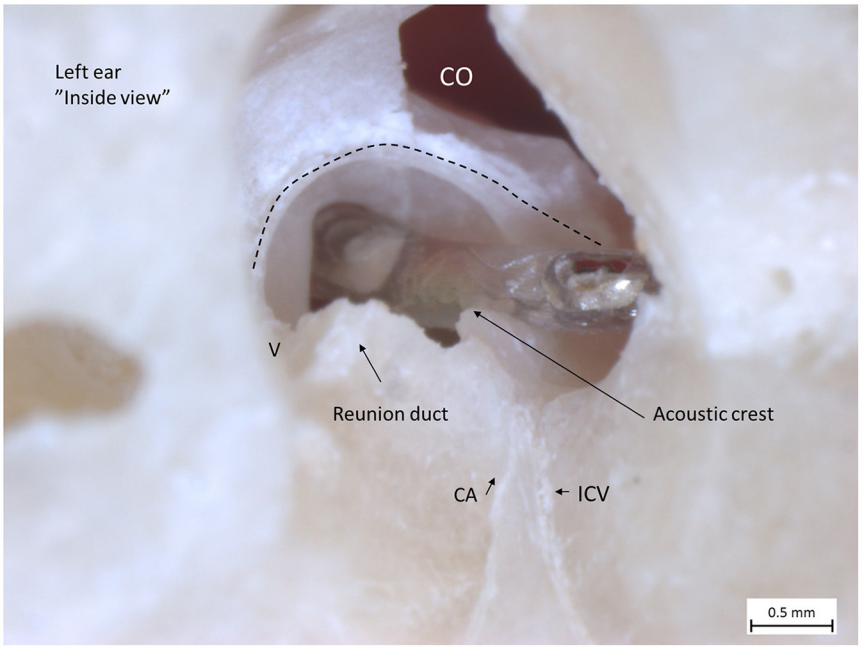

FIGURE 5 | Left human micro-dissected temporal bone (taken from the temporal bone collection of Uppsala Museum) shows the RW and acoustic crest from "inside" the labyrinth. The OSL was resected, with the secondary lamina partially preserved along the rim of the RW. The broken line shows the attachment of the BM around the RW. The electrode was inserted via the RW. It rides upon the acoustic crest before reaching the ST. An anterior CO was drilled. The CA and the inferior cochlear vein (ICV) channels were dissected as well as the RD.

lateral wall of the saccule is visualized through the OW, reaching cranially to the floor of the utricle. The inferior cochlear and saccular veins in the floor of the ST were found to be at low risk for damage.

DISCUSSION

To minimize damage during CI, it is important that the electrode is retained within the ST and that the integrity of the endolymph space is maintained. The surgical area at RW insertion is located ∼2.7 mm from the rim of the saccule membrane. At AICO and ACO, this distance is longer, but the risk for breaking the endolymph barrier is higher. Synchrotron imaging shows that the saccule wall consists of a thin and a thick portion. The thick portion lies near the bony margins of the spherical recess, and the thin portion faces the middle ear. The latter shows extreme fragility and may protect saccular receptors from high-energy stapes vibrations (32). This portion may be damaged or ruptured even by forceful mechanical pressure changes such as the "cork effect" at stapes removal. Entering the vestibular scala during cochleostomy increases the risk of bone dust entering the vestibule, which may lead to acute pro-inflammatory reactions and contribute to symptom manifestations. Moreover, the vibration produced by the milling process may cause statoconia dislocation and consequent vertigo. It may even explain benign positional vertigo, transient dizziness (33), and EH caused by dislocated saccular statoconia in the RD (34) (**Figure 10**). Therefore, direct drilling on the cochlear capsule should probably be kept to a minimum.

There are other explanations for acute or persistent dizziness following CI surgery, such as fistulae in patients with large vestibular aqueduct syndrome (LVAS) (35) or EH (7, 36). The saccular receptors seem particularly vulnerable, reflected by changes in vestibular-evoked myogenic potentials (VEMPs) (37). Alterations such as new bone formation, vestibular fibrosis, saccule membrane distortion, and sub-epithelial thickening were described in studies where the CO technique was mostly performed (8). The authors suggested that the saccule is at greater risk for damage than the utricle or semicircular canals. According to Todt et al. (38), CO may degrade saccular function demonstrated by affected VEMP, and this was correlated with persistent dizziness. Similar results were noted by Jin et al. (39) studying 12 children undergoing CI and by Meli et al. in adults showing lack or reduction of VEMP responses (40). Licamelli et al. (41) found a majority of patients had vestibular impairment with altered saccular function indicated by VEMP as well as reduced vestibule-ocular reflex (VOR) gain. Our 3D study revealed the small distance between the most proximal region of the RW and the saccule (**Figure 11**), which may suggest that this region of the RW should be avoided during surgery. In some children with inner ear dysplasia, VEMP responses were also observed at electrical stimulation, suggesting that the vestibular nerve may be stimulated (39). This may be explained by the posterior ampulla and nerve positioned near the RW (**Figure 11**, **Supplementary Tables 1, 2**).

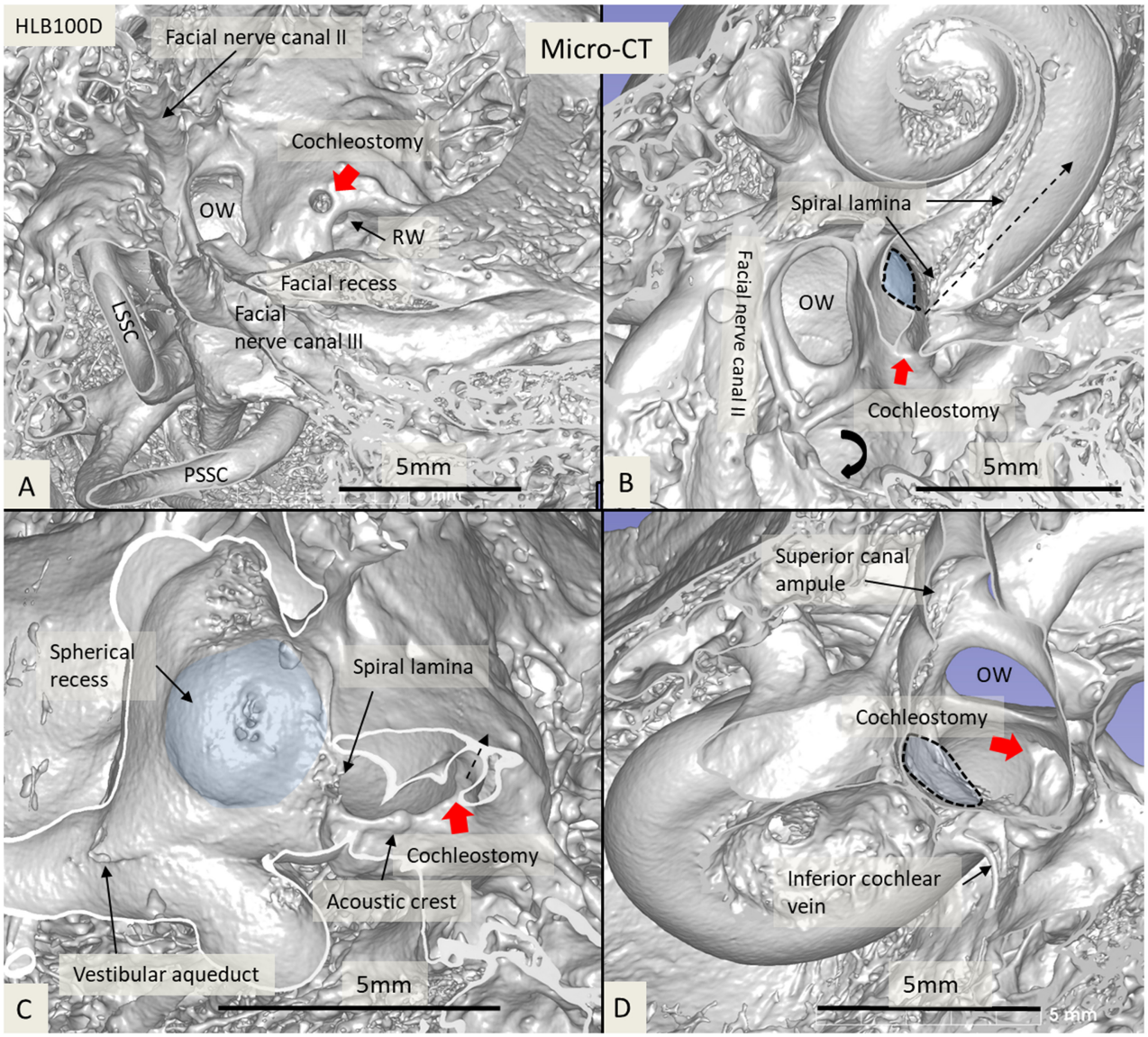

FIGURE 6 | Micro-CT and 3D reconstruction of a macerated human temporal bone (right ear). An anterior CO was made (red arrow), and its relation to the spherical recess (blue) and saccule was studied. **(A)** Surgical view shows the CO and the RW. **(B)** Lateral cropping demonstrates the entrance canal of the CO and its relation to the spherical recess. The bold arrow shows the tympanic sinus. **(C)** Medial cropping shows the spherical recess (blue) with bony foramina of the saccular nerve. The broken arrow shows the direction of the scala tympani. **(D)** Medial view shows CO and spherical recess (dashed line). OW, oval window; RW, round window; LSSC, lateral semicircular canal; PSSC, posterior semicircular canal.

Optimal preservation of residual hearing requires a more atraumatic CI surgery which can be expected to diminish injury to the vestibular organ as well. However, there are indications of some damage to the vestibular receptors of the otolith organs and semicircular canals even when using soft surgery techniques (42). Insertion speed was found to influence hearing preservation and vestibular function. A slow electrode insertion speed seemed to facilitate complete insertion, and improved preservation of residual hearing and vestibular function after CI (43). Fortunately, patients with vertigo usually undergo central vestibular compensation and recover with little or no postural deficit (40). However, it has not been determined whether the surgical approach and design of electrodes influence the prevalence of vestibular problems. Synchrotron 3D analyses show that the RW approach may be less damaging to the inner ear compared with CO (15, 23), which is in accordance with the vestibular results obtained by Todt et al. (38). Batuecas-Caletrio et al. (44) found the RW approach safer and less traumatic than CO. However, no correlation between the surgical approach and occurrence of postoperative vertigo was found by Veroul et al. (45) or by Nassif et al. (46), who investigated children. Rah et al. (7) found that the RW approach resulted in less postoperative

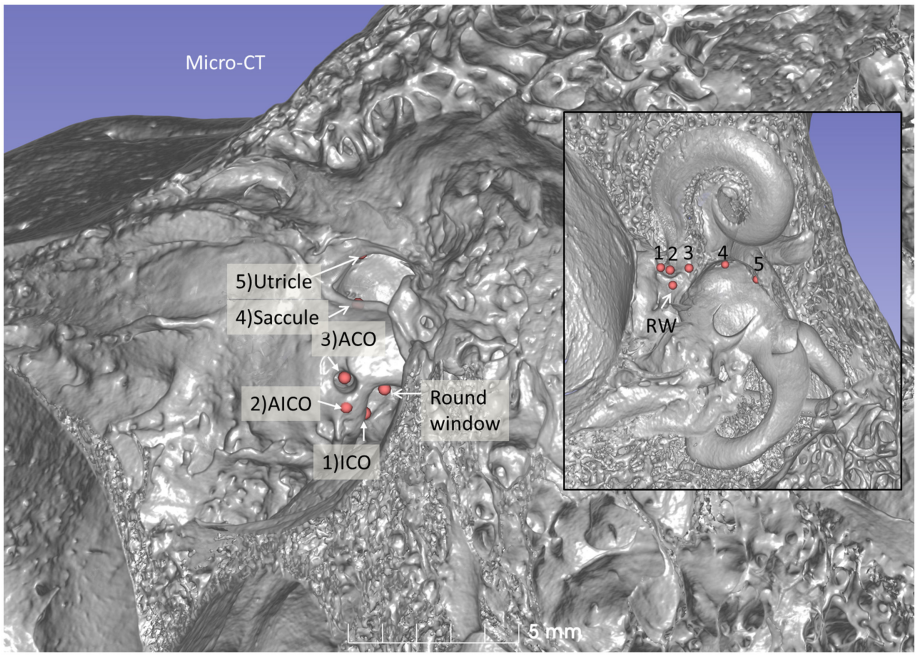

FIGURE 7 | Micro-CT 3D reconstruction of a left human temporal bone (lateral view). An ACO (3) was made, and the distances to the saccular (4) and utricular (5) nerve foramina can be assessed (inset). Virtual AICO (2) and ICO (1) are shown with fiducials.

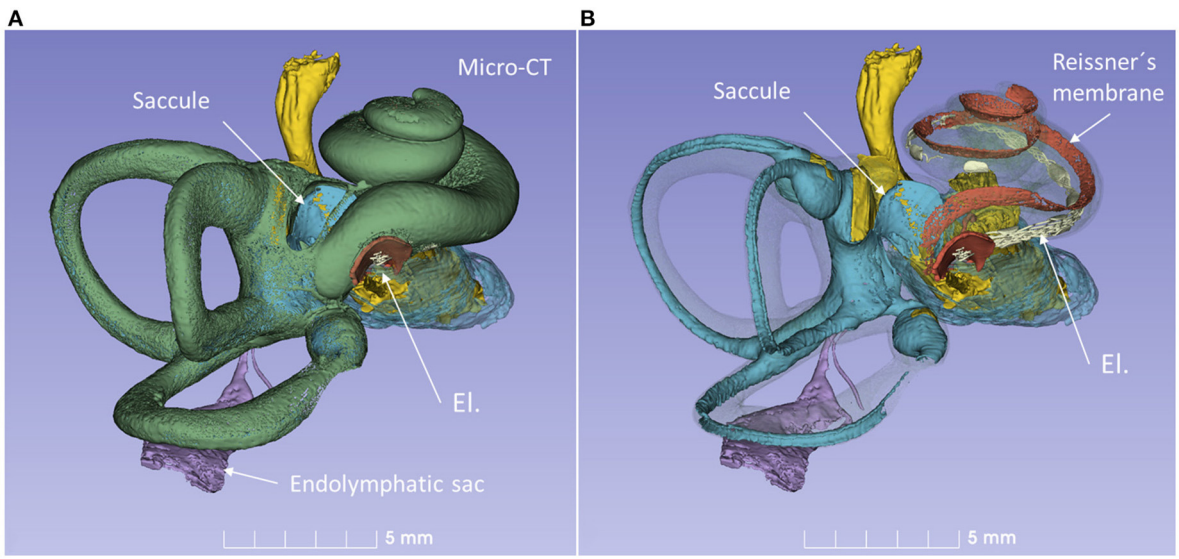

FIGURE 8 | 3D model of a right human temporal bone from micro-CT. Increased penetration time of aqueous I_2KI improved visualization of soft tissue structures. The cochlea was virtually implanted with an electrode (El) through the RW. **(A)** With bone capsule. **(B)** Bone capsule was made transparent to visualize the inner ear soft tissues.

dizziness, but this was not statistically significant due to the small numbers of RW insertions. Hänsel et al. (47) performed a meta-analysis and showed a low incidence of postoperative vertigo, but it was slightly higher in the CO group compared with the RW group. A CO closer to the RW was said to reduce the BM penetrations (48). In our opinion, it is difficult to foresee the extent of the damage that may occur from using the CO technique even if drilling is performed far inferiorly near the acoustic crest at the RW (22, 49). It may appear possible to directly enter the ST, however due to the surgical angle and curved outline of the SL, it may not actually be the case. Nonetheless, there may be anatomical limitations that necessitate a CO, such as facial recess exposure, cochlear malformations, and angles reducing the visibility of the RW.

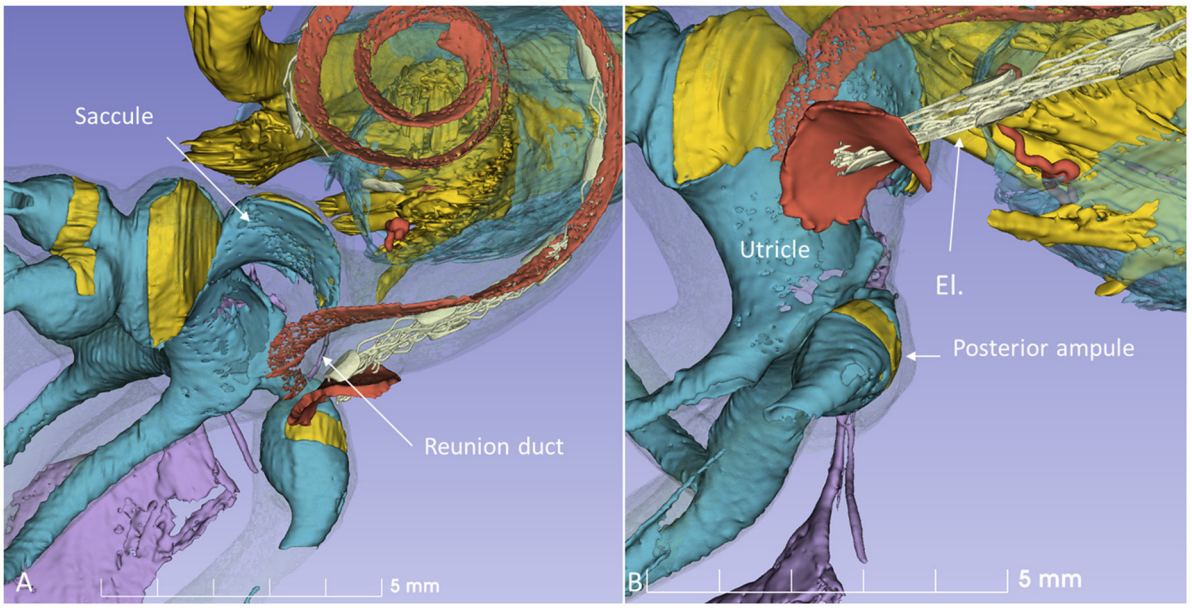

FIGURE 9 | 3D model in **Figure 8** is shown at higher magnification. **(A)** The modeled RD is seen. **(B)** The posterior ampule and its relation to the RW can be seen. El, cochlear implant electrode.

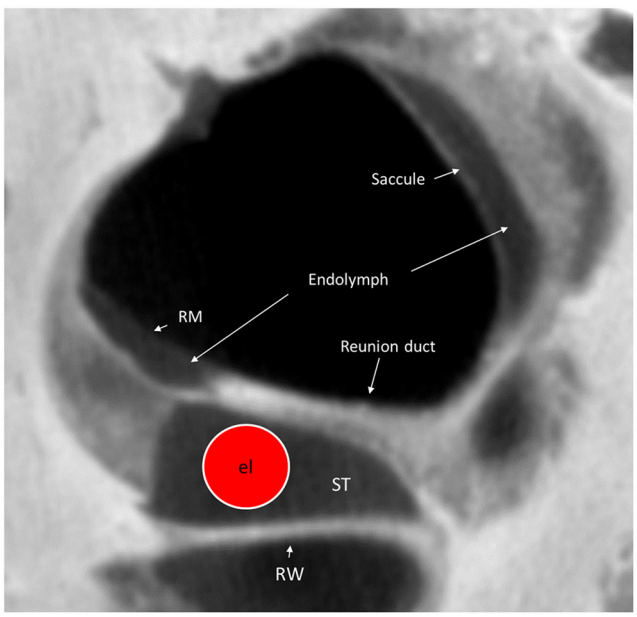

FIGURE 10 | Micro-CT cross-section of the cochlear base at the RW. A virtual CI electrode (el) is placed in the scala tympani. The RD can hardly be seen on the superior surface of the OSL. RM, Reissner's membrane; ST, scala tympani; RW, Round window.

CI can also influence horizontal semicircular canal function, and the video head impulse test (vHIT) and caloric test have been recommended for a complete vestibular analysis (50). RW surgery may change canal and otolith organ function, as shown by Dagkiran et al. (51). They found that the posterior and superior semicircular canal functions were more affected than the lateral canal, recommending the use of a test battery capable of evaluating all five vestibular end-organs pre- and postoperatively. In a recent study in patients undergoing unilateral or bilateral CI, there was no significant impairment of lateral semicircular canal function as demonstrated by high-frequency VOR and vHIT compared with normal hearing individuals in the long term (46, 52). According to Nassif et al. (46), vHIT results suggest there is little impairment of LSSC function compared with normal hearing children (52). From an anatomical standpoint, a functional deterioration of the lateral and horizontal canals is likely to be caused by an indirect trauma caused by perilymph drain or contamination at surgery. Interestingly, SR-PCI revealed that the vestibular membrane apparatus is anchored by several gracile tissue pillars reaching the interior surface of the bony labyrinth. A massive drain of perilymph could rupture this fine network and lead to organ displacement and vestibular dysfunction. These findings may further point to the importance of a slow electrode insertion to minimize perilymph displacement and allow adaptation inside the scala and vestibule to reduce trauma.

Today, most congenitally deaf children receive implants in both ears. Vestibular concerns may arise if the patient is operated on in both ears simultaneously, or in the only vestibular functioning ear. Signs of damage to the saccule with loss of VEMP are common but seemingly with a limited correlation to vertigo, possibly due to transient disturbances (53) and central compensation (37, 41, 54). Colin et al. (4) prospectively tested vestibular function, using pre- and postoperative neuro-vestibular examination and clinical tests, and found no correlation between postoperative test results and postoperative vertigo. Occasionally, there was even improved balance following electric stimulation (4, 55, 56).

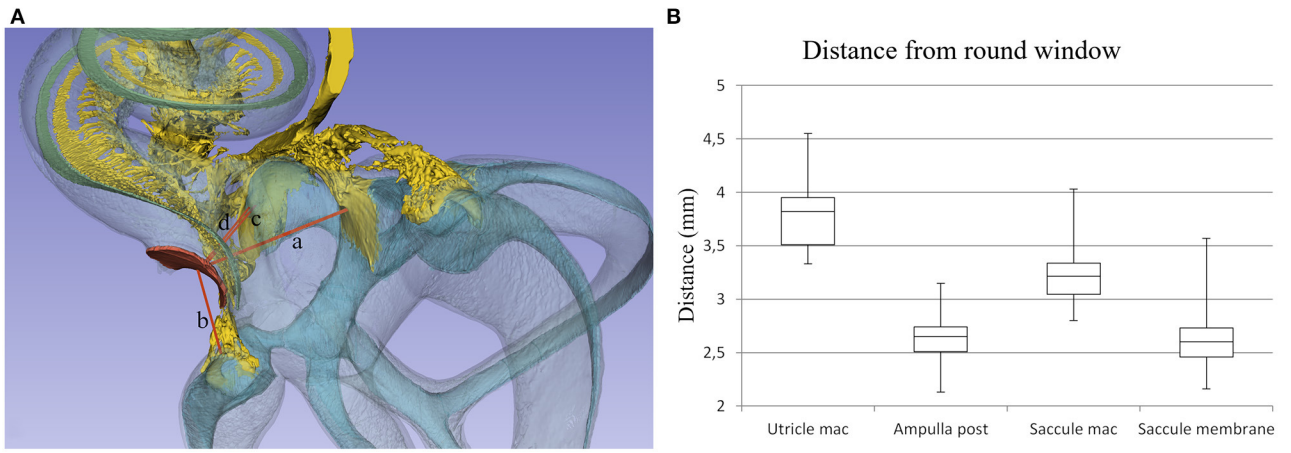

FIGURE 11 | (A) Distances from the (a) utricle macula, (b) posterior semicircular canal ampulla, (c) saccule macula, and (d) saccule membrane to the middle of the RW were assessed. **(B)** Box plot showing measurements in 22 temporal bones.

The present results using SR-PCI and micro-CT imaging three-dimensionally display the intriguing and difficult anatomy of the base of the cochlea and vestibular end-organs. This study may hopefully contribute to a better understanding of the spatial organization, thereby increasing surgical safety. Enhancement of surgical techniques, approaches, and design of CI electrodes may further lessen surgical trauma in the future.

DATA AVAILABILITY STATEMENT

The data supporting the conclusions of this article will be made available by the authors, upon request to the corresponding author.

ETHICS STATEMENT

The study was approved by Western University, London, Ontario, Canada, in accordance with the Anatomy Act of Ontario and Western's Committee for Cadaveric Use in Research (approval no. 06092020).

AUTHOR CONTRIBUTIONS

GR and JS performed micro-CT of human cadavers. HML and JS performed image processing and 3D visualization of scanned objects provided by SA, HL, SR, and JS. HR-A and NS-M planned the project. Microdissections with cochleostomies were provided by FA and HR-A. HR-A, SA, and HL analyzed the images and wrote the manuscript.

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SUPPLEMENTARY MATERIAL

The Supplementary Material for this article can be found online at: https://www.frontiersin.org/articles/10.3389/fneur.2021.663722/full#supplementary-material

REFERENCES

1. Dutt SN, Ray J, Hadjihannas E, Cooper H, Donaldson I, Proofs DW. Medical and surgical complications of the second 100 adult cochlear implant patients in Birmingham. *J Laryngol Otol.* (2005) 119:759–64. doi: 10.1258/002221505774481291
2. Enticott JC, Tari S, Koh SM, Dowell RC, O'Leary SJ. Cochlear implant and vestibular function. *Otol Neurotol.* (2006) 27:824–30. doi: 10.1097/01.mao.0000227903.47483.a6
3. Ibrahim I, Da Silva SD, Segal B, Zeitouni A. Effect of cochlear implant surgery on vestibular function: Meta-analysis study. *J Otolaryngol Head Neck Surg.* (2017) 46:44. doi: 10.1186/s40463-017-0224-0
4. Colin V, Bertholon P, Roy S, Karkas A. Impact of cochlear implantation on peripheral vestibular function in adults. *Eur Ann Otorhinolaryngol Head Neck Dis.* (2018) 135:417–20. doi: 10.1016/j.anorl.2018.10.007
5. Binnetoglu A, Demir B, Batman C. Surgical complications of cochlear implantation: a 25-year retrospective analysis of cases in a tertiary academic center. *Eur Arch Oto Rhino Laryngol.* (2020) 277:1917–23. doi: 10.1007/s00405-020-05916-w
6. Farinetti A, Ben Gharbia D, Mancini J, Roman S, Nicollas R, Triglia JM. Cochlear implant complications in 403 patients: comparative study of adults and children and review of the literature. *Eur Ann Otorhinolaryngol Head Neck Dis.* (2014) 131:177–82. doi: 10.1016/j.anorl.2013.05.005
7. Rah YC, Park JH, Park JH, Choi BY, Koo JW. Dizziness and vestibular function before and after cochlear implantation. *Eur Arch Oto Rhino Laryngol.* (2016) 273:3615–21. doi: 10.1007/s00405-016-3988-3
8. Tien HC, Linthicum FH. Histopathologic changes in the vestibule after cochlear implantation. *Otolaryngol Head Neck Surg.* (2002) 127:260–4. doi: 10.1067/mhn.2002.128555
9. Handzel O, Burgess BJ, Nadol JB. Histopathology of the peripheral vestibular system after cochlear implantation in the human. *Otol Neurotol.* (2006) 27:57–64. doi: 10.1097/01.mao.0000188658.36327.8f
10. Vogel U. New approach for 3D imaging and geometry modeling of the human inner ear. *ORL.* (1999) 61:259–67. doi: 10.1159/000027683
11. Müller B, Lareida A, Beckmann F, Diakov GM, Kral F, Schwarm F, et al. Anatomy of the murine and human cochlea visualized at the cellular level by synchrotron-radiation-based micro-computed tomography. In: *Developments in X-Ray Tomography V*. San Diego, CA: SPIE Optics + Photonics (2006). p. 631805. doi: 10.1117/12.680540
12. Lareida A, Beckmann F, Schrott-Fischer A, Glueckert R, Freysinger W, Muller B. High-resolution X-ray tomography of the human inner ear: synchrotron radiation-based study of nerve fibre bundles, membranes and ganglion cells. *J Microsc.* (2009) 234:95–102. doi: 10.1111/j.1365-2818.2009.03143.x
13. Koch RW, Elfarnawany M, Zhu N, Ladak HM, Agrawal SK. Evaluation of cochlear duct length computations using synchrotron radiation phase-contrast imaging. *Otol Neurotol.* (2017) 38:e92–9. doi: 10.1097/MAO.0000000000001410
14. Li H, Schart-Morén N, Rohani SA, Ladak HM, Rask-Andersen H, Agrawal S. Synchrotron radiation-based reconstruction of the human spiral ganglion: implications for cochlear implantation. *Ear Hear.* (2018) 41:173–81. doi: 10.1097/AUD.0000000000000738
15. Agrawal S, Schart-Morén N, Liu W, Ladak HM, Rask-Andersen H, Li H. The secondary spiral lamina and its relevance in cochlear implant surgery. *Ups J Med Sci.* (2018) 123:9–18. doi: 10.1080/03009734.2018.1443983
16. Elfarnawany M, Alam SR, Rohani SA, Zhu N, Agrawal SK, Ladak HM. Micro-CT versus synchrotron radiation phase contrast imaging of human cochlea. *J Microsc.* (2017) 265:349–57. doi: 10.1111/jmi.12507
17. Rau C, Robinson IK, Richter C-P. Visualizing soft tissue in the mammalian cochlea with coherent hard X-rays. *Microsc Res Tech.* (2006) 69:660–5. doi: 10.1002/jemt.20336
18. Iyer JS, Zhu N, Gasilov S, Ladak HM, Agrawal SK, Stankovic KM. Visualizing the 3D cytoarchitecture of the human cochlea in an intact temporal bone using synchrotron radiation phase contrast imaging. *Biomed Opt Express.* (2018) 9:3757. doi: 10.1364/BOE.9.003757
19. Enghag S, Strömbäck K, Li H, Rohani SA, Ladak HM, Rask-Andersen H, et al. Incus necrosis and blood supply: a micro-CT and synchrotron imaging study. *Otol Neurotol.* (2019) 40:E713–22. doi: 10.1097/MAO.0000000000002292
20. Rohani SA, Allen D, Gare B, Zhu N, Agrawal S, Ladak H. High-resolution imaging of the human incudostapedial joint using synchrotron-radiation phase-contrast imaging. *J Microsc.* (2020) 277:61–70. doi: 10.1111/jmi.12864
21. Anschuetz L, Demattè M, Pica A, Wimmer W, Caversaccio M, Bonnin A. Synchrotron radiation imaging revealing the sub-micron structure of the auditory ossicles. *Hear Res.* (2019) 383. doi: 10.1016/j.heares.2019.107806
22. Atturo F, Barbara M, Rask-Andersen H. On the anatomy of the "hook" region of the human cochlea and how it relates to cochlear implantation. *Audiol Neurotol.* (2014) 19:378–85. doi: 10.1159/000365585
23. Schart-Morén N, Agrawal SK, Ladak HM, Li H, Rask-Andersen H. Effects of various trajectories on tissue preservation in cochlear implant surgery: a micro-computed tomography and synchrotron radiation phase-contrast imaging study. *Ear Hear.* (2019) 40:393–400. doi: 10.1097/AUD.0000000000000624
24. Fedorov A, Beichel R, Kalpathy-Cramer J, Finet J, Fillion-Robin JC, Pujol S, et al. 3D Slicer as an image computing platform for the quantitative imaging network. *Magn Reson Imaging.* (2012) 30:1323–41. doi: 10.1016/j.mri.2012.05.001
25. Camilieri-Asch V, Shaw JA, Mehnert A, Yopak KE, Partridge JC, Collin SP. Dicect: A valuable technique to study the nervous system of fish. *eNeuro.* (2020) 7:1–23. doi: 10.1523/ENEURO.0076-20.2020
26. Culling CFA, Charles FA, Dunn WL. Developments in X-Ray tomography V. *In: SPIE Optics + Photonics. Vol. 6318.* Bonse U, (editor). San Diego, CA. (1974).
27. Wilbrand HF. Multidirectional tomography of the facial canal. *Acta Radiol Diagn.* (1975) 16:654–72. doi: 10.1177/028418517501600613
28. Rask-Andersen H, Stahle J, Wilbrand H. Human cochlear aqueduct and its accessory canals. *Ann Otol Rhinol Laryngol.* (1977) 86:1–16. doi: 10.1177/00034894770860S501
29. Atturo F, Barbara M, Rask-Andersen H. Is the human round window really round? An anatomic study with surgical implications. *Otol Neurotol.* (2014) 35:1354–60. doi: 10.1097/MAO.0000000000000332
30. Adunka OF, Radeloff A, Gstoettner WK, Pillsbury HC, Buchman CA. Scala tympani cochleostomy II: topography and histology. *Laryngoscope.* (2007) 117:2195–200. doi: 10.1097/MLG.0b013e3181453a53
31. Basura GJ, Adunka OF, Buchman CA. Scala tympani cochleostomy for cochlear implantation. *Oper Tech Otolaryngol Head Neck Surg.* (2010) 21:218–22. doi: 10.1016/j.otot.2010.08.001
32. Perlman HB. The saccule: observations on a differentiated reenforced area of the saccular wall in man. *Arch Otolaryngol Head Neck Surg.* (1940) 32:678–91. doi: 10.1001/archotol.1940.00660020683005
33. Limb CJ, Francis HF, Lustig LR, Niparko JK, Jammal H. Benign positional vertigo after cochlear implantation. *Otolaryngol Head Neck Surg.* (2005) 132:741–5. doi: 10.1016/j.otohns.2005.01.004
34. Yamane H, Takayama M, Sunami K, Sakamoto H, Mochizuki K, Inoue Y. Three-dimensional images of the reuniting duct using cone beam CT. *Acta Otolaryngol.* (2009) 129:493–6. doi: 10.1080/00016480802294393
35. Kusuma S, Liou S, Haynes DS. Disequilibrium after cochlear implantation caused by a perilymph fistula. *Laryngoscope.* (2005) 115:25–6. doi: 10.1097/01.mlg.0000150680.68355.cc
36. Fina M, Skinner M, Goebel JA, Piccirillo JF, Neely JG. Vestibular dysfunction after cochlear implantation. *Otol Neurotol.* (2003) 24:234–42. doi: 10.1097/00129492-200303000-00018
37. Basta D, Todt I, Goepel F, Ernst A. Loss of saccular function after cochlear implantation: the diagnostic impact of intracochlear electrically elicited vestibular evoked myogenic potentials. *Audiol Neurotol.* (2008) 13:187–92. doi: 10.1159/000113509
38. Todt I, Basta D, Ernst A. Does the surgical approach in cochlear implantation influence the occurrence of postoperative vertigo? *Otolaryngol Head Neck Surg.* (2008) 138:8–12. doi: 10.1016/j.otohns.2007.09.003
39. Jin Y, Nakamura M, Shinjo Y, Kaga K. Vestibular-evoked myogenic potentials in cochlear implant children. *Acta Otolaryngol.* (2006) 126:164–9. doi: 10.1080/00016480500312562
40. Meli A, Aud BM, Aud ST, Aud RG, Cristofari E. Vestibular function after cochlear implant surgery. *Cochlear Implants Int.* (2016) 17:151–7. doi: 10.1179/1754762815Y.0000000014

41. Licameli G, Zhou G, Kenna MA. Disturbance of vestibular function attributable to cochlear implantation in children. *Laryngoscope*. (2009) 119:740–5. doi: 10.1002/lary.20121
42. Sosna M, Tacikowska G, Pietrasik K, Skarzyński H, Lorens A, Skarzyński PH. Effect on vestibular function of cochlear implantation by partial deafness treatment–electro acoustic stimulation (PDT–EAS). *Eur Arch Oto Rhino Laryngol*. (2019) 276:1951–9. doi: 10.1007/s00405-019-05425-5
43. Rajan GP, Kontorinis G, Kuthubutheen J. The effects of insertion speed on inner ear function during cochlear implantation: a comparison study. *Audiol Neurotol*. (2012) 18:17–22. doi: 10.1159/000342821
44. Batuecas-Caletrio A, Klumpp M, Santacruz-Ruiz S, Gonzalez FB, Sánchez EG, Arriaga M. Vestibular function in cochlear implantation: correlating objectiveness and subjectiveness. *Laryngoscope*. (2015) 125:2371–5. doi: 10.1002/lary.25299
45. Veroul E, Sabban D, Blexmann L, Frachet B, Poncet-Wallet C, Mamelle E. Predictive factors of vertigo following cochlear implantation in adults. *Eur Arch Oto Rhino Laryngol*. (2020) 1:3. doi: 10.1007/s00405-020-06449-y
46. Nassif N, Balzanelli C, Redaelli De Zinis LO. Long-Term lateral semicircular canal function in children with cochlear implants: results of video head impulse test. *Eur J Investig Heal Psychol Educ*. (2021) 11:12–9. doi: 10.3390/ejihpe11010002
47. Hänsel T, Gauger U, Bernhard N, Behzadi N, Romo Ventura ME, Hofmann V, et al. Meta-analysis of subjective complaints of vertigo and vestibular tests after cochlear implantation. *Laryngoscope*. (2018) 128:2110–23. doi: 10.1002/lary.27071
48. Richter B, Aschendorff A, Lohnstein P, Husstedt H, Nagursky H, Laszig R. The nucleus contour electrode array: a radiological and histological study. *Laryngoscope*. (2001) 111:508–14. doi: 10.1097/00005537-200103000-00023
49. Rask-Andersen H, Liu W, Erixon E, Kinnefors A, Pfaller K, Schrott-Fischer A, et al. Human cochlea: anatomical characteristics and their relevance for cochlear implantation. *Anat Rec*. (2012) 295:1791–811. doi: 10.1002/ar.22599
50. Zeng J, Huang HM, Wang XQ, Zhong KB, Wu PN. [Assessment of the horizontal semicircular canal function after cochlear implantation by video head impulse test and caloric test]. *Lin Chung Er Bi Yan Hou Tou Jing Wai Ke Za Zhi*. (2018) 32:86–90. doi: 10.13201/j.issn.1001-1781.2018.02.002
51. Dagkiran M, Tuncer U, Surmelioglu O, Tarkan O, Ozdemir S, Cetik F, et al. How does cochlear implantation affect five vestibular end-organ functions and dizziness? *Auris Nasus Larynx*. (2019) 46:178–85. doi: 10.1016/j.anl.2018.07.004
52. Nassif N, Balzanelli C, Redaelli de Zinis LO. Preliminary results of video head Impulse TESTING (vHIT) in children with cochlear implants. *Int J Pediatr Otorhinolaryngol*. (2016) 88:30–3. doi: 10.1016/j.ijporl.2016.06.034
53. Jacot E, Van Den Abbeele T, Debre HR, Wiener-Vacher SR. Vestibular impairments pre- and post-cochlear implant in children. *Int J Pediatr Otorhinolaryngol*. (2009) 73:209–17. doi: 10.1016/j.ijporl.2008.10.024
54. Ajalloueyan M, Saeedi M, Sadeghi M, Zamiri Abdollahi F. The effects of cochlear implantation on vestibular function in 1–4 years old children. *Int J Pediatr Otorhinolaryngol*. (2017) 94:100–3. doi: 10.1016/j.ijporl.2017.01.019
55. Buchman CA, Joy J, Hodges A, Telischi FF, Balkany TJ. Vestibular effects of cochlear implantation. *Laryngoscope*. (2004) 114:1–22. doi: 10.1097/00005537-200410001-00001
56. Krause E, Louza JPR, Wechtenbruch J, Hempel JM, Rader T, Grkov R. Incidence and quality of vertigo symptoms after cochlear implantation. *J Laryngol Otol*. (2009) 123:278–82. doi: 10.1017/S00222151080 0296X

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Influence of Cochlear Implantation on Vestibular Function in Children With an Enlarged Vestibular Aqueduct

Ruijie Wang†, Daogong Zhang†, Jianfen Luo, Xiuhua Chao, Jiliang Xu, Xianfeng Liu, Zhaomin Fan, Haibo Wang and Lei Xu**

Department of Otolaryngology-Head and Neck Surgery, Shandong Provincial ENT Hospital, Cheeloo College of Medicine, Shandong University, Jinan, China

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Robert Gürkov,
Bielefeld University, Germany

***Correspondence:**
Haibo Wang
whboto11@163.com
Lei Xu
sdphxl@126.com

†*These authors have contributed equally to this work and share first authorship*

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Wang R, Zhang D, Luo J, Chao X, Xu J, Liu X, Fan Z, Wang H and Xu L (2021) Influence of Cochlear Implantation on Vestibular Function in Children With an Enlarged Vestibular Aqueduct. Front. Neurol. 12:663123. doi: 10.3389/fneur.2021.663123

Background: Cochlear implantation (CI) is becoming increasingly used in the rehabilitation of hearing-impaired patients. Children with an enlarged vestibular aqueduct (EVA) need CI for severe or profound hearing loss, with excellent outcomes in hearing rehabilitation. However, vestibular function influenced by CI in children with EVA has not been clarified. We compared the characteristics of vestibular function in implanted children with EVA and those with a normal cochlea.

Methods: In this retrospective case-control study, 16 children with large vestibular aqueduct syndrome (LVAS) and 16 children with a normal cochlea were recruited as the Study and Control Group, respectively. All children (mean age, 10.3 ± 4.4 years) had bilateral profound sensorineural hearing loss (SNHL) and normal pre-operative vestibular functions and underwent unilateral CI. Otolith and canal functions were assessed before CI and 12 months thereafter. Cervical vestibular-evoked myogenic potential (cVEMP), ocular vestibular-evoked myogenic potential (oVEMP), and video head impulse test (vHIT) were evaluated.

Results: Full insertion of the electrode array was achieved in all the cases. Preoperatively, no significant differences in parameters in cVEMP between the Study and Control Group were revealed ($p > 0.05$). In pre-operative oVEMP, shorter N1 latencies ($p = 0.012$), shorter P1 latencies ($p = 0.01$), and higher amplitudes ($p = 0.001$) were found in the Study than in the Control Group. The Study Group had shorter P1 latency in cVEMP ($p = 0.033$), and had lower amplitude in oVEMP after implantation ($p = 0.03$). Statistically significant differences were not found in VOR gains of all three semicircular canals before and after surgery ($p > 0.05$). VEMP results revealed that the Control Group had significantly lower deterioration rates after CI ($p < 0.05$). The surgical approach and electrode array had no statistically significant influence on the VEMP results ($p > 0.05$).

Conclusion: oVEMP parameters differed between children with EVA and children with a normal cochlea before surgery. Systematic evaluations before and after CI showed that otolith function was affected, but all three semicircular canals functions were essentially

undamaged after implantation. In contrast to subjects with a normal cochlea, children with EVA are more likely to preserve their saccular and utricular functions after CI surgery. Possible mechanisms include less pressure-related damage, a reduced effect in terms of the air-bone gap (ABG), or more sensitivity to acoustic stimulation.

Keywords: cochlear implant, vestibular function, EVA, child, vestibular-evoked myogenic potential

INTRODUCTION

Cochlear implantation (CI) is a gold standard therapy for total or severe sensorineural hearing loss (SNHL). In congenitally deaf children, early intervention enables communication, oral language, and cognitive function development. Although studies have shown that CI is effective and safe, the potential effects on vestibular function are of clinical concern (1). Because of the proximity of the cochlea and vestibule, a vestibular impairment may occur after CI, leading to disorders of environmental perception and balance ability (2). Possible reasons include electrode insertion, intraoperative perilymphatic loss, labyrinthitis, endolymphatic hydrops, or electrical stimulation (3).

The vestibular aqueduct is a bony canal in the temporal bone. Arrested development during the fifth week of gestation, before narrowing occurs, results in large vestibular aqueduct syndrome (LVAS) (4). An enlarged vestibular aqueduct (EVA) is the most common inner ear malformation associated with early-onset SNHL, as first described by Mondini (5). As children with EVA become progressively deafer through childhood, they would be ideal candidates for CI (6). Studies have described excellent speech perception outcomes in patients with EVA who had undergone CI (7). However, patients with EVA may have vestibular dysfunctions. According to previous reviews, adverse vestibular signs and symptoms varied from 0 to 100% (8–10). Post-operative vertigo was observed to be increased significantly after CI (11). Some studies have demonstrated that individuals with vestibular impairments showed worse performances in terms of visuospatial ability, attention, executive function, and memory (2). With unilateral or bilateral CI in children with EVA, this risk needs to be carefully taken into account.

Vestibular impairment can be investigated by objective tests. Vestibular-evoked myogenic potential (VEMP) parameters in an EVA patient were recently discussed. A few studies have demonstrated different parameters in VEMPs between patients with EVA and those with a normal cochlea (12–14). The VEMP is used to evaluate the otolith system quantitatively and includes the cervical VEMP (cVEMP) and ocular VEMP (oVEMP). The cVEMP is derived from the saccule and mainly reflects saccular function and inferior vestibular nerve. The oVEMP is derived from the utricle and mainly reflects utricular function and superior vestibular nerve (15). Normal cVEMP and oVEMP responses have been detected in 46.7–100% and 63.5% of children with SNHL compared to 15.6–83% and 45.5% of children with CI (16). However, systematic objective evaluations of peripheral vestibular organ function in children with EVA before CI have seldom been performed.

In the present research, we compared the pre- and post-operative cVEMP, oVEMP, and video head impulse test (vHIT) results in pediatric populations with EVA and a normal cochlea, to gain insight into the vestibular function of these children.

METHODS

Participants

This retrospective study included 32 children (32 ears), who underwent unilateral CI in our department between November 2016 and November 2019. Across all subjects, the mean age at implantation was 10.3 ± 4.4 years (range: 5–18 years). The indication for CI was based on severe-to-profound bilateral deafness with little benefit from hearing aids. Patients were excluded if they were ≥ 18 years, unable to participate in vestibular assessments, or had undergone previous otologic surgery. Computed tomography (CT) scans of the temporal bone and magnetic resonance imaging (MRI) were performed before surgery. EVA was defined as a vestibular aqueduct diameter > 1.5 mm at the midpoint between the posterior cranial fossa and the vestibule of the inner ear, or an otherwise grossly malformed morphology of the vestibular aqueduct (8). The surgical technique was identical in all patients and was performed by one senior surgeon. All children had normal otolith and canal functions before implantation. All participants underwent vestibular assessments prior to CI and again at 12 months post-surgery. The CIs were all switched off during tests after processor activation.

We divided children into the Study Group and the Control Group. The Study Group included 16 patients (5 females and 11 males; 4 left and 12 right ears). The mean age was 9.2 ± 4.4 years (range, 5–17 years). Pre-operative CT and MRI showed bilateral EVA in all 16 children. There were 13 subjects with congenital deafness and 3 subjects with progressive deafness. In 12 children, the round window (RW) surgical approach was used, and in 4 the extended RW approach was used. A total of 11 children were implanted with a Nucleus CI422, 1 child with a Med-EL FLEX28, 1 child with a Nurotron CS-10A, and 3 children with a Nucleus CI24RECA electrode. In the Control Group, 16 recipients (5 females and 11 males; 5 left and 11 right ears) were included. Pre-operative imaging was normal in all these children. Their mean age was 11.4 ± 4.4 years (range, 5–18 years). There were seven subjects with congenital deafness and nine subjects with progressive deafness. In 10 children, the RW surgical approach was used, and in 6 the extended RW approach was used. A total of seven children were implanted with a Nucleus CI422, one child with a Med-EL FLEX28, two

children with a Nurotron CS-10A, and six children with a Nucleus CI24RECA electrode.

cVEMP

cVEMP was recorded using the Neuro-Audio auditory evoked potential equipment (Neurosoft LTD, Ivanov, Russia). The test was performed with the patients in a seated position. Tone burst stimuli (93 dB nHL and 500 Hz) were delivered via a standard insert earphone (ER-3A). Active recording electrodes with respect to the examination were placed on the region of the upper third of the sternocleidomastoid muscle (SCM) on both sides. The reference electrodes were placed on the upper sternum. The ground electrode was on the nasion. The head was rotated toward the contralateral side of the stimulated ear to achieve tonic contraction of the SCM during recording. The stimulation rate was 5.1 Hz. Bandpass filtering was 30–2,000 Hz. An amplitude ratio over 30% was considered abnormal if the weaker response was from the implanted ear. In the event of bilaterally reduced responses where the asymmetry ratio would be normal, absent responses were considered abnormal (17).

oVEMP

oVEMP was recorded using the Neuro-Audio auditory evoked potential equipment (Neurosoft LTD, Ivanov, Russia). The electromyographic activity of the extraocular muscle was recorded with the patients in the seated position. Tone burst stimuli (93 dB nHL and 500 Hz) were delivered via a standard insert earphone (ER-3A). The active recording electrodes were placed on the infra-orbital ridge 1 cm below the center of each lower eyelid. The reference electrodes were positioned approximately 1 cm below them. The ground electrode was on the nasion. The results were recorded with eyes open and maximal gaze upwards. The stimulation rate was 5.1 Hz. Bandpass filtering was 1–1,000 Hz. An amplitude ratio over 30% was considered abnormal if the weaker response was from the implanted ear. In the event of bilaterally reduced responses where the asymmetry ratio would be normal, absent responses were considered abnormal (17).

vHIT

The vHIT device (Ulmer II Evolution, France) was used. The VHIT Ulmer II was equipped with an ultra-sensitive camera that filmed the patient's face from a distance of ∼90 cm. The patient was instructed to maintain eye focusing on a stationary object on a screen at about 1 m distance while the examiner manipulated the patient's head with quick and precise head movements. The vestibulo-ocular reflex (VOR) gain was calculated by vHIT software based on head velocity and eye velocity curves. When the head was turned to one side in the plane of the semicircular canal to be tested, the VOR maintained visual fixation. The breaking of visual fixation, shown by a corrective saccade, indicated a respective canal disorder. This test was possible as soon as the child could hold his head steady. The VOR gain of a horizontal semicircular canal (HSC) <0.8 was considered to be abnormal. Both the VOR gain of the superior semicircular canal (SSC) and the posterior semicircular canal (PSC) <0.7 were considered to be abnormal (18).

Statistical Analyses

Data were analyzed using the Statistical Package for the Social Sciences (SPSS), version 23.0 (SPSS, Inc., Chicago, IL). Statistical comparisons on parameters were performed using the paired-samples test and the independent-samples test as appropriate. The variables in response rates between groups were compared by the chi-square test. The influence factors on the results were analyzed by the chi-square test. Statistical significance was considered at $p < 0.05$.

RESULTS

This study was conducted in two groups of children, who had similar baseline characteristics (**Table 1**). For all children, each implanted electrode reached full insertion without any resistance or complication. Specific parameters of VEMPs in the Study Group and the Control Group before and after implantation are presented in **Table 2**. The VOR gains in the vHIT in the Study Group and the Control Group before and after implantation are presented in **Table 3**. The VEMP response in 32 implanted children and correlation to the electrode and surgical approach after CI are shown in **Table 4**. The response rates of cVEMP and oVEMP at postoperative month 12 are shown in **Figure 1**.

VEMP Parameters Before Surgery

In the pre-operative cVEMP test, the means of P1 latencies, N1 latencies, and amplitudes of the Study Group ($n = 16$) and Control Group ($n = 16$) were 15.04 ± 2.79 ms vs. 14.24 ± 1.62 ms, 22.86 ± 4.59 ms vs. 21.72 ± 2.08 ms, and 94.99 ± 49.40 μV vs. 88.61 ± 86.82 μV, respectively. The independent-samples test showed that there were no significant differences between the pre-operative parameters of these two groups ($p > 0.05$). In the pre-operative oVEMP test, the N1 latencies, P1 latencies, and amplitudes of the Study Group ($n = 16$) and Control Group ($n = 16$) were 9.92 ± 0.62 ms vs. 11.26 ± 1.68 ms, 14.52 ± 1.21 ms vs. 15.65 ± 1.29 ms, and 13.87 ± 8.71 μV vs. 5.63 ± 6.63 μV, respectively. The independent-samples test showed that N1 latencies ($p = 0.012$) and P1 latencies ($p = 0.01$) were shorter, and amplitudes ($p = 0.001$) were higher in the Study Group than the Control Group.

Changes in VEMP Parameters Between Pre- and Post-CI

In the Study Group, two children with normal VEMPs before CI had absent VEMPs (cVEMP or oVEMP) postoperatively. Paired-samples test showed that shorter P1 latency in cVEMP ($n = 14$, $p = 0.033$) and lower amplitude in oVEMP ($n = 14$, $p = 0.03$) were found after implantation in the Study Group (**Table 2**). In the Control Group, 11 children with normal VEMPs before CI had absent VEMPs (cVEMP or oVEMP) postoperatively. The paired-samples test showed that no significant changes in all three parameters (P1, N1, amplitude) after as compared to before surgery ($n = 5$, $p > 0.05$; **Table 2**).

Six children implanted with the Nucleus CI 422 electrode (RW approach), five children implanted with the Nucleus CI24RECA electrode (extended RW approach), one child implanted with

TABLE 1 | Demographic characteristics of the 32 patients in this study.

Group	Subject number	Gender	Ear tested	Hearing loss	Age at implantation (yrs)	CT scan	Electrode	Surgical approach
Study	S1	M	L	Congenital	6	EVA	CI422	RW
	S2	M	R	Congenital	7	EVA	CI422	RW
	S3	M	L	Congenital	5	MD, EVA	CI422	RW
	S4	M	L	Congenital	8	EVA	CI24RECA	Extended
	S5	M	R	Congenital	5	EVA	CI422	RW
	S6	M	L	Congenital	11	MD, EVA	CS-10A	RW
	S7	F	R	Congenital	5	MD, EVA	CI422	RW
	S8	M	R	Congenital	6	EVA	CI24RECA	Extended
	S9	M	R	Progressive	15	MD, EVA	CI24RECA	Extended
	S10	F	R	Congenital	13	MD, EVA	CI422	RW
	S11	F	R	Progressive	17	MD, EVA	CI422	RW
	S12	F	R	Congenital	6	MD, EVA	FLEX F28	Extended
	S13	M	R	Congenital	7	MD, EVA	CI422	RW
	S14	M	R	Congenital	14	MD, EVA	CI422	RW
	S15	M	R	Progressive	16	EVA	CI422	RW
	S16	F	R	Congenital	6	MD, EVA	CI422	RW
Control	C1	F	R	Progressive	18	Normal	CI24RECA	Extended
	C2	M	L	Progressive	12	Normal	CS-10A	RW
	C3	M	R	Progressive	16	Normal	CS-10A	RW
	C4	F	R	Progressive	12	Normal	CI24RECA	Extended
	C5	M	R	Congenital	5	Normal	CI24RECA	Extended
	C6	M	L	Progressive	18	Normal	CI422	RW
	C7	M	R	Progressive	17	Normal	CI422	RW
	C8	M	R	Congenital	7	Normal	CI422	RW
	C9	F	R	Congenital	6	Normal	CI24RECA	Extended
	C10	M	R	Progressive	13	Normal	CI422	RW
	C11	M	R	Progressive	12	Normal	CI422	RW
	C12	M	L	Progressive	13	Normal	CI422	RW
	C13	F	R	Congenital	11	Normal	CI24RECA	Extended
	C14	M	L	Congenital	10	Normal	CI24RECA	Extended
	C15	M	R	Congenital	7	Normal	FLEX F28	RW
	C16	F	L	Congenital	6	Normal	CI422	RW

RW, round window; Extended, extended RW; EVA, enlarged vestibular aqueduct; MD, Mondini; M, male; F, female; L, left; R, right.

TABLE 2 | Specific parameters of VEMPs in the Study Group and the Control Group before and after implantation.

VEMP	Group	T▼	P1-pre	N1-pre	Amplitude-pre	P1-post	N1-post	Amplitude-post
cVEMP	Study	14	15.38 ± 2.82	23.55 ± 4.48	94.04 ± 51.27	13.66 ± 0.71*	25.77 ± 16.54	110.96 ± 60.94
	Control	5	13.85 ± 2.58	21.55 ± 2.59	162.19 ± 122.92	15.38 ± 2.82	21.76 ± 1.59	89.90 ± 43.11
oVEMP	Study	14	14.28 ± 0.96	9.86 ± 0.51	15.18 ± 8.51	14.79 ± 1.33	10.39 ± 1.25	8.16 ± 5.49*
	Control	5	15.87 ± 1.42	11.80 ± 2.26	9.04 ± 10.73	15.03 ± 1.48	11.48 ± 1.61	10.50 ± 13.03

*The first positive wave in the cVEMP waveform is P1, and the first negative wave is N1. The first negative wave in the oVEMP waveform is N1, and the first positive wave is P1. P1, ms; N1, ms; Amplitude, μV. T▼, tested ears of patients with both pre-operative and post-operative present VEMPs; patients with present VEMPs preoperatively and absent VEMPs postoperatively were not included. cVEMP, cervical vestibular-evoked myogenic potential; oVEMP, ocular vestibular-evoked myogenic potential; pre, pre-operation; post, post-operation; *$p < 0.05$.*

the Nurotron CS-10A electrode (RW approach), and one child implanted with the Med-EL FLEX 28 electrode (RW approach) demonstrated present VEMPs preoperatively and absent postoperatively (cVEMP or oVEMP), and were excluded from analysis of VEMP parameter changes.

Response Rates of VEMP

In the Study Group, three children had abnormal cVEMP responses and four children had abnormal oVEMP responses after surgery. Two showed decreases in the amplitude of cVEMP and one showed no response, while two showed decreases in

TABLE 3 | The VOR gains in the vHIT in the Study Group and the Control Group before and after implantation.

vHIT	Group	T	SSC-pre	HSC-pre	PSC-pre	SSC-post	HSC-post	PSC-post
	Study	16	1.03 ± 0.08	1.02 ± 0.06	0.98 ± 0.09	0.98 ± 0.18	0.90 ± 0.28	0.94 ± 0.13
	Control	16	1.01 ± 0.07	0.98 ± 0.08	0.99 ± 0.10	1.05 ± 0.07	1.01 ± 0.08	1.00 ± 0.09

Pre, pre-operation; post, post-operation; T, test ears; vHIT, video head impulse test; HSC, horizontal semicircular canal; SSC, superior semicircular canal; PSC, posterior semicircular canal.

TABLE 4 | The VEMP response in 32 implanted children and correlation to electrode and surgical approach after CI.

Factor	cVEMP-normal (n)	cVEMP-abnormal (n)	oVEMP-normal (n)	oVEMP-abnormal (n)
CI422	12	6	11	7
CI24RECA	4	5	4	5
FLEX 28	1	1	1	1
CS-10A	3	0	2	1
RW	15	7	13	9
Extended RW	5	5	5	5

Chi-square test. cVEMP, cervical vestibular-evoked myogenic potential; oVEMP, ocular vestibular-evoked myogenic potential; RW, round window; Extended, extended RW; n, number of patient.

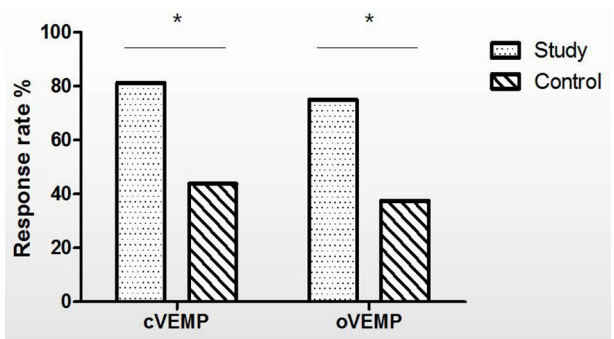

FIGURE 1 | The response rates of cVEMP and oVEMP at postoperative month 12 (%). Chi-square test, the response rate of cVEMP (Study Group vs. Control Group, $p = 0.028$), the response rate of oVEMP (Study Group vs. Control Group, $p = 0.033$), $^*p < 0.05$. cVEMP, cervical vestibular-evoked myogenic potential; oVEMP, ocular vestibular-evoked myogenic potential; Study, Study Group; Control, Control Group.

the amplitude of oVEMP and two showed no responses. The response rates of cVEMP and oVEMP decreased to 81.25 and 75.00%, respectively, after CI.

In the Control Group, 9 children had abnormal cVEMP responses and 10 had abnormal oVEMP responses after surgery. Two children showed decreased and seven had absent cVEMP responses, while one child had decreased response and nine had absent oVEMP responses. The response rates of cVEMP and oVEMP decreased to 43.75 and 37.50%, respectively, after CI.

After CI, children with abnormal VEMP responses included these 13 children who had present VEMP preoperatively but absent VEMP postoperatively (cVEMP or oVEMP). There were 2 children with EVA and 11 children with a normal cochlea.

The chi-square test showed that the response rate of cVEMP was statistically significantly lower in the Control Group than in the Study Group ($p = 0.028$), and the response rate of oVEMP was statistically significantly lower in the Control Group than in the Study Group after CI surgery ($p = 0.033$) (**Figure 1**).

VOR Gains and Response Rates of vHIT

The pre-operative SSC VOR gain was compared between the two groups, but the independent-samples test showed that the difference was not statistically significant (mean gain in the Study Group = 1.03 ± 0.08, mean gain in the Control Group = 1.01 ± 0.07, $p = 0.402$). The pre-operative HSC VOR gain was not statistically significantly different between the two groups (mean gain in the Study Group = 1.02 ± 0.06, mean gain in the Control Group = 0.98 ± 0.08, $p = 0.08$). The pre-operative PSC VOR gain was also not statistically significantly different between the two groups (mean gain in the Study Group = 0.98 ± 0.09, mean gain in the Control Group = 0.99 ± 0.10, $p = 0.642$) (**Table 3**). The paired-samples test showed that VOR gains in the HSC, SSC, and PSC did not differ differently before and after surgery within groups ($p > 0.05$) (**Table 3**).

In the Study Group, one child with EVA had post-operative abnormal VOR gains in all three semicircular canals, and one child with EVA had post-operative abnormal VOR gains in the HSC. The response rates of all three semicircular canals were all 100% in the Control Group postoperatively.

Influence of Surgical Approach and Electrode Array on VEMP Results

The electrode array and surgical approach used had no statistically significant impact on the changes pre- and post-CI in the patients overall (chi-square test, $p > 0.05$) (**Table 4**).

DISCUSSION

In this study, we compared the vestibular function characteristics in implanted children with EVA and those with a normal cochlea. We found that oVEMP parameters differed between children with EVA and children with a normal cochlea before surgery. Systematic evaluations before and after CI showed that otolith function was affected, but all three semicircular canals functions were essentially undamaged after implantation. In contrast to normal children, children with EVA were more likely to have preserved saccular and utricular functions after CI.

Cochlear implants are hearing prostheses that bypass defective sensory hair cells in the cochlea, allowing individuals with severe to profound SNHL to regain much of their hearing. Effects of CI on pediatric and adult vestibular receptors were discussed in researches before. Previous studies have shown that most patients experience vertigo symptoms and the canal and otolith function could be damaged after CI (19–23). In a previous study, vHIT revealed that 30% of patients demonstrated a post-operative change in vestibular function (24). However, few studies have investigated the vestibular function in children with CI. Most of these studies analyzed the caloric and cVEMP results in children and showed deteriorated HSC and saccular functions after CI (25–29). A few reports have studied oVEMP and vHIT tests in children with CI (28, 30, 31). It has been suggested that doctors should be aware of potential vestibular dysfunction in LVAS patients (9). Systematic studies of post-CI peripheral vestibular organ function in children with EVA have been rare.

In the present study, before CI, shorter P1 latencies, shorter N1 latencies, and higher amplitudes of oVEMP were found in LVAS children than in children with a normal cochlea. Taylor et al. (13) and Zhou et al. (12) found higher oVEMP amplitudes in patients with LVAS, similar to our present findings. However, another report showed no significant difference in oVEMP parameters in children with EVA (14). Higher cVEMP amplitudes have also been reported in children with EVA (12, 32, 33), which was in contrast to our findings. The reasons for the disparate findings among studies are unknown. The largest cVEMP amplitude in response to tone bursts occurred between 600 and 1,000 Hz, while the largest oVEMP amplitude in response to tone bursts was found at 500–1,000 Hz (34). A recent report demonstrated that cVEMP showed more disparities in parameters. Adult patients had more severe impairment of the vestibular apparatus with aging (14). Different ranges of frequencies are needed at different ages to evoke the best VEMP responses (35). Recently, some studies have shown that the observed modulation of oVEMP responses by increased intracranial pressure (ICP) is primarily due to the effect of an increased intralabyrinthine pressure on the stiffness of the inner ear contents and the middle ear-inner ear junction. Reduction in ICP by lumbar cerebrospinal fluid (CSF) drainage has a systemic effect on VEMP amplitudes. Increasing ICP systematically alters oVEMP in terms of absolute amplitudes and frequency tuning characteristics (36–39). In this report, in terms of differences in oVEMP parameters between children with EVA and those with a normal cochlea, we speculated that the presence of a third window in the inner ear labyrinth might allow for activation of vestibular receptors in LVAS patients (40). LVAS is regarded as a third-window lesion disease: this refers to an additional opening to the inner ear except for the first and second windows. A similar characteristic can be found in other third window diseases, such as SSC or PSC dehiscence (10). The sound energy could be shunted away from the cochlea to the vestibule, making the vestibular system organs more excitable and sensitive, leading to a shorter latency or higher amplitude. In this study, a stronger oVEMP response was demonstrated in children with EVA. This phenomenon implied that the utricular function might be more sensitive to sound in children with EVA than in those with a normal cochlea.

In this report, all children had normal otolith and canal functions before surgery. In LVAS children, the response rates of cVEMP and oVEMP decreased to 81.25 and 75.00% after CI. In children with a normal cochlea, the cVEMP and oVEMP response rates decreased to 43.75 and 37.50%, respectively. We found that otolith function was markedly affected after CI, particularly in children with a normal cochlea. Several studies have described the otolith organs as being the most frequent site of damage (41). Otolith sensors can be susceptible to surgical damage following electrode insertion, drilling, variation of the inner ear environment, or electrical stimulation related to CI. Significantly lower VEMP response rates were found in subjects with a normal cochlea. It seemed that otolith function was relatively less damaged after CI in children with EVA. A series of recent investigations have reported that the pressure within the cochlea may change during the insertion of CI electrodes (42–44). It has also been verified that the vestibular end organs are at risk to be injured by the pressure-related trauma during cochlear implant insertion (45). The pressure energy was confirmed to be propagated from the cochlea to the vestibular labyrinth in the absence of a third window (46). Based on our results, we hypothesized that the pressure change generated during the insertion of electrodes might be released through the EVA or released into the endolymph fluid in patients with EVA. Therefore, children with EVA might eventually protect against vestibular function loss due to cochlear implantation by equalizing the pressure inside the inner ear. However, decreased or absent VEMP responses may not necessarily reflect otolith dysfunctions. Furthermore, previous studies confirmed that the sensitivities to acoustic stimulation of the utricle and semicircular canal can be increased in the presence of a third window (47, 48). Since then, it was speculated that although the impairment of otolith function occurred, children with EVA were more sensitive to acoustic stimulation and had less change in VEMP results, as discussed aforementioned. It has been proposed that the air-bone gap (ABG) might adversely affect the air conduction stimulation (ACS) responses of VEMP (49). A study found that mechanical changes could lead to an ABG, which varied across patients, with an unclear mechanism (50). VEMPs were reported to be present in ears with ABG and LVAS (10). Hence, we considered that CI affected ABG in a different manner in children with EVA. Our data suggested that the post-CI otolith function in children with EVA might be less susceptible to ABG. The mechanism for the different performances between children with EVA and

children with a normal cochlea remains unknown and needs further in-depth research in the future.

A shorter P1 latency of cVEMP and lower amplitude of oVEMP were seen in children with EVA in this study. The decrease in oVEMP amplitude was consistent with a previous report of children with SNHL (31). We excluded 13 children with present VEMP preoperatively but absent VEMP postoperatively when comparing the parameters. Different surgical approaches and electrode arrays were used in them. Some studies failed to find a correlation between the post-operative vestibular symptoms and gender, implanted side, age, implant type, and the results of Caloric and VEMP test before (21, 26). The data on the relationship between VEMP response and different influence factors is currently lacking. We analyzed the influence of the surgical approach and electrode array on the changes in VEMP response but found no effect on the changes from pre- to post-operation in this study.

vHIT is a fast, practical, and non-invasive test used to evaluate all three semicircular canals. It uses a more physiological stimulus, testing higher frequencies (> 1 Hz), which is similar to the physiological stimuli of daily life (51). HSC VOR gain observed by vHIT was studied in a previous case report (52). In this study with the aid of vHIT, the VOR gains of all three semicircular canals were not statistically significantly different between groups. The post-operative response rates of all three semicircular canals were 100% in normal children. In children with EVA, there were no statistically significant response rate variations of any of the three semicircular canals from pre- to post-operation. However, HSC functions (two children), SSC function (one child), and PSC function (one child) were damaged in children with EVA after CI. Post-mortem temporal bone studies suggested that CI can cause structural damage to the inner ear, including the posterior labyrinth (53, 54). The HSC function might be easily influenced after surgery, as this is the explored part of the posterior labyrinth. The mechanism involving the function of all three semicircular canals in children is still being studied.

LIMITATIONS

When we compared the changes of parameters in VEMP from pre- to post-CI, we excluded 11 children in the Control Group and 2 children in the Study Group who demonstrated normal VEMP responses preoperatively but absent postoperatively. Therefore, the numbers of children were different between groups. We observed the changes in latency and amplitude in the two groups separately.

CONCLUSION

Our research findings further validated the value of VEMP and vHIT tests in the clinical application of vestibular evaluations in children. The utricular function was found to be more sensitive to sound in children with EVA. Although otolith function was affected, the overall damages to all three semicircular canals functions were slight after implantation. In contrast to subjects with a normal cochlea, the otolith sensor function was less seriously affected in children with EVA after CI surgery. Possible mechanisms include less pressure-related damage, less of an effect resulting from ABG, or more sensitivity to acoustic stimulation.

DATA AVAILABILITY STATEMENT

The raw data supporting the conclusions of this article will be made available by the authors, without undue reservation.

ETHICS STATEMENT

The studies involving human participants were reviewed and approved by the ethics committee of Shandong Provincial ENT Hospital. Written informed consent to participate in this study was provided by the participants' legal guardian/next of kin.

AUTHOR CONTRIBUTIONS

LX, HW, RW, and DZ contributed to the conception of the work. JL, XC, and ZF contributed to the experimental design. JX and XL selected data and performed the analysis. All authors contributed to the interpretation of the data and were involved in writing the manuscript.

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REFERENCES

1. Webb RL, Clark GM, Shepherd RK, Franz BK, Pyman BC. The biologic safety of the cochlear corporation multiple-electrode intracochlear implant. *Am J Otol.* (1988) 9:8–13.
2. Bigelow RT, Agrawal Y. Vestibular involvement in cognition: visuospatial ability, attention, executive function, and memory. *J Vestib Res.* (2015) 25:73–89. doi: 10.3233/VES-150544
3. Fina M, Skinner M, Goebel JA, Piccirillo JF, Neely JG, Black O. Vestibular dysfunction after cochlear implantation. *Otol Neurotol.* (2003) 24:234–42. doi: 10.1097/00129492-200303000-00018
4. Jackler RK, De La Cruz A. The large vestibular aqueduct syndrome. *Laryngoscope.* (1989) 99:1238–43. doi: 10.1288/00005537-198912000-00006
5. Mondini C. Anatomic surdi nati sectio. *De Bononiensi Scientarium et Artium Instituto atque Academia Commenarii.* (1791) 7:417.
6. Govaerts PJ, Casslman J, Daemers K, Caulaer GD, Somers T, Offeciers FE. Audiological findings in large vestibular aqueduct syndrome. *Int J Pediatr. Otorhinolaryngol.* (1999) 51:157–64. doi: 10.1016/S0165-5876(99)00268-2
7. Hall AC, Kenway B, Sanli H, Birman CS. Cochlear implant outcomes in large vestibular aqueduct syndrome-should we provide cochlear implant earlier? *Otol Neurotol.* (2019) 40:e769–73. doi: 10.1097/MAO.0000000000002314

8. Valvassori GE, Clemis JD. The large vestibular aqueduct syndrome. *Laryngoscope.* (1978) 88:723–8. doi: 10.1002/lary.1978.88.5.723
9. Zalewski CK, Chien WW, King KA, Muskett JA, Baron RE, Butman JA, et al. Vestibular dysfunction in patients with enlarged vestibular aqueduct. *Otolaryngol Head Neck Surg.* (2015) 153:257–62. doi: 10.1177/0194599815585098
10. Sheykholeslami K, Schmerber S, Habiby Kermany M, Kaga K. Vestibular-evoked myogenic potentials in three patients with large vestibular aqueduct syndrome. *Hear Res.* (2004) 190:161–8. doi: 10.1016/S0378-5955(04)00018-8
11. Hansel T, Gauger U, Bernhard N, Behzadi N, Ventrura MEO, Hofmann V, et al. Meta-analysis of subjective complaints of vertigo and vestibular tests after cochlear implantation. *Laryngoscope.* (2018) 128:2110–23. doi: 10.1002/lary.27071
12. Zhou YJ, Wu YZ, Cong N, Yu J, Gu J, Wang J, et al. Contrasting results of tests of peripheral vestibular function in patients with bilateral large vestibular aqueduct syndrome. *Clin Neurophysiol.* (2017) 128:1513–8. doi: 10.1016/j.clinph.2017.05.016
13. Taylor RL, Bradshaw AP, Magnussen JS, Gibson WP, Halmagyi GM, Welgampola MS. Augmented ocular vestibular evoked myogenic potentials to air-conducted sound in large vestibular aqueduct syndrome. *Ear and Hearing.* (2012) 33:768–71. doi: 10.1097/AUD.0b013e31825ce613
14. Zhang Y, Chen ZC, Zhang YZ, Hu J, Wang JL, Xu M, et al. Vestibular-evoked myogenic potentials in patients with large vestibular aqueduct. *Acta Oto-laryngoligia.* (2020) 140:40–5. doi: 10.1080/00016489.2019.1687937
15. Curthoys IS, Iwasaki S, Chihara Y, Ushio M, McGarvie LA, Burgess AM. The ocular vestibular-evoked myogenic potential to air-conducted sound probable superior vestibular nerve origin. *Clin Neurophysiol.* (2011) 122:611–6. doi: 10.1016/j.clinph.2010.07.018
16. Verbecque E, Marijnissen T, De Belder N, Van Rampaey V, Boudewyns A, van de Heyning P, et al. Vestibular (dys) function in children with sensorineural hearing loss: a systematic review. *Int J Audiol.* (2017) 56:361–8. doi: 10.1080/14992027.2017.1281444
17. Zhang DG, Lv YF, Han YC, Li YW, Li XF, Jing W, et al. Long-term outcomes of triple semicircular canal plugging for the treatment if intractable Meniere's disease: a single center experience of 361 cases. *Journal of vestibular research.* (2019) 29:315–22. doi: 10.3233/VES-190682
18. Sichnarek J, Mrazkova E, Zathurecky E, Tomaskova H. Comparing results from vestibular caloric stimulation and vHIT from a specialised outpatient clinic. *Int Tinnitus J.* (2019) 23:1–5. doi: 10.5935/0946-5448.20190001
19. Louza J, Mertes L, Braun, Gurkov R, Krause E. Influence of insertion depth in cochlear implantation on vertigo symptoms and vestibular function. *Am J Otolaryngol.* (2015) 36:254–8. doi: 10.1016/j.amjoto.2014.11.007
20. Colin V, Bertholon P, Karkas A. Impact of cochlear implantation on peripheral vestibular function in adults. *Eur Annals Otorhinolaryngol Head Neck Dis.* (2018) 135:417–20. doi: 10.1016/j.anorl.2018.10.007
21. Chen XL, Chen XH, Zhang F, Qin ZB. Influence of cochlear implantation on vestibular function. *Acta Oto-Laryngol.* (2016) 136:655–9. doi: 10.3109/00016489.2016.1154186
22. Krause E, Louza JP, Wechtenbruch J, Gorkov R. Influence of cochlear implantation on peripheral vestibular receptor function. *Otolaryngol Head Neck Surg.* (2010) 142:809–13. doi: 10.1016/j.otohns.2010.01.017
23. Dagkiran M, Tuncer U, Surmelioglu O, Tarkan O, Ozdemir S, Cetik F et al. How dose cochlear implantation affect five vestibular end-organ functions and dizziness? *Auris Nasus Larynx.* (2019) 46:178–85. doi: 10.1016/j.anl.2018.07.004
24. Batuecas-Caletrio A, Klumpp M, Santacruz-Ruiz S, Gonzalez FB, Sanchez EG, Arriage M. Vestibular function in cochlear implantation: correlating objectiveness and subjectiveness. *Laryngoscope.* (2015) 125:2371–5. doi: 10.1002/lary.25299
25. Jin Y, Nakamura M, Shinjo Y, Kaga K. Vestibular-evoked myogenic potentials in cochlear implant children. *Acta Otolaryngol.* (2006) 126:164–9. doi: 10.1080/00016480500312562
26. Jacot E, Van Den Abbeele T, Debre HR, Wiener SR. Vestibular impairments pre- and post-cochlear implant in children. *Int J Pediatr Otorhinolaryngol.* (2009) 73:209–17. doi: 10.1016/j.ijporl.2008.10.024
27. Gupta A, Raj P. Compensated vestibular dysfunction post cochlear implantation in children with sensorineural hearing loss: a prospective study. *Indian J Otolaryngol Head Neck Surg.* (2018) 2:200–4. doi: 10.1007/s12070-017-1054-0
28. Ajalloueyan M, Saeedi M, Sadeqhi M, Zamiri Abdollahi F. The effects of cochlear implantation on vestibular function in 1-4 years old children. *Int J Pediatr Otorhinolaryngol.* (2017) 94:100–3. doi: 10.1016/j.ijporl.2017.01.019
29. Licameli G, Zhou G, Kenna MA. Disturbance of vestibular function attributable to cochlear implantation in children. *Laryngoscope.* (2009) 119:740–5. doi: 10.1002/lary.20121
30. Xu X, Zhang X, Zhang Q, Hu J, Chen Y, Xu M. Ocular and cervical vestibular-evoked myogenic potentials in children with cochlear implant. *Clin Neurophysiol.* (2015) 126:1624–31. doi: 10.1016/j.clinph.2014.10.216
31. Li X, Gong S. The effect of cochlear implantation on vestibular evoked myogenic potential in children. *Laryngoscope.* (2020) 130:e918–25. doi: 10.1002/lary.28520
32. Liu XH, Ren LL, Li JN, Ji F, Liu XJ, Du Y, et al. Air and bone-conducted vestibular evoked myogenic potentials in children with large vestibular aqueduct. *Acta Oto-laryngol.* (2021) 141:50–6. doi: 10.1080/00016489.2020.1815836
33. Zhou GW Gopen Q. Characteristics of vestibular evoked myogenic potentials in children with large vestibular aqueduct. *Laryngoscope.* (2011) 121:220–5. doi: 10.1002/lary.21184
34. Park HJ, Lee IS, Shin JE, Lee YJ, Park MS. Frequency-tuning characteristics of cervical and ocular vestibular evoked myogenic potentials induced by air-conducted tone bursts. *Clin Neurophysiol.* (2010) 121:85–9. doi: 10.1016/j.clinph.2009.10.003
35. Piker EG, Jccobson GP, Burkard RF, McCaslin DL, Hood LJ. Effects of age on the tuning of the cVEMP and oVEMP. *Ear Hear.* (2013) 34:e65–73. doi: 10.1097/AUD.0b013e31828fc9f2
36. Gurkov R, Wittwer L, Speierer G, Müri R, Mantokoudis G, Kalla R. Idiopathic intracranial hypertension: ocular vestibular evoked myogenic potentials as a new evaluation tool. *Clin Neurophysiol.* (2017) 128:2048–9. doi: 10.1016/j.clinph.2017.07.415
37. Gurkov R, Speierer G, Wittwer L, Muri R, Kalla R. Differential effect of elevated intralabyrinthine pressure on ocular vestibular evoked myogenic potentials elicited by air conducted sound and bone conducted vibration. *Clin Neurophysiol.* (2016) 127:2115–8. doi: 10.1016/j.clinph.2015.12.019
38. Gurkov R, Speierer G, Wittwer L, Kalla R. Effect of elevated intracranial pressure on amplitudes and frequency tuning of ocular vestibular evoked myogenic potentials elicited by bone-conducted vibration. *Ear Hear.* (2016) 37:e409–13. doi: 10.1097/AUD.0000000000000326
39. G. Jerin C, Wakili R, Kalla R, Gurkov R. Effect of increasing intracranial pressure on vestibular-evoked myogenic potential frequency tuning. *Ear Hear.* (2015) 36:336–41. doi: 10.1097/AUD.0000000000000190
40. Govender S, Fernando T, Dennis DL, Welgampola MS, Colebatch JG. Properties of 500 Hz air- and bone-conducted vestibular evoked myogenic potentials (VEMPs) in superior canal dehiscence. *Clin Neurophysiol.* (2016) 127:2522–31. doi: 10.1016/j.clinph.2016.02.019
41. Yong M, Young E, Lea J, Foggin H, Zaia E, Kozak FE, et al. Subjective and objective vestibular changes that occur following paediatric cochlear implantation: systematic review and meta-analysis. *J Otolaryngol Head Neck Surg.* (2019) 48:22. doi: 10.1186/s40463-019-0341-z
42. Greene NT, Mattingly JK, Banakis Hartl RM, Tollin DJ, Cass SP. Intracochlear pressure transients during cochlear implant electrode insertion. *Otol Neurotol.* (2016) 37:1541–8. doi: 10.1097/MAO.0000000000001232
43. Mittmann M, Ernst A, Mittmann P, Todt I. Insertional depthdependent intracochlear pressure changes in a model of cochlear implantation. *Acta Otolaryngol.* (2017) 137:113–8. doi: 10.1080/00016489.2016.1219918
44. Mittmann P, Mittmann M, Ernst A, Todt I. Intracochlear pressure changes due to 2 electrode types: an artificial model experiment. *Otolaryngol Head Neck Surg.* (2017) 156:712–6. doi: 10.1177/0194599816684104
45. Banakis Hartl RM, Greene NT, Jenkins HA, Cass SP, Tollin DJ. Lateral semicircular canal pressure during cochlear implant electrode insertion: a possible mechanism for post-operative vestibular loss. *Otol Neurotol.* (2018) 39:755–64. doi: 10.1097/MAO.0000000000001807
46. Maxwell AK, Banakis Hartl RM, Greene NT, Benichoux V, Mattingly JK, Cass SP, et al. Semicircular canal pressure changes during high-intensity acoustic stimulation. *Otol Neurotol.* (2017) 38:1043–51. doi: 10.1097/MAO.0000000000001456

47. Halmagyi GM, Curthoys IS, Colebatch JG, Aw ST. Vestibular responses to sound. *Ann NY Acad Sci.* (2005) 1039:54–67. doi: 10.1196/annals.1325.006
48. Minor LB. Superior canal dehiscence syndrome. *Am J Otol.* (2000) 21:9–19. doi: 10.1016/S0196-0709(00)80068-X
49. Hartl RMB, Mattingly JK, Greene NT, Jenkins HA, Cass SP, Tollin DJ. A preliminary investigation of the air-bone gap: changes in intracochlear sound pressure with air- and bone-conducted stimuli after cochlear implantation. *Otol Neurotol.* (2016) 37:1291–9. doi: 10.1097/MAO.0000000000001184
50. Merchant GR, Schulz KM, Patterson JN, Fitzpatrick D, Janky KL. Effect of cochlear implantation on vestibular evoked myogenic potentials and wideband acoustic immittance. *Ear Hear.* (2020) 41:1111–24. doi: 10.1097/AUD.0000000000000831
51. Zellhuber S, Mahringer A, Rambold HA. Relation of video-head-impulse test and caloric irrigation: a study on the recovery in unilateral vestibular neuritis. *Eur Arch Otorhinolaryngol.* (2014) 271:2375–83. doi: 10.1007/s00405-013-2723-6
52. Weber KP, Macdougall HG, Halmagyi GM, Curthoys IS. Impulse testing of semicircular-canal function using video-oculography. *Ann NY Acad of Sci.* (2009) 1164:486–91. doi: 10.1111/j.1749-6632.2008.03730.x
53. Tien HC, Linthicum FH Jr. Histopathologic changes in the vestibule after cochlear implantation. *Otolaryngol Head Neck Surg.* (2002) 127:260–4. doi: 10.1067/mhn.2002.128555
54. Handzel O, Burgess BJ, Nadol JB. Histopathology of the peripheral vestibular system after cochlear implantation in the human. *Otol Neurotol.* (2006) 27:57–64. doi: 10.1097/01.mao.0000188658.36327.8f

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Vestibular Preservation After Cochlear Implantation Using the Round Window Approach

Keita Tsukada[1] *and Shin-ichi Usami*[1,2]*

[1] *Department of Otolaryngology, Shinshu University School of Medicine, Matsumoto, Japan,* [2] *Department of Hearing Implant Sciences, Shinshu University School of Medicine, Matsumoto, Japan*

Background: The development of less traumatic surgical techniques, such as the round window approach (RWA), as well as the use of flexible electrodes and post-operative steroid administration have enabled the preservation of residual hearing after cochlear implantation (CI) surgery. However, consideration must still be given to the complications that can accompany CI. One such potential complication is the impairment of vestibular function with resulting vertigo symptoms. The aim of our current study was to examine the changes in vestibular function after implantation in patients who received CI using less traumatic surgery, particularly the RWA technique.

Methods: Sixty-six patients who received CI in our center were examined by caloric testing, cervical vestibular evoked myogenic potential (cVEMP) and ocular VEMP (oVEMP) before or after implantation, or both, to obtain data on semicircular canal, saccular and utricular function, respectively. Less traumatic CI surgery was performed by the use of the RWA and insertion of flexible electrodes such as MED-EL FLEX soft, FLEX 28, and FLEX 24 (Innsbruck, Austria).

Results: Caloric response and the asymmetry ratio of cVEMP and oVEMP were examined before and after implantation using less traumatic surgical techniques. Compared with before implantation, 93.9, 82.4, and 92.5% of the patients showed preserved vestibular function after implantation based on caloric testing, cVEMP and oVEMP results, respectively. We also examined the results for vestibular function by a comparison of the 66 patients using the RWA and flexible electrodes, and 17 patients who underwent cochleostomy and insertion of conventional or hard electrodes. We measured responses using caloric testing, cVEMP and oVEMP in patients after CI. There were no differences in the frequencies of abnormal caloric and oVEMP results in the implanted ears between the RWA and cochleostomy. On the other hand, the frequency of abnormal cVEMP responses in the implanted ears in the patients who received implantation by cochleostomy was significantly higher than that in the patients undergoing surgery using the RWA.

Conclusion: Patients receiving CI using less traumatic surgical techniques such as RWA and flexible electrodes have reduced risk of damage to vestibular function.

Keywords: cochlear implant, vestibular function, round window approach, caloric testing, cVEMP, oVEMP

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***Correspondence:**
Shin-ichi Usami
usami@shinshu-u.ac.jp

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INTRODUCTION

Recently, the development of techniques such as less traumatic surgery has enabled the preservation of residual hearing and of cochlear structures after cochlear implantation (CI) surgery (1, 2). These techniques include the use of flexible electrodes (3, 4), the round window approach (RWA) (5) and steroid administration. However, consideration must still be given to the non-hearing vestibular complications that can accompany CI, resulting in balance symptoms. The incidence of vestibular symptoms, as reported previously, varies quite widely from 0.33 to 75% (6).

While there have been numerous reports evaluating the effects of CI on vestibular function, there have been few reports examining the post-operative effects of the use of a less traumatic surgical technique on vestibular function. Our previous preliminary report showed that a less traumatic technique involving the RWA is preferable from the viewpoint of vestibular preservation (7).

The aim of this study was to evaluate vestibular function before and after implantation by use of less traumatic surgical techniques, and whether such surgical techniques, particularly the RWA, result in less trauma to the vestibular end organs.

MATERIALS AND METHODS

Patients

A total of 66 patients (21 males and 45 females) who underwent unilateral CI surgery in our center between 2009 and 2019 were included in this study after obtaining informed written consent. The 66 patients included part of the study population for whom the results of vestibular function were previously published in 2013 (8). The age at CI surgery ranged from 7 to 70 years, with a mean age of 46.6 ± 18.3 years. Twenty-five patients received implants in the right ear and forty-one in the left ear.

To preserve hearing and/or inner ear structures, we used less traumatic techniques for these patients. The less traumatic surgeries were performed by the use of flexible electrodes such as MED-EL FLEX 24™ and FLEX 28™ or FLEX soft™ electrodes (Innsbruck, Austria). The FLEX 24 electrode was implanted in 24 patients, FLEX 28 in 38, and FLEX soft in 5 patients. The full insertion of electrodes was achieved in all patients. All surgeries involving the RWA were performed by a single surgeon (S.U). With regard to steroids, systemic steroid administration was applied in patients receiving electric acoustic stimulation (EAS) using FLEX24 (2). However, steroids were not routinely used for conventional CI.

In this study, hearing thresholds, assessed by pure-tone audiometry (PTA), were measured pre- and at 6 months to 1 year post-operatively. The hearing levels were calculated by the average hearing levels (HL) at 500, 1,000, and 2,000 Hz, and the average low-frequency hearing thresholds of 125, 250, and 500 Hz (LFA) were also calculated.

The final position of the implanted electrode array was assessed by X-ray images of the horizontal plane of the cochlear basal turn obtained using the modified Stenver's view. We measured the insertion depth angel (IDA) based on the method for the determination of insertion depth described by Trieger et al. (9).

To compare surgical techniques, we also evaluated post-operative vestibular function in 17 age-matched patients (mean age: 41.6 ± 21.1, six males and eleven females) who underwent cochleostomy between 2001 and 2009. These patients had MED-EL standard™, CI24M™ or CI24R(CS)™ (Sydney, Australia) electrodes inserted.

Vestibular Testing

The patients underwent caloric testing, cervical vestibular evoked myogenic potential (cVEMP), and ocular VEMP (oVEMP) both before or at 6 months−1 year after CI surgery, or both, to obtain data on semicircular canal function, saccular function and utricular function, respectively.

With regard to cVEMP testing, electromyography (EMG) was performed using a pair of surface electrodes mounted on the upper half and the sternal head of the sternocleidomastoid (SCM) muscle. The electrographic signal was recorded using a Neuropack evoked potential recorder (Nihon Kohden Co. Ltd., Tokyo, Japan). The method was described in detail in our previous report (8). The amplitude between the 13 ms positive peak and the 23 ms peak, and the background integrated EMG were measured, and the correction of the amplitude was calculated as follows (10):

Corrected amplitude = amplitude of the averaged unrectified EMG (micro V)/background integrated EMG (micro V)

oVEMP testing was measured by bone-conductive vibration (BCV). BCV was delivered in 4 ms tone bursts of 500 Hz vibration (rise/fall time = 1 ms and plateau time = 2 ms) by a hand-held 4810 mini-shaker (Bruel and Kjaer, Naerum, Denmark), which was placed on the forehead midline (Fz). The active electrode was located over the inferior orbital margin and a reference electrode was placed 2 cm below the active electrode. The ground electrode was placed on the chin. The patients lay in a supine position on the bed and looked up with head raised at ∼30 degrees above straight-ahead during recording. The signals were amplified and bandpass filtered between 20 and 2,000 Hz. The stimulus intensity was 115 dB force level for 500 Hz, with an analysis time of 40 ms, and 50 responses were averaged for each run. For oVEMP, the amplitude was defined as the difference between the 10 ms negative peak (n10) and the 15 ms positive peak (p15).

The cVEMP and oVEMP asymmetry ratio was calculated as follows:

*asymmetry ratio (AR) = (amplitude of CI side – amplitude of non-CI side)*100/(amplitude of CI side + amplitude of non-CI side).*

In this study, an asymmetry ratio of below −30% was defined as a decreased reaction on the CI side, that of over 30% as a decreased reaction on the non-CI side, and no reaction in amplitude bilaterally as bilaterally absent.

With regard to the caloric testing, the maximum slow phase velocity (mSPV) was measured by cold water irrigation (20°C, 5 ml, 20 s) (8) and was calculated as the percentage of canal paresis (CP%):

*CP% = (mSPV of CI side – mSPV of non-CI side) * 100/(mSPV of CI side + mSPV of non-CI side).*

We defined a CP% of below −25% as canal paresis (CP) on the CI side, over 25% as CP on the non-CI side, and below 10 deg/s of mSPV bilaterally as bilateral CP.

Statistical Analysis

For all analyses, IBM SPSS version 26 for Windows software (Chicago, IL, USA) was used and the Wilcoxon signed-rank test applied when comparing differences between pre-operative and post-operative CP% for caloric testing or between pre- and post-operative AR for cVEMP and oVEMP. The Fisher's exact test was applied when comparing the frequencies of vestibular dysfunction and electrode length. The Mann-Whitney U-test was applied when comparing the frequencies of vestibular function and age, pre- and post-operative HL and LFA, and IDA. Statistical significance was set at $p < 0.05$.

RESULTS

Vestibular Function Before CI Surgery

A summary of pre-operative vestibular function is shown in **Table 1**, and detailed data for each subject are shown in **Supplementary Table 1**.

Sixty-five patients were evaluated by caloric testing before CI surgery. Twenty of the 65 patients (30.8%) showed canal paresis (CP) on caloric testing, 5 patients had bilateral CP, 9 had CP on the CI side only, and 6 had CP on the non-CI side only. In the pre-operative cVEMP, 25 of the 66 patients (37.9%) had no response or decreased reaction bilaterally or unilaterally; 12 patients bilaterally, 8 patients on the CI-side, and five patients on the non-CI side. Sixteen of 48 patients (33.3%) who were evaluated pre-operatively by oVEMP showed absent or decreased reaction; seven patients on the CI side, two patients on the non-CI side, and the other seven patients bilaterally. With regard to vestibular symptoms before CI surgery, 7 of 45 (15.6%) patients with normal reactions and 10 of 20 (50.0%) patients with abnormal reactions on caloric testing had experienced some vestibular symptoms in the past. Seven of 41 (17.1%) patients with normal reactions and 10 of 25 (40.0%) with abnormal reactions on cVEMP, and 8 of 32 (25.0%) with normal reactions and 7 of 16 (43.8%) with abnormal reactions on oVEMP also had some vestibular symptoms before CI surgery. Although there was no significantly difference in vestibular symptoms between patients with normal and those with abnormal reactions on oVEMP ($p = 0.21$), the patients with abnormal reactions complained of significantly greater vestibular symptoms than did the patients with normal reactions on pre-operative caloric testing ($p = 0.006$) and cVEMP ($p = 0.048$). For the pre-operative caloric testing and oVEMP results, no significant differences between normal and abnormal reactions for sex, age, pre-operative mean HL, or pre-operative mean LFA were observed (**Table 1**). There were significant differences in the pre-operative cVEMP results between normal and abnormal reactions for age ($p = 0.002$) and pre-operative mean LFA ($p = 0.005$).

Vestibular Preservation After CI Surgery

A summary of vestibular preservation is shown in **Table 2** and detailed data for each subject are shown in **Supplementary Table 1**.

All of the patients who underwent vestibular testing both before and after CI surgery had received CI by the RWA method and had had a FLEX 24, FLEX 28 or FLEX soft electrode inserted. We excluded the patients showing bilateral absent or unilateral absent reactions on the CI side before CI surgery. In this study, a post-operative CP% on caloric testing and AR on the cVEMP and oVEMP of 30% or more lower than the pre-operative results were defined as a decreased post-operative response.

Caloric testing was performed before and after CI surgery in 49 patients. **Figure 1A** shows caloric responses before and after implantation. The pre-operative and post-operative CP% values were 2.09 ± 19.6 and 1.00 ± 23.0, respectively. There were no significant differences between caloric responses before and after implantation on caloric testing ($p = 0.76$). Compared with before implantation, the results after implantation were unchanged in 46 of 49 patients (93.9%) who underwent both pre- and post-operative testing. In the other 3 patients, the post-operative CP% was 30% or more lower than the pre-operative value.

Sixty-six patients underwent cVEMP before and after CI surgery, and we excluded 15 patients showing bilateral absent or unilateral absent reactions on the CI side before surgery. Thus, the AR values for cVEMP were compared before and after CI surgery for 51 patients (**Figure 1B**). The mean AR was 3.36 (SD = 34.7) pre-operatively and −4.56 (SD = 35.6) post-operatively. The post-operative AR was significantly lower than the pre-operative value on the cVEMP testing ($p = 0.029$). Forty-two of the 51 patients (82.4%) showed unchanged reactions before and after CI surgery. The other 9 patients showed decreased reactions; 8 patients showed a 30% or more reduction in AR, and the remaining patient, who had unilateral absent reaction on the non-CI side and a normal reaction on the CI side before surgery, changed to an absent reaction on the CI side, resulting in bilateral absent reaction after CI surgery.

A comparison of pre- and post-operative oVEMP results is shown in **Figure 1C**. Among the 48 patients who underwent oVEMP both pre- and post-operatively, we evaluated 40 patients (excluding 8 patients who had bilateral or unilateral absent reactions on the CI side before CI surgery). The pre- and post-operative AR on oVEMP was −3.60 (SD 21.5) and −6.24 (SD 26.4), respectively, and there were no significant differences observed ($p = 0.64$). Although 3 patients showed an AR reaction of 30% or more lower post-operatively when compared with the pre-operative AR, 37 of the 40 patients (92.7%) showed no change in reaction between the pre- and post-operative AR values.

Gender, implanted side, age at CI surgery, vestibular symptoms after CI surgery, and pre- and post-operative HL and LFA were compared between patients with and without preservation of vestibular function, but there were no significant differences in the results for caloric testing, cVEMP or oVEMP (**Table 2**). We compared results between those fitted with a shorter electrode (FLEX 24:24 mm) and those fitted with longer electrodes (FLEX 28:28 mm or FLEX soft:31.5 mm), but again no

TABLE 1 | Summary of vestibular function before CI surgery.

	Caloric testing			cVEMP			oVEMP		
	Normal	**Abnormal**	***p*-value**	**Normal**	**Abnormal**	***p*-value**	**Normal**	**Abnormal**	***p*-value**
***n* (%)**	**45 (69.2)**	**20 (30.8)**		**41 (62.1)**	**25 (37.9)**		**32 (66.7)**	**16 (33.3)**	
Sex (male/female)	17/28	4/16	$p = 0.25$	13/28	8/17	$p = 1.00$	11/21	4/12	$p = 0.74$
Median age at implant	50 ± 18.4	54 ± 16.4	$p = 0.23$	45 ± 19.9	57 ± 9.7	$p = 0.002$	43 ± 21.1	55 ± 18.1	$p = 0.19$
Vestibular symptoms before CI (+/–)	7/38	10/10	$p = 0.006$	7/34	10/15	$p = 0.048$	8/24	7/16	$p = 0.21$
Pre-operative median HL (dB)	95.0 ± 9.6	91.3 ± 13.6	$p = 0.21$	91.3 ± 12.8	95.0 ± 11.7	$p = 0.059$	93.2 ± 10.6	95.0 ± 8.7	$p = 0.37$
Pre-operative median LFA (dB)	61.6 ± 26.1	71.6 ± 20.5	$p = 0.19$	55 ± 24.7	90 ± 20.8	$p = 0.005$	71.1 ± 25.1	85.0 ± 16.7	$p = 0.28$

HL, average thresholds of 500, 1,000, 2,000 Hz; LFA, average low-frequency hearing thresholds of 125, 250, and 500 Hz.
+, with vestibular symptoms; –, without vestibular symptoms.

TABLE 2 | The results of vestibular changes after CI surgery.

	Caloric testing			cVEMP			oVEMP		
	No change	**Decreased**	***p*-value**	**No change**	**Decreased**	***p*-value**	**No change**	**Decreased**	***p*-value**
***n* (%)**	**46 (93.9)**	**3 (6.1)**	–	**42 (82.4)**	**9 (17.6.)**	–	**37 (92.5)**	**3 (7.5)**	–
Sex (male/female)	16/30	0/3	$p = 0.54$	14/28	2/7	$p = 1.00$	11/26	2/1	$p = 0.24$
implanted side (R/L)	17/29	1/2	$p = 1.00$	11/31	5/4	$p = 0.12$	15/22	2/1	$p = 0.57$
Vestibular symptoms after CI (+/–)	8/38	1/2	$p = 0.46$	6/36	3/6	$p = 0.19$	8/29	0/3	$p = 1.00$
Median age at implant	51 ± 18.6	57 ± 20.78	$p = 0.95$	50 ± 18.7	36 ± 20.5	$p = 0.39$	52 ± 18.5	61 ± 6.7	$p = 0.35$
Pre-operative median HL (dB)	91.9 ± 13.9	100 ± 5.0	$p = 0.094$	90 ± 13.3	95 ± 13.3	$p = 0.096$	93.8 ± 10.5	87.5 ± 10.5	$p = 0.96$
Pre-operative median LFA (dB)	67.5 ± 25.3	76.6 ± 20.4	$p = 0.57$	54.2 ± 24.3	68.3 ± 26.2	$p = 0.47$	77.3 ± 24.6	90.0 ± 5.8	$p = 0.25$
Post-operative median HL (dB)	97.2 ± 9.5	105 ± 4.3	$p = 0.62$	96.9 ± 10.0	102 ± 3.8	$p = 0.15$	103.1 ± 7.4	105 ± 3.6	$p = 0.16$
Post-operative median LFA (dB)	83 ± 20.7	90 ± 9.5	$p = 0.25$	75.9 ± 20.3	86.6 ± 21.4	$p = 0.74$	90 ± 18.5	90 ± 0.0	$p = 0.45$
Electrodes (FLEX24/FLEX28 or soft)	18/28	1/2	$p = 1.00$	18/24	3/6	$p = 0.72$	9/28	0/3	$p = 1.00$
Median IDA (deg)	579.8 ± 78.7	657.9 ± 104.2	$p = 0.36$	564.1 ± 81.4	590.4 ± 95.9	$p = 0.89$	596.7 ± 82.2	603.3 ± 63.7	$p = 0.74$

HL, average thresholds of 500, 1,000, 2,000 Hz; LFA, average low-frequency hearing thresholds of 125, 250, and 500 Hz. IDA, insertion depth angle.
+, with vestibular symptoms; –, without vestibular symptoms.

significant differences were observed between them on caloric testing ($p = 1.00$), cVEMP ($p = 0.72$) or oVEMP ($p = 1.00$). IDA was also compared between patients with and without vestibular preservation. Median IDA was 579.8 ± 78.7 deg in patients with vestibular preservation on caloric testing and 657.9 ± 104.2 deg in patients without vestibular preservation. Further, median IDA was 564.1 ± 81.4 deg and 590.4 ± 95.2 deg in patients with and without vestibular preservation on cVEMP, and 596.7 ± 82.2 deg and 603.3 ± 63.7 deg in patients with and without vestibular preservation on oVEMP, respectively (**Table 2**). There was no difference in IDA between the two groups on caloric testing ($p = 0.36$), cVEMP ($p = 0.89$) or oVEMP ($p = 0.74$).

A Comparison Between RWA and Cochleostomy

As we could not evaluate pre-operative vestibular function in patients who underwent cochleostomy, we compared the post-operative vestibular function in 66 patients (mean age: 46.6 ± 18.3) who underwent CI with the RWA and 17 age-matched patients (mean age: 41.6 ± 21.1) who underwent cochleostomy. The detailed results for patients receiving cochleostomy are shown in **Supplementary Table 2**.

The post-operative results for vestibular function are shown in **Figure 2**. The frequencies of abnormal reactions on post-operative caloric testing on the CI side were 12.5% in the cochleostomy patients and 17.2% in the RWA patients (**Figure 2A**), and those on post-operative oVEMP were 11.8% in the cochleostomy patients and 11.1% in the RWA patients (**Figure 2C**). There were no significant differences in the frequencies of post-operative abnormal reactions on the CI side ($p = 1.00$ on caloric testing and oVEMP), the non-CI side ($p = 0.689$ for caloric testing, $p = 1.00$ for oVEMP), or bilaterally ($p = 0.061$, $p = 0.162$), or of bilateral normal reactions ($p = 0.577$, $p = 0.263$) between RWA patients and cochleostomy patients. On the other hand, the frequencies of decreased or absent cVEMP responses on the CI side in the RWA patients and cochleostomy cases were 18 and 47%, respectively. The frequency of abnormal post-operative cVEMP responses on the CI side in cochleostomy patients was significantly higher than that in RWA cases ($p = 0.023$), even though there were no differences in the frequency of decreased cVEMP responses on the non-CI side ($p = 0.63$) or of bilateral abnormal responses ($p = 0.74$) between the cochleostomy patients and RWA patients (**Figure 2B**).

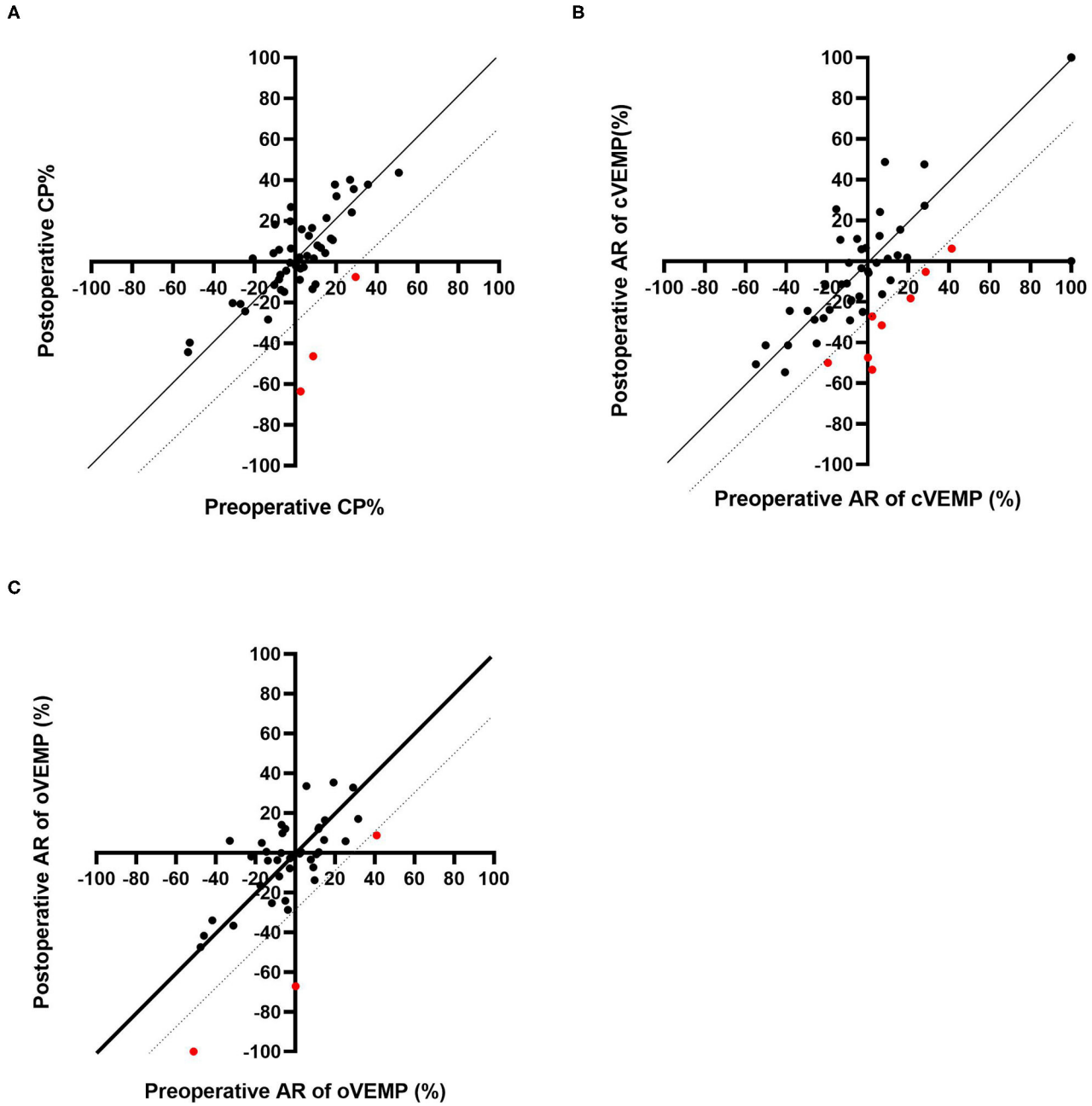

FIGURE 1 | Pre-operative and post-operative CP% based on caloric testing **(A)**. Pre-operative and post-operative AR based on cVEMP **(B)** and oVEMP **(C)**. The dotted line indicates the line where the post-operative result is 30% lower than that before CI. The red dots indicate the patients who showed decreased responses post-operatively.

DISCUSSION

Previous reports showed that the frequency of normal pre-operative vestibular function in patients who were candidates for CI was about 41–84% based on caloric testing (11–20), 35–89% based on cVEMP (12, 14–17, 19–23), and 50–71% based on oVEMP (19, 20, 23). In the present study, we found that the pre-operative frequencies of normal vestibular function in patients who received CI were 69.2, 62.1, and 66.7% for caloric testing (semicircular function), cVEMP (saccular function) and oVEMP (utricular function), respectively. Although the frequencies of normal responses showed some variations from those in previous studies, similar results were obtained in this study. We previously reported that patients who were candidates

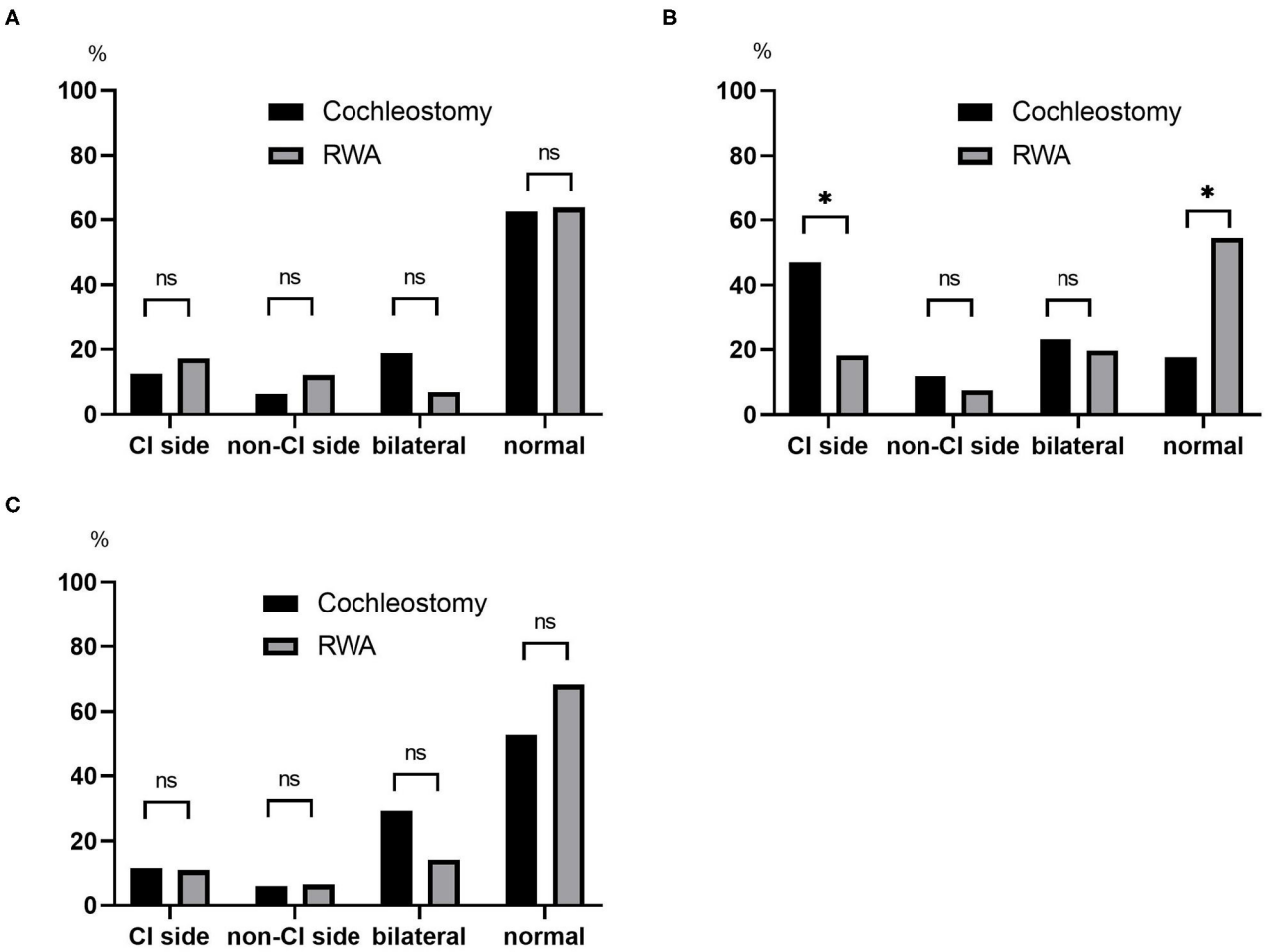

FIGURE 2 | The frequencies of post-operative abnormal results on the CI side, non-CI side, bilaterally absent and post-operative normal reactions based on **(A)** caloric testing, **(B)** cVEMP, **(C)** oVEMP were compared between the RWA and cochleostomy. The frequency of abnormal post-operative cVEMP responses on the CI side in cochleostomy patients was significantly higher than that in RWA patients ($p = 0.023$). ns, not significant; *$p < 0.05$.

for EAS had relatively good vestibular function before CI surgery (8). We also evaluated the relationship between residual hearing at low frequencies and vestibular function. Although no significant differences were shown on caloric testing or oVEMP, it was found that the greater the residual hearing, the more saccular function is preserved based on pre-operative cVEMP results. Thus, we have to pay attention to the preservation of vestibular function, particularly in patients with residual hearing.

In this study, to preserve vestibular function, less traumatic CI surgical techniques (the RWA with a flexible thin electrode) were performed, and the frequencies of post-operative preservation of semicircular function, saccular function and utricular function were 93.9, 82.4, and 92.5%, respectively.

Further, in this study, we are able to perform comprehensive vestibular testing (including semicircular function, saccular function and utricular function). There have been few previous reports to date on comprehensive vestibular function. Chen et al. reported that among the vestibular functions, the semicircular canal function was more frequently damaged (19). Sonsa et al. showed that the frequencies of post-operative damage to these three vestibular functions were almost equal (20). Our present study showed that saccular function was more frequently damaged post-operatively. A previous histopathological study also showed that the saccule was the most frequently damaged organ, followed by the utricle and semicircular canals (24). The saccule is anatomically and embryologically closer to the cochlea than is the utricle or semicircular canals (25). Cytologically, dark cells, which secrete potassium and create homeostasis in the endolymph, are present in the utricle and semicircular canal ampulla, but not in the saccule (26). It is proposed that saccular endolymph originates from the cochlea by longitudinal flow or diffusion and is not produced in this organ. Based on these anatomical, embryological, and cytological aspects, it is speculated that the saccule is more susceptible to environmental changes in the cochlea due to CI surgery than are the utricle and semicircular canals.

TABLE 3 | The frequencies of post-operative vestibular preservation in the literature.

Preservation rate % (*n*)			Surgical approach	References
Semicircular canal function	Saccular function	Utricular function		
66% (24)			Unknown	(27)
44% (66)			Unknown	(28)
77% (60)			Unknown	(29)
62% (8)			Cochleostomy	(11)
43% (14)			Cochleostomy	(30)
	0% (12)		Cochleostomy	(31)
68% (86)			cochleostomy	(32)
57% (21)	50% (16)		Cochleostomy	(12)
91% (27)	87% (23)		RWA	(12)
	0% (18)		Cochleostomy	(33)
42% (12)	50% (8)		Cochleostomy	(21)
68% (38)			Cochleostomy	(13)
	18% (17)		Cochleostomy	(22)
61% (89)	49% (89)		Cochleostomy	(34)
94% (16)	69% (16)		RWA	(14)
50% (16)	14% (14)		Cochleostomy	(16)
94% (17)	77% (11)		RWA	(15)
40% (20)	40% (20)		Unknown	(35)
	39% (26)	13% (22)	Cochleostomy	(23)
27% (30)	38% (29)		RWA	(36)
28% (22)	41% (22)		RWA	(17)
82% (17)	24% (17)		RWA	(18)
7% (29)	58% (22)	63% (19)	RWA	(19)
62% (21)	54% (26)		RWA	(37)
80% (10)	42% (12)		RWA	(38)
86% (10)	56% (9)		Cochleostomy	(38)
84% (55)	84% (55)	81% (55)	RWA	(20)
	88% (42)	95% (42)	RWA	(39)
79% (120)			RWA	(40)
89% (49)	84% (51)	91% (40)	RWA	This study

The previously reported frequencies of post-operative preservation of vestibular functions are shown in **Table 3**. Post-operative preservation was found in 7–94% based on caloric testing, 0–88% based on cVEMP, and 13–95% based on oVEMP. Our results showed relatively better preservation of post-operative vestibular functions compared with those of previous reports. When considering factors related to vestibular preservation, there were no significant differences between vestibular preservation for age at implant, implanted side, gender, and pre- and post-operative HL and LFA in the present study.

Thus, one of the reasons for such better outcomes is probably the surgical technique applied, such as the RWA and the use of flexible electrodes.

In our present study, the frequencies of post-operative abnormal reactions on caloric testing and oVEMP in the implanted ears did not significantly differ regardless of whether the patients received the RWA or cochleostomy. On the other hand, the frequency of abnormal post-operative cVEMP results in the implanted ears was significantly higher in the cochleostomy patients than in the RWA patients. Todt et al. reported that decreased function based on post-operative cVEMP was seen in 50% of patients who received cochleostomy and in 13% of those receiving the RWA, while abnormal post-operative caloric testing results were seen in 42.9 and 9.4% of cochleostomy and RWA patients, respectively (12). We also confirmed that the RWA is a preferable approach for the preservation of vestibular function (7, 8). We compared the frequencies of vestibular preservation between RWA and cochleostomy patients in the literature (**Figure 3**) (11–23, 27–40). The median preservation rates for RWA and cochleostomy patients were 81 and 61% based on caloric testing, and 63.5 and 39% based on cVEMP, respectively. Although there were few oVEMP results available, the preservation rates for RWA patients were better than those for cochleostomy patients in terms of vestibular function. These results suggested that the RWA results, including those from

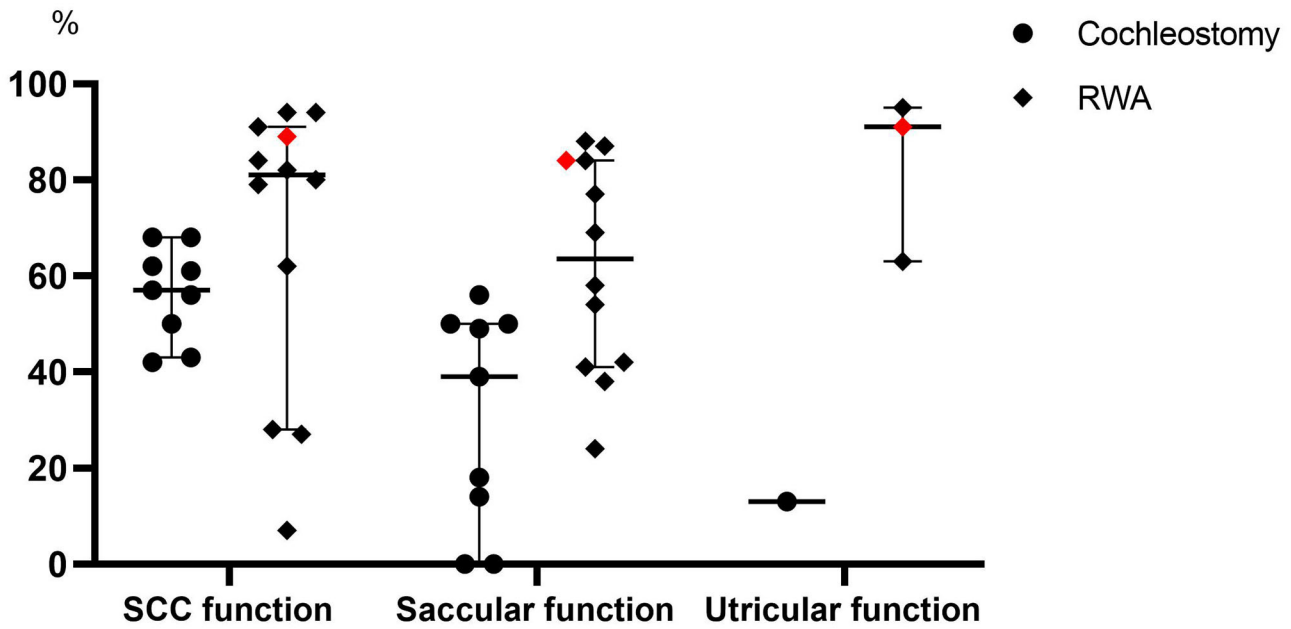

FIGURE 3 | A comparison of the frequencies of vestibular preservation between patients undergoing the RWA and cochleostomy in the literature. The red dots indicate the present results. SCC, Semicircular canal.

our study, indicated less trauma to post-operative vestibular function than did those for cochleostomy, particularly in terms of saccular function.

Ishiyama previously reported that a histopathological study showed secondary fibrosis and endolymphatic hydrops when the cochleostomy involves the scala vestibuli (SV) (41). Other temporal bone studies have also shown that electrode insertion into the SV involves damage to the vestibular receptors. However, when the electrode was inserted into the scala tympani (ST), no vestibular damage was found (24). When considering the results of histopathological studies of cochleostomy and the RWA, Ishiyama reported that cochleostomy was significantly associated with SV fibrosis and hydrops whereas round window insertion was not (41). Adunka evaluated CI electrode insertions through the round window membrane histologically and reported that smooth implantations via the round window membrane resulted in deep, atraumatic insertions into the ST, and unintentional lesions to the basilar membrane could be avoided by using the round window as an exact anatomical landmark that is always in direct continuity with the ST (42). These histological studies imply that one of the reasons for our worse results on cVEMP testing among cochleostomy cases may be the dislocation of electrodes.

Thus, the histopathological and clinical results in previous studies have shown that the RWA preserves vestibular functions to the greatest extent and, therefore, is superior to cochleostomy.

In our study, all the patients who underwent RWA had flexible electrodes such as FLEX soft, FLEX28, and FLEX24 inserted, whereas the patients who underwent cochleostomy mainly had conventional or hard, peri-modiolar electrodes [MED-EL standard, CI24M and CI24R (CS)] inserted. In most of the previous studies of vestibular preservation in CI surgery, the type of electrode used varied within each study to include hard electrodes, whereas our preservation study used only flexible electrodes. A previous review of electrode designs reported that hard, peri-modiolar electrodes had a higher incidence of translocation from the ST to the SV, and also showed that the insertion force of the electrodes was lower for flexible electrodes (35–55 mN) than for other electrodes (over 75 mN) (43). Histological study and dissection of human temporal bones performed by Adunka et al. (3) confirmed the atraumatic nature of flexible electrodes. Insertion forces with the conventional standard array and FLEX array were measured in an acrylic model of the ST, demonstrating that the insertion force could be reduced significantly by more than 40% with the FLEX electrode (3). This indicates that the flexible electrodes result in less trauma to the structure of the cochlea. One of the reasons of our better preservation results using the RWA than cochleostomy in the present study and other previous reports may be that the use of such less traumatic flexible electrodes reduces trauma not only to the cochlear but also to the vestibular receptors. Thus, the use of both RWA and a flexible electrode reduced the risk of damage to vestibular function.

In this study, we also evaluated the relationship between vestibular symptoms and vestibular function. Forty to 50% of the patients who complained of some vestibular symptoms before CI surgery had vestibular dysfunction pre-operatively. They had a significantly higher frequency of vestibular dysfunction compared to patients who had not complained of vestibular symptoms. However, there were no differences in post-operative vestibular symptoms between patients with and without vestibular preservation. Therefore, vestibular symptoms

are not due to operative trauma, but are due to the pre-operative pathology of the patients.

Regarding the electrode length and IDA, the preservation rates of post-operative semicircular canal function were 95 and 90% in the patients receiving FLEX 24 and FELX 28/FLEX soft electrodes, respectively. Meanwhile, 86% of patients receiving a FLEX 24 and 80% with a FLEX 28/soft, and 100% receiving a FLEX24 and 90% with a FLEX 28/soft showed preserved post-operative saccular or utricular functions, respectively, based on cVEMP and oVEMP results. We also evaluated the relationship between IDA and vestibular preservation. There were no significant differences in IDA between patients with and without vestibular preservation based on caloric testing, cVEMP and oVEMP. In our previous study (44), we reported that 17 of 18 (94.4%) patients who had residual hearing in the low frequencies retained low-frequency hearing when implanted with longer electrodes such as FLEX 28 and FLEX soft electrodes. There were no significant differences between the shorter and longer electrodes in these patients. Similarly, the cochlear function in the present results indicates that vestibular functions can be preserved even when applying longer electrodes or with deeper insertion using flexible electrodes. A previous report by Nordfald also showed that there was no significant differences in the residual hearing and vestibular function between the FLEX 28 and the FLEX soft electrodes based on caloric testing, cVEMP and SVH/SVV results (37). These results indicate that it is possible to preserve not only residual hearing but also vestibular function by use of a longer electrode. Although it cannot be excluded that cochleosotomy insertion using atraumatic electrodes will not produce the same result, preservation of vestibular function is not influenced by electrode length, but is thought to be due to the surgical technique used, such the RWA, and the use of flexible electrodes.

CONCLUSION

The above results indicate that less traumatic surgical techniques such as RWA and flexible electrodes can reduce the risk of damage to vestibular function. It is important to preserve not only hearing but also vestibular function by using such techniques. Further, there were no significant differences in the frequencies of vestibular dysfunction in terms of the length of the flexible electrodes used.

DATA AVAILABILITY STATEMENT

The raw data supporting the conclusions of this article will be made available by the authors, without undue reservation.

ETHICS STATEMENT

The studies involving human participants were reviewed and approved by Shinshu University Ethical Committee. Written informed consent to participate in this study was provided by the participants' legal guardian/next of kin.

AUTHOR CONTRIBUTIONS

KT designed the study, collected the data, performed data analysis, wrote the manuscript, created the figures, and performed the literature search. S-iU designed the study and revised the manuscript. All authors contributed to the article and approved the submitted version.

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SUPPLEMENTARY MATERIAL

The Supplementary Material for this article can be found online at: https://www.frontiersin.org/articles/10.3389/fneur.2021.656592/full#supplementary-material

REFERENCES

1. von Ilberg CA, Baumann U, Kiefer J, Tillein J, Adunka OF. Electric-acoustic stimulation of the auditory system: a review of the first decade. *Audiol Neurootol.* (2011) (16 Suppl. 2):1–30. doi: 10.1159/000327765
2. Usami S, Moteki H, Tsukada K, Miyagawa M, Nishio SY, Takumi Y, et al. Hearing preservation and clinical outcome of 32 consecutive electric acoustic stimulation (EAS) surgeries. *Acta Otolaryngol.* (2014) 134:717–27. doi: 10.3109/00016489.2014.894254
3. Adunka O, Kiefer J, Unkelbach MH, Lehnert T, Gstoettner W. Development and evaluation of an improved cochlear implant electrode design for electric acoustic stimulation. *Laryngoscope.* (2004) 114:1237–41. doi: 10.1097/00005537-200407000-00018
4. Baumgartner WD, Jappel A, Morera C, Gstottner W, Muller J, Kiefer J, et al. Outcomes in adults implanted with the FLEXsoft electrode. *Acta Otolaryngol.* (2007) 127:579–86. doi: 10.1080/00016480600987784
5. Skarzynski H, Lorens A, Piotrowska A, Anderson I. Preservation of low frequency hearing in partial deafness cochlear implantation (PDCI) using the round window surgical approach. *Acta Otolaryngol.* (2007) 127:41–8. doi: 10.1080/00016480500488917
6. Buchman CA, Joy J, Hodges A, Telischi FF, Balkany TJ. Vestibular effects of cochlear implantation. *Laryngoscope.* (2004) 114 (10 Pt 2 Suppl. 103):1–22. doi: 10.1097/00005537-200410001-00001
7. Usami S, Moteki H, Suzuki N, Fukuoka H, Miyagawa M, Nishio SY, et al. Achievement of hearing preservation in the presence of an electrode covering the residual hearing region. *Acta Otolaryngol.* (2011) 131:405–12. doi: 10.3109/00016489.2010.539266
8. Tsukada K, Moteki H, Fukuoka H, Iwasaki S, Usami S. Effects of EAS cochlear implantation surgery on vestibular function. *Acta Otolaryngol.* (2013) 133:1128–32. doi: 10.3109/00016489.2013.824110
9. Trieger A, Schulze A, Schneider M, Zahnert T, Murbe D. *In vivo* measurements of the insertion depth of cochlear implant arrays using

flat-panel volume computed tomography. *Otol Neurotol.* (2011) 32:152–7. doi: 10.1097/MAO.0b013e3181fcf04d
10. Shojaku H, Takemori S, Kobayashi K, Watanabe Y. Clinical usefulness of glycerol vestibular-evoked myogenic potentials: preliminary report. *Acta Otolaryngol Suppl.* (2001) 545:65–8. doi: 10.1080/000164801750388144
11. Vibert D, Hausler R, Kompis M, Vischer M. Vestibular function in patients with cochlear implantation. *Acta Otolaryngol Suppl.* (2001) 545:29–34. doi: 10.1080/000164801750388063
12. Todt I, Basta D, Ernst A. Does the surgical approach in cochlear implantation influence the occurrence of postoperative vertigo? *Otolaryngol Head Neck Surg.* (2008) 138:8–12. doi: 10.1016/j.otohns.2007.09.003
13. Krause E, Louza JP, Hempel JM, Wechtenbruch J, Rader T, Gurkov R. Effect of cochlear implantation on horizontal semicircular canal function. *Eur Arch Otorhinolaryngol.* (2009) 266:811–7. doi: 10.1007/s00405-008-0815-5
14. Melvin TA, Della Santina CC, Carey JP, Migliaccio AA. The effects of cochlear implantation on vestibular function. *Otol Neurotol.* (2009) 30:87–94. doi: 10.1097/MAO.0b013e31818d1cba
15. Wagner JH, Basta D, Wagner F, Seidl RO, Ernst A, Todt I. Vestibular and taste disorders after bilateral cochlear implantation. *Eur Arch Otorhinolaryngol.* (2010) 267:1849–54. doi: 10.1007/s00405-010-1320-1
16. Krause E, Louza JP, Wechtenbruch J, Gurkov R. Influence of cochlear implantation on peripheral vestibular receptor function. *Otolaryngol Head Neck Surg.* (2010) 142:809–13. doi: 10.1016/j.otohns.2010.01.017
17. Robard L, Hitier M, Lebas C, Moreau S. Vestibular function and cochlear implant. *Eur Arch Otorhinolaryngol.* (2015) 272:523–30. doi: 10.1007/s00405-014-3040-4
18. Meli A, Aud BM, Aud ST, Aud RG, Cristofari E. Vestibular function after cochlear implant surgery. *Cochlear Implants Int.* (2016) 17:151–7. doi: 10.1179/1754762815Y.0000000014
19. Chen X, Chen X, Zhang F, Qin Z. Influence of cochlear implantation on vestibular function. *Acta Otolaryngol.* (2016) 136:655–9. doi: 10.3109/00016489.2016.1154186
20. Sosna M, Tacikowska G, Pietrasik K, Skarzynski H, Lorens A, Skarzynski PH. Effect on vestibular function of cochlear implantation by partial deafness treatment-electro acoustic stimulation (PDT-EAS). *Eur Arch Otorhinolaryngol.* (2019) 276:1951–9. doi: 10.1007/s00405-019-05425-5
21. Krause E, Wechtenbruch J, Rader T, Gurkov R. Influence of cochlear implantation on sacculus function. *Otolaryngol Head Neck Surg.* (2009) 140:108–13. doi: 10.1016/j.otohns.2008.10.008
22. Licameli G, Zhou G, Kenna MA. Disturbance of vestibular function attributable to cochlear implantation in children. *Laryngoscope.* (2009) 119:740–5. doi: 10.1002/lary.20121
23. Xu XD, Zhang XT, Zhang Q, Hu J, Chen YF, Xu M. Ocular and cervical vestibular-evoked myogenic potentials in children with cochlear implant. *Clin Neurophysiol.* (2015) 126:1624–31. doi: 10.1016/j.clinph.2014.10.216
24. Tien HC, Linthicum FH, Jr. Histopathologic changes in the vestibule after cochlear implantation. *Otolaryngol Head Neck Surg.* (2002) 127:260–4. doi: 10.1067/mhn.2002.128555
25. Gulya AJ. Developmental anatomy of the temporal bone and skull base. In: Gulya AJM, Lloyd B, Poe, Dennis S, editor. *Glasscock-Shambaugh's Surgery of the Ear*. 6th ed. Shelton, CT: People's Medical Publishing House. (2010). p. 3–27.
26. Kimura RS. Distribution, structure, and function of dark cells in the vestibular labyrinth. *Ann Otol Rhinol Laryngol.* (1969) 78:542–61. doi: 10.1177/000348946907800311
27. Ito J. Influence of the multichannel cochlear implant on vestibular function. *Otolaryngol Head Neck Surg.* (1998) 118:900–2. doi: 10.1016/S0194-5998(98)70295-5
28. Fina M, Skinner M, Goebel JA, Piccirillo JF, Neely JG, Black O. Vestibular dysfunction after cochlear implantation. *Otol Neurotol.* (2003) 24:234–42. Discussion 42. doi: 10.1097/00129492-200303000-00018
29. Szirmai A, Ribari O, Repassy G. Air caloric computer system application in monitoring vestibular function changes after cochlear implantation. *Otolaryngol Head Neck Surg.* (2001) 125:631–4. doi: 10.1067/mhn.2001.120429
30. Filipo R, Patrizi M, La Gamma R, D'Elia C, La Rosa G, Barbara M. Vestibular impairment and cochlear implantation. *Acta Otolaryngol.* (2006) 126:1266–74. doi: 10.1080/00016480600678789
31. Jin Y, Nakamura M, Shinjo Y, Kaga K. Vestibular-evoked myogenic potentials in cochlear implant children. *Acta Otolaryngol.* (2006) 126:164–9. doi: 10.1080/00016480500312562
32. Enticott JC, Tari S, Koh SM, Dowell RC, O'Leary SJ. Cochlear implant and vestibular function. *Otol Neurotol.* (2006) 27:824–30. doi: 10.1097/01.mao.0000227903.47483.a6
33. Basta D, Todt I, Goepel F, Ernst A. Loss of saccular function after cochlear implantation: the diagnostic impact of intracochlear electrically elicited vestibular evoked myogenic potentials. *Audiol Neurootol.* (2008) 13:187–92. doi: 10.1159/000113509
34. Jacot E, Van Den Abbeele T, Debre HR, Wiener-Vacher SR. Vestibular impairments pre- and post-cochlear implant in children. *Int J Pediatr Otorhinolaryngol.* (2009) 73:209–17. doi: 10.1016/j.ijporl.2008.10.024
35. Katsiari E, Balatsouras DG, Sengas J, Riga M, Korres GS, Xenelis J. Influence of cochlear implantation on the vestibular function. *Eur Arch Otorhinolaryngol.* (2013) 270:489–95. doi: 10.1007/s00405-012-1950-6
36. Louza J, Mertes L, Braun T, Gurkov R, Krause E. Influence of insertion depth in cochlear implantation on vertigo symptoms and vestibular function. *Am J Otolaryngol.* (2015) 36:254–8. doi: 10.1016/j.amjoto.2014.11.007
37. Nordfalk KF, Rasmussen K, Hopp E, Bunne M, Silvola JT, Jablonski GE. Insertion Depth in Cochlear Implantation and Outcome in Residual Hearing and Vestibular Function. *Ear Hear.* (2016) 37:e129–37. doi: 10.1097/AUD.0000000000000241
38. Nordfalk KF, Rasmussen K, Bunne M, Jablonski GE. Deep round window insertion versus standard approach in cochlear implant surgery. *Eur Arch Otorhinolaryngol.* (2016) 273:43–50. doi: 10.1007/s00405-014-3451-2
39. Dagkiran M, Tuncer U, Surmelioglu O, Tarkan O, Ozdemir S, Cetik F, et al. How does cochlear implantation affect five vestibular end-organ functions and dizziness? *Auris Nasus Larynx.* (2019) 46:178–85. doi: 10.1016/j.anl.2018.07.004
40. Stuermer KJ, Kluenter HD, Lang-Roth R, Schwarz D, Huttenbrink KB, Anagiotos A. Preservation of vestibular function and residual hearing after round window cochlear implantation. *Otol Neurotol.* (2019) 40:878–82. doi: 10.1097/MAO.0000000000002257
41. Ishiyama A, Doherty J, Ishiyama G, Quesnel AM, Lopez I, Linthicum FH. Post hybrid cochlear implant hearing loss and endolymphatic hydrops. *Otol Neurotol.* (2016) 37:1516–21. doi: 10.1097/MAO.0000000000001199
42. Adunka O, Unkelbach MH, Mack M, Hambek M, Gstoettner W, Kiefer J. Cochlear implantation via the round window membrane minimizes trauma to cochlear structures: a histologically controlled insertion study. *Acta Otolaryngol.* (2004) 124:807–12. doi: 10.1080/00016480410018179
43. Dhanasingh A, Jolly C. An overview of cochlear implant electrode array designs. *Hear Res.* (2017) 356:93–103. doi: 10.1016/j.heares.2017.10.005
44. Moteki H, Nishio SY, Miyagawa M, Tsukada K, Noguchi Y, Usami SI. Feasibility of hearing preservation for residual hearing with longer cochlear implant electrodes. *Acta Otolaryngol.* (2018) 138:1080–5. doi: 10.1080/00016489.2018.1508888

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Vestibular Function in Children and Adults Before and After Unilateral or Sequential Bilateral Cochlear Implantation

Ruirui Guan, Yanqi Wang, Sasa Wu, Bo Zhang, Jingwu Sun, Xiaotao Guo* and Jiaqiang Sun**

Department of Otolaryngology Head and Neck Surgery, The First Affiliated Hospital of USTC, Division of Life Sciences and Medicine, University of Science and Technology of China, Hefei, China

Background: Cochlear implantation (CI) helps patients with severe or profound sensorineural hearing loss (SNHL) restore hearing and speech abilities. However, some patients exhibit abnormal vestibular functions with symptoms such as dizziness or balance disorders, after CI. Whether age at CI and CI approach (unilateral or sequential bilateral) affect vestibular functions in users with cochlear implants remains unclear.

Objectives: To investigate the vestibular functions in children and adults before and after unilateral or sequential bilateral CI.

Materials and Methods: Thirty-seven patients with severe or profound SNHL who were candidates for a first- or second-side CI were divided into three groups: first-side CI-implanted adults (≥18 years), first-side CI-implanted children (6–17 years), and second-side CI-implanted children (6–17 years). All cases were implanted with the round window approach to minimize damage to the intra-cochlear structures. The caloric test, vestibular evoked myogenic potential (VEMP) test, video head impulse test (vHIT), Dizziness Handicap Inventory (DHI), Pediatric Vestibular Symptom Questionnaire (PVSQ), and audiometric tests were performed before and 1 month after CI.

Results: The abnormal rates of caloric test and VEMP test after CI in the first-side CI-implanted adults and children significantly increased compared with those before CI. The pre-implantation VEMP test showed significantly higher abnormal rates between first- and second-side CI-implanted children. No other significant differences of abnormal rates between first- and second-side CI-implanted children or between first-side CI-implanted adults and children were found. In second-side CI-implanted children, PVSQ scores significantly increased at day 3 post-implantation but decreased at day 30.

Conclusion: CI has a negative effect on the results of caloric and VEMP tests, but not on vHIT, indicating that the otolith and low-frequency semicircular canal (SCC) are more vulnerable to damage from CI. The alterations of vestibular functions resulting from CI surgery may be independent of age at CI and CI approach (unilateral or sequential bilateral). Long-term impacts on the vestibular function from CI surgery, as well as the chronic electrical stimulation to the cochlea, are still to be investigated.

Keywords: cochlear implant, vestibular function, children, adults, unilateral implantation, sequential bilateral implantation

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Manohar Bance, University of Cambridge, United Kingdom

****Correspondence:***
Jingwu Sun
sunjingwuustc@163.com
Xiaotao Guo
gxt2012@mail.ustc.edu.cn
Jiaqiang Sun
sunjq0605@126.com

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INTRODUCTION

Cochlear implantation (CI) is successfully used as a treatment option for restoring hearing in patients with severe or profound sensorineural hearing loss (SNHL). While CI restores hearing, in some patients, it negatively affects vestibular functions, resulting in dizziness, or balance disorders. In 1971, Michelson first reported that a CI patient developed vertigo and tinnitus symptoms after CI surgery (1). Terry et al. analyzed delayed complications after CI in a review capturing 88 studies and found that vestibular complications were the most common phenomenon (2). Sokolov et al. reported that deaf children are more likely to have vestibular disorders (3). Modifications and areflexia of vestibular functions have been previously reported (4). The CI electrode stimulates the spiral ganglion in the central modiolus trunk, which affects the stability of the endolymphatic environment, possibly resulting in histopathological changes after CI.

With the popularization of CI, vestibular dysfunction has attracted much attention recently. Most studies, however, have focused on vestibular functions in adults rather than in children because of the often-poor co-operation and unreliable responses of children during testing. The effect of CI on vestibular functions in children remains unclear. The advantages of binaural hearing through bilateral CI are widely accepted, and more patients choose bilateral CI. Simultaneous bilateral implantation may cause more risks to patients compared with sequential bilateral implantation from the surgical point of view (5). But considering the health economics and the process of learning to use CI, simultaneous bilateral CI is considered better (6). Clinical studies showed that the incidence of vertigo after CI was 2–35%, but the incidence of vestibular dysfunction was 20–80% (5, 7, 8). The results of subjective and objective tests for evaluating vestibular function seem inconsistent.

Obviously, the incidence of vestibular dysfunction after CI changes greatly, and the reasons are multifactorial. In this study, to investigate the effects of age at CI and CI approach (unilateral or sequential bilateral) on vestibular functions, we evaluated vestibular functions of five vestibular end organs (saccule, utricle, and semicircular canals) in children and adults before and after unilateral or sequential bilateral CI.

MATERIALS AND METHODS

Patients

In this study, 37 patients (23 males and 14 females) with bilateral severe or profound SNHL receiving CI in our hospital from October 2020 to January 2021 were included. No patients had inner ear malformations and all had normal eardrums and middle ear pressures before and 1 month after CI. Patients had no pathological features of the vestibular, oculomotor or neuromuscular system except for one adult patient with Meniere's disease. Children in this study were more than 6 years old. They had good comprehension and expression abilities and could clearly describe their vertigo symptoms. Each patient was implanted with a 28 mm long electrode array (FLEX28) through the round window (RW) approach to minimize damage to the intra-cochlear structures. The implanted devices were produced by MED-EL (Innsbruck, Austria). No serious complications after CI surgery were found. Each patient underwent audiometric tests (tympanometry and pure tone audiometry) and a series of vestibular function tests 1–3 days before surgery and 29–37 days after surgery. The vestibular function tests included the caloric test, vestibular evoked myogenic potential (VEMP) test, video head impulse test (vHIT), Dizziness Handicap Inventory (DHI) for adults, and Pediatric Vestibular Symptom Questionnaire (PVSQ) for children.

Patients were divided into three groups according to the age at implantation and the first- or second-side CI: first-side CI-implanted adults ($\geq$18 years, $n = 15$), first-side CI-implanted children (6–17 years, $n = 10$), and second-side CI-implanted children (6–17 years, $n = 12$). First-side CI-implanted adults and children received a unilateral CI, and second-side CI-implanted children received a sequential bilateral CI. The mean ($\pm$SD) ages of first-side CI-implanted adults, first-side CI-implanted children, and second-side CI-implanted children were 37.46 $\pm$ 15.32 years (ranging from 18 to 70 years), 10.00 $\pm$ 4.24 years (ranging from 6 to 16 years), and 8.92 $\pm$ 4.11 years (ranging from 6 to 17 years), respectively. The pure tone averages (PTAs) at 500 Hz, 1, 2, and 4 kHz for all patients were 102.3 $\pm$ 13.65 dB HL (left side) and 102.1 $\pm$ 20.89 dB HL (right side), ranging from 75 to 120 dB HL. The demographic information of patients is listed in **Table 1**. The protocols and experimental procedures in the present study were reviewed and approved by the Anhui Provincial Hospital Ethics Committee. Each participant or his/her guardians had filled out informed consent carefully before the experiment.

Vestibular Function Tests

Caloric Test

The caloric test was employed to evaluate the horizontal semicircular canal (SCC). The patients took supine position and raised their head to 30 degrees with a pillow. The right and left ears of the patients were stimulated with cool air (24°C) and warm air (50°C) by using an air caloric irrigator system (Micromedical Technologies Inc., Chatham, IL, USA). We used videonystagmography (VNG) (VisualEyesTM VNG, Micromedical Technologies Inc., USA) to record horizontal eye movements during the test. The subjects were perfused four times for 60 s. After perfusion, the nystagmus was observed for 60 s. Unilateral Weakness (UW) was calculated using the maximal slow phase eye velocity: UW = | (RC + RW) – (LC + LW) | / (RC + RW +LC + LW) × 100%, where RC = right cool, RW = right warm, LC = left cool, and LW = left warm. UW >25% was considered abnormal (9).

VEMP

VEMP was recorded by using a SmartEP equipment (Intelligent Hearing Systems, Miami, FL, USA). All patients were tested with air-conducted tone bursts of 105 dB nHL at 500 Hz administered by plug-in earphones. The resistance of the electrode was <5 kΩ. For ocular VEMP (oVEMP), the first negative waveform is N1 (at the latency of about 10 ms) and the first positive waveform is P1 (at the latency of about 15 ms). For cervical

TABLE 1 | The demographic information of participants with cochlear implants.

Subject	Gender	Etiology	Age at first/second CI (years)	First/second implanted side	First/second Implant type
First-side CI-implanted adults					
1	M	Hereditary	22/	R/	SONATATi100
2	M	Unknown	33/	L/	SONATAtTi100
3	F	Unknown	18/	R/	CONCERTOMi1000
4	M	Meniere's disease	70/	R/	CONCERTOMi1000
5	F	Unknown	56/	R/	CONCERTOMi1000
6	M	Unknown	19/	R/	SONATATi100
7	M	Noise induced	46/	R/	CONCERTOMi1000
8	F	Unknown	40/	L/	SONATATi100
9	M	Noise induced	44/	L/	CONCERTOMi1000
10	F	Sudden deafness	48/	L/	CONCERTOMi1000
11	M	Unknown	20/	R/	CONCERTOMi1000
12	F	Unknown	43/	R/	CONCERTOMi1000
13	M	Drug-induced	24/	R/	CONCERTOMi1000
14	F	Sudden deafness	48/	R/	CONCERTOMi1000
15	M	Unknown	31/	L/	SONATATi100
First-side CI-implanted children					
1	M	Unknown	16/	R/	CONCERTOMi1000
2	M	Hereditary	6/	L/	CONCERTOMi1000
3	F	Unknown	8/	R/	SONATATi100
4	F	Unknown	6/	R/	CONCERTOMi1000
5	M	Hereditary	8/	L/	CONCERTOMi1000
6	M	Viral infection	13/	R/	SONATATi100
7	M	Hereditary	16/	L/	CONCERTOMi1000
8	M	Viral infection	6/	R/	CONCERTOMi1000
9	F	Unknown	14/	L/	SONATATi100
10	M	Viral infection	7/	R/	CONCERTOMi1000
Second-side CI-implanted children					
1	F	Unknown	1/6	R/L	SONATAti100/CONCERTOMi1000
2	M	Viral infection	9/12	L/R	CONCERTOMi1000 (Bi)
3	M	Drug-induced	1/6	R/L	SONATAti100 (Bi)
4	M	Unknown	1/6	L/R	SONATAti100 (Bi)
5	M	Unknown	10/16	R/L	CONCERTOMi1000 (Bi)
6	F	Hereditary	3/8	L/R	CONCERTOMi1000 (Bi)
7	F	Unknown	3/6	R/L	CONCERTOMi1000 (Bi)
8	M	Viral infection	10/11	R/L	CONCERTOMi1000 (Bi)
9	F	Unknown	2/9	R/L	CONCERTOMi1000 (Bi)
10	M	Unknown	1/7	R/L	SONATAti100 (Bi)
11	M	Unknown	2/8	R/L	SONATAti100/CONCERTOMi1000
12	M	Hereditary	16/17	R/L	SONATAti100 (Bi)

CI, cochlear implant; F, female; M, male; L, left; R, right; Bi, bilateral.

VEMP (cVEMP), the first positive waveform is P1 (at the latency of about 13 ms) and the first negative wave is N1 (at the latency of about 23 ms). Whereas, oVEMP can be used to evaluate the function of the utricle and the superior vestibular nerve pathway, cVEMP is mainly used to evaluate the function of the saccule and the inferior vestibular nerve pathway. The amplitude asymmetry ratio (AR) was calculated as follows: | (right amplitude - left amplitude) | /(right amplitude + left amplitude) × 100%. The response was regarded as abnormal for AR >0.34 or no repeatable waveforms (10).

vHIT

All subjects were tested for vHIT by using the EyeSeeCam system (EyeSeeCam, Interacoustics Inc., Assens, Denmark) to record the gain of vestibulo-ocular reflex (VOR) of each SCC. The subjects took seated position and wore a light glass, which was about 1–1.5 m away from the fixed point. After the calibration according to the software requirements, three pairs of semicircular canals in the horizontal and vertical directions were tested. During the test, subjects were asked to keep their eyes fixed in front of the target and relax their necks. At least 10 impulses with peak velocity

ranging from 150 to 250/s were collected from each canal. In our study, the vHIT results were classified based on the gain of vHIT. We classified abnormal values as follows: the gain of the horizontal canal (HC) was <0.8; the gain of the anterior canal (AC) or posterior canal (PC) was <0.7 (11). We measured the gains of both ears at the same time and regarded the vestibular function as abnormal if either ear showed an abnormal value.

Vertigo Disorders Scale Assessment

The DHI was used to evaluate the impact of dizziness or vertigo on the quality of life for adult patients. DHI includes 25 items: 9 items of emotion (E), 9 items of function (F), and 7 items of physical (P). Each item has three options, namely, "yes," "sometimes," and "none," which are scored as 4 points, 2 points, and 0 points, respectively. The maximum score is 100 points. 0 points indicates that vertigo symptoms have no effect on patients. The higher the score, the more serious the impact of vertigo on patients.

The PVSQ is a measure of the severity of vestibular symptoms (dizziness, instability) in children ages 6–17 years old. There are 11 questions in this questionnaire (10 multiple-choice questions, 1 subjective question). In this study, only 10 multiple-choice questions were selected. Each question has four options. Each item is rated on a scale of 0 (never) to 3 (most of the time) (12). The answer to each item of the PVSQ was obtained from the guardians by full communication between children and guardians.

Data Processing and Analysis

The ratio of patients with abnormal vestibular functions to total subjects in each group was regarded as the abnormal rate. Because the pre-implantation abnormal rates of vestibular functions for different groups may be different, we also assessed the growth rate which was calculated by subtracting the pre-implantation abnormal rate from the post-implantation abnormal rate. We used the SPSS software package (version 17.0 for Windows; SPSS Inc., Chicago, IL, USA) to analyze the data. Because of the small sample size, the Fisher's exact test was used to assess the differences of abnormal rates and growth rates. Among all patients, 12 first-side CI-implanted adults, 8 first-side CI-implanted children, and 9 second-side CI-implanted children completed vertigo disorders scale assessment before implantation, at day 3 after implantation, and at day 30 after implantation. The difference of DHI or PVSQ scores among three periods for each group was assessed by using a non-parametric Friedman test, and the difference of PVSQ scores between first- and second-side CI-implanted children at each period was further assessed by using a non-parametric Mann-Whitney *U*-test. If the DHI or PVSQ scores were significantly different among three periods, a Wilcoxon signed rank test was further used to assess scores between any two periods. For hypothesis testing, $p < 0.05$ was considered significantly different.

RESULTS

Abnormal Rates of Vestibular Functions Before and After CI

The caloric test and the VEMP test showed that the abnormal rates significantly increased from pre- to post-implantation in the first-side CI-implanted adults (caloric test: pre: 26.67%, post: 80%, $p = 0.009$; oVEMP: pre: 33.33%, post: 100%, $p < 0.001$; cVEMP: pre: 33.33%, post: 100%, $p = 0.001$) and in the first-side CI-implanted children (caloric test: pre: 40%, post: 100%, $p = 0.011$; oVEMP: pre: 20%, post: 90%, $p = 0.005$; cVEMP: pre: 0%, post: 70%, $p = 0.003$) (**Figure 1**). For the second-side CI-implanted children, the abnormal rate was higher in post- than in pre-implantation caloric test (pre: 58.33%, post: 91.67%, $p = 0.155$) and VEMP test (oVEMP: pre: 75%, post: 91.67%, $p = 0.590$; cVEMP: pre: 66.67%, post: 100%, $p = 0.093$), but the difference was not significant. The vHIT test showed no significant difference between pre- and post-implantation abnormal rates in the first-side CI-implanted adults (HC: pre:

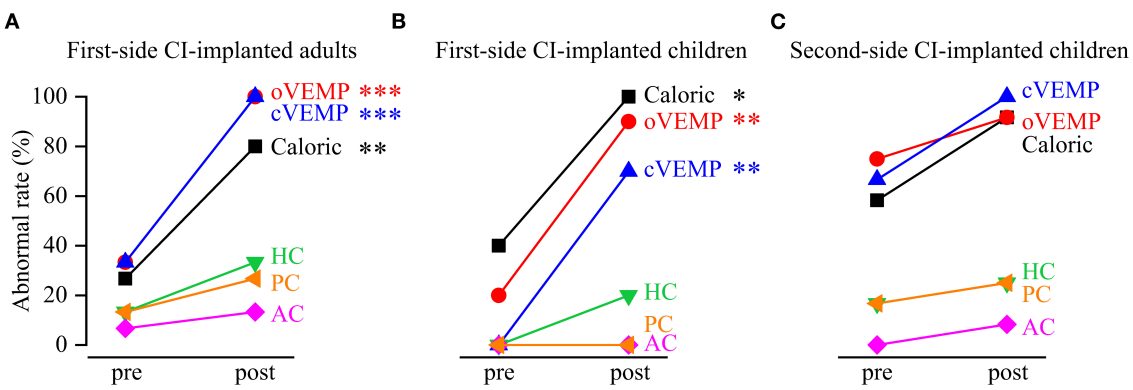

FIGURE 1 | Abnormal rates of vestibular functions revealed by the caloric test, vestibular evoked myogenic potential (VEMP) test and video head impulse test (vHIT) before and after cochlear implantation (CI). The abnormal rates significantly increased from pre- to post-implantation in **(A)** first-side CI-implanted adults and **(B)** first-side CI-implanted children, as revealed by the caloric test, ocular VEMP (oVEMP) and cervical VEMP (cVEMP). The pre- and post-implantation abnormal rates of functions of horizontal canal (HC), anterior canal (AC) and posterior canal (PC) in vHIT were not significantly different. **(C)** No significant difference of the abnormal rates was found between pre- and post-implantation tests in the second-side CI-implanted children. *$p < 0.05$, **$p < 0.01$, ***$p < 0.001$.

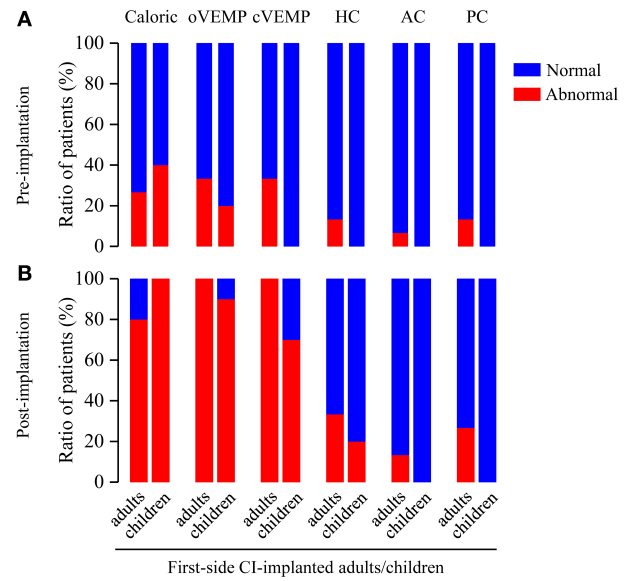

FIGURE 2 | Ratio of patients with abnormal vestibular functions revealed by pre- and post-implantation caloric test, VEMP test, and vHIT in first-side CI-implanted adults and children. **(A)** Pre- and **(B)** post-implantation tests showed no significant difference of abnormal rates between first-side CI-implanted adults and children.

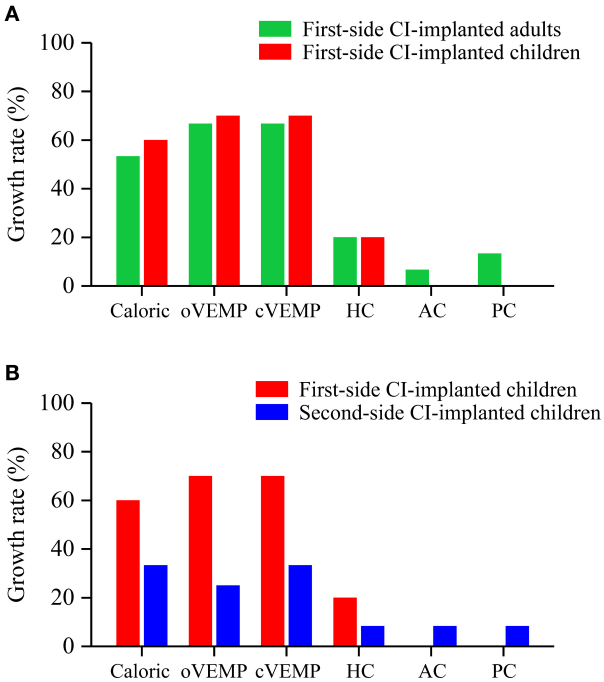

FIGURE 3 | Growth rates of abnormal vestibular functions revealed by the caloric test, VEMP test and vHIT. No significant difference of growth rates was found **(A)** between first-side CI-implanted adults and children or **(B)** between first- and second-side CI-implanted children.

13.33%, post: 33.33%, $p = 0.390$; AC: pre: 6.67%, post: 13.33%, $p > 0.999$; PC: pre: 13.33%, post: 26.67%, $p = 0.651$), in the first-side CI-implanted children (HC: pre: 0%, post: 20%, $p = 0.474$; AC: pre: 0%, post: 0%, $p > 0.999$; PC: pre: 0%, post: 0%, $p > 0.999$) or in the second-side CI-implanted children (HC: pre:16.67%, post: 25%, $p > 0.999$; AC: pre: 0%, post: 8.33%, $p > 0.999$; PC: pre: 16.67%, post: 25%, $p > 0.999$).

Abnormal Rates of Vestibular Functions Between First-Side CI-Implanted Adults and Children

To assess the effect of age at CI on the vestibular functions, we analyzed the differences of abnormal rates between first-side CI-implanted adults and children. The pre-implantation caloric test, VEMP test and vHIT showed no significant difference of the abnormal rates between first-side CI-implanted adults and children (caloric test: 26.67 vs. 40%, $p = 0.667$; oVEMP: 33.33 vs. 20%, $p = 0.659$; cVEMP: 33.33 vs. 0%, $p = 0.061$; HC: 13.33 vs. 0%, $p = 0.500$; AC: 6.67 vs. 0%, $p > 0.999$; PC: 13.33 vs. 0%, $p = 0.500$) (**Figure 2**). Furthermore, no significant difference of the post-implantation abnormal rates between these two groups was found (caloric test: 80 vs. 100%, $p = 0.250$; oVEMP: 100 vs. 90%, $p = 0.400$; cVEMP: 100 vs. 70%, $p = 0.052$; HC: 33.33 vs. 20%, $p = 0.659$; AC: 13.33 vs. 0%, $p = 0.500$; PC: 26.67 vs. 0%, $p = 0.125$, respectively).

The growth rates in the first-side CI-implanted adults and children were 53 and 60% for caloric test, 67 and 70% for oVEMP, 67 and 70% for cVEMP, 20 and 20% for HC, 6.67 and 0% for AC, and 13.33 and 0% for PC, respectively (**Figure 3A**). No significant difference of the growth rates between these two groups was found ($p > 0.05$).

Abnormal Rates of Vestibular Functions Between First- and Second-Side CI-Implanted Children

To further assess the effect of CI approach on the vestibular functions, we analyzed the differences of abnormal rates between first- and second-side CI-implanted children. Before CI, the VEMP test showed significant differences of the abnormal rates between first- and second-side CI-implanted children (oVEMP: 20 vs. 75%, $p = 0.030$; cVEMP: 0 vs. 66.67%, $p = 0.002$, respectively) (**Figure 4**). No other significant difference of pre- (caloric test: 40 vs. 58.33%, $p = 0.670$; HC: 0 vs. 16.67%, $p = 0.481$; AC: 0 vs. 0%, $p > 0.999$; PC: 0 vs. 16.67%, $p = 0.481$) or post-implantation (caloric test: 100 vs. 91.67%, $p > 0.999$; oVEMP: 90 vs. 91.67%, $p > 0.999$; cVEMP: 70 vs. 100%, $p = 0.078$; HC: 20 vs. 25%, $p > 0.999$; AC: 0 vs. 8.33%, $p > 0.999$; PC: 0 vs. 25%, $p = 0.221$) abnormal rates between these two groups was found.

The growth rates in the first- and second-side CI-implanted children were 60 and 33% for caloric test, 70 and 25% for oVEMP, 70 and 33% for cVEMP, 20 and 8.33% for HC, 0 and 8.33% for AC, and 0 and 8.33% for PC, respectively (**Figure 3B**). No significant difference of the growth rates between these two groups was found ($p > 0.05$).

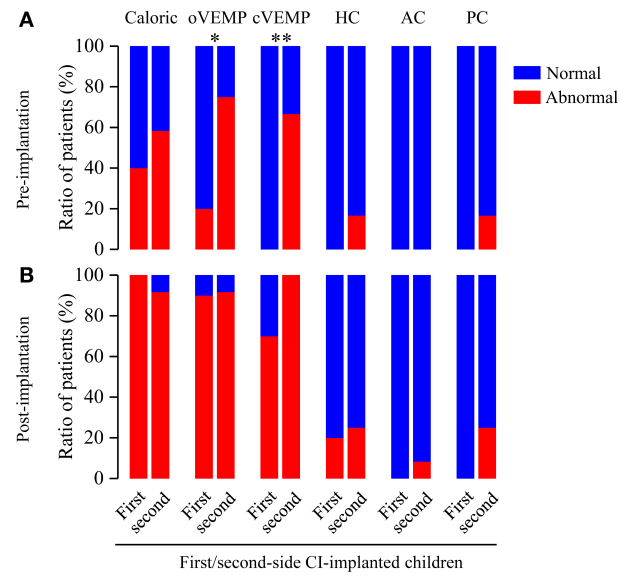

FIGURE 4 | Ratio of patients with abnormal vestibular functions revealed by pre- and post-implantation caloric test, VEMP test and vHIT in first- and second-side CI-implanted children. **(A)** Higher abnormal rates for pre-implantation oVEMP and cVEMP were found in first-side CI-implanted children than in second-side CI-implanted children. **(B)** Post-implantation tests showed no significant difference of abnormal rates between these two groups. $^{*}p < 0.05$, $^{**}p < 0.01$.

Vertigo Questionnaires Before and After CI

The average DHI and PVSQ scores for three groups at three periods (before implantation, at day 3 after implantation and at day 30 after implantation) are shown in **Table 2**. The DHI scores for first-side CI-implanted adults ($p = 0.066$) and the PVSQ scores for first-side CI-implanted children ($p = 0.206$) were not significantly different among the three periods. However, we found significant differences of PVSQ scores for second-side CI-implanted children among the three periods ($p = 0.014$). The further tests showed that PVSQ score for second-side CI-implanted children at day 3 after implantation was significantly higher than that before implantation ($p = 0.021$) and that at day 30 after implantation ($p = 0.035$), respectively. There was no significant difference of the PVSQ scores between first- and second-side CI-implanted children before implantation ($p = 0.226$), at day 3 after implantation ($p = 0.411$), or at day 30 after implantation ($p = 0.664$).

A Spearman's correlation test further showed a significantly positive correlation between the DHI score and the UW of the caloric test at day 30 after implantation in first- side CI-implanted adults ($r = 0.619$, $p = 0.032$).

DISCUSSIOIN

CI is the preferred method of treatment for patients with severe and profound SNHL to regain hearing and speech abilities, and it has been accepted universally. However, the post-operative complications have greatly concerned clinicians and patients. Vertigo is one of the most common complications (13). The vestibule and the cochlea share a continuous membranous structure and have similar receptor cells. However, the mechanism underlying vestibular symptoms caused by CI remains unclear. A histopathological study of temporal bone specimens of CI users suggests that cochlear hydrops accompanied by saccular collapse may cause attacks of vertigo with delayed onset (14). Therefore, pre-operative and post-operative assessment of vestibular functions can be made clinically mandatory.

The abnormal rates in the caloric and VEMP tests greatly increased from pre- to post-implantation for first-side CI-implanted adults and children, indicating the negative effect of CI surgery on vestibular functions. Stultiens et al. found deteriorated vestibular functions after CI using the caloric test (15). The caloric test is based on thermal conductance which may alter after CI surgery (16) and the VEMP response may be also affected by residual blood or conductive loss in the middle ear. It should be noted that the patients had normal middle ear pressures revealed by the tympanometry before and after CI in our study, suggesting normal middle-ear conduction function. Therefore, the differences between pre- and post-operative caloric and VEMP tests may mainly reflect vestibular dysfunction resulting from CI surgery. However, we cannot completely rule out the effect of changes in thermal conductance between the external auditory canal and the labyrinth and those in the middle ear structure on the post-operative results. Moreover, there was no significant difference of the abnormal rates before and after CI in second-side CI-implanted children. This may be explained by the ceiling effect that the vestibular functions of these children already had been negatively affected by the first CI. The vHIT test showed no significant difference of the abnormal rates between pre- and post-implantation, consistent with previous findings (17). Jutila et al. reported that only 10% of patients had a reduction in VOR gain after CI (18). These findings suggest that damaged vestibular functions caused by CI may be better reflected by the caloric test compared with vHIT. Tsuji et al. analyzed the vestibular hair cells of 30 patients with Meniere's disease and found that the number of type II hair cells in patients with endolabyrinthine hydrops was significantly lower than that in the control group, whereas the numbers of type I hair cells were similar between the two groups (19). Type I hair cells (for high frequency) are located at the crest of the crista ampullaris and type II hair cells (for low frequency) are mainly located at the periphery of the crista ampullaris. Therefore, type II hair cells are closer to the perilymph space compared with type I hair cells and may be more vulnerable to endolabyrinthine hydrops. Similar to Meniere's disease, CI can also result in hydrops (14), possibly causing damage to type II hair cells. Our results are also consistent with the findings of Kuang et al. (20). Ibrahim et al. also concluded that CI surgery affects the results of caloric and VEMP tests, but not those of vHIT (17). These findings indicate that otolith and low-frequency SCC are more vulnerable to CI.

Many factors, such as age, affect the vestibular functions revealed by the VEMP test (21). With the increase of age, the hardness of the otolith structure will increase and the VEMP response rate will decrease (22). In the present study, we

TABLE 2 | The pre- and post-implantation (at day 3 and at day 30) scores of Dizziness Handicap Inventory (DHI) for adults and Pediatric Vestibular Symptom Questionnaire (PVSQ) for children.

Group	*N*	Scores of DHI/PVSQ		
		Pre-implantation	**post-implantation (at day 3)**	**post-implantation (at day 30)**
First-side CI-implanted adults	12	18.83 ± 25.99	43.33 ± 32.84	16.00 ± 17.66
First-side CI-implanted children	8	7.00 ± 4.24	11.63 ± 4.72	8.00 ± 4.11
Second-side CI-implanted children	9	6.22 ± 9.27	14.11 ± 6.66*	8.22 ± 8.61#

*Data are expressed as mean ± standard deviation. *$p < 0.05$ vs. pre-implantation. #$p < 0.05$ vs. post-implantation (at day 3).*

investigated whether the age at CI affects the vestibular functions by comparing the abnormal rates between adults and children who underwent first-side CI. The first-side CI-implanted adults and children showed similar abnormal rates and growth rates in all tests, indicating that CI damages the vestibular functions independent of age at CI. This finding may be explained by the acute injury. The abnormal rates in caloric and VEMP tests were very high within 1 month after CI (all ≥70%) and it was difficult to observe a difference between two groups. Xu et al. also reported that the response rates of oVEMP and cVEMP declined 1 month after CI (23). A follow-up study is needed to assess the long-term effects of CI on the age of implantation.

In our study, first-side CI-implanted adults and children showed abnormal vestibular functions before CI, suggesting that severe or profound hearing loss could be accompanied by vestibular dysfunction (24). Yu and Li reported that patients with sudden deafness could show vertigo (25). Meil et al. performed a series of SCC function tests before CI and found that the abnormal rate in the caloric test was 32% (26). These studies are consistent with our findings. The vestibular organs are adjacent to the cochlea anatomically, and the factors causing severe or profound hearing loss may also damage the structure and function of the vestibular systems.

With the increasing acceptance of CI, the advantages of bilateral hearing are becoming widely recognized. We found no significant difference of abnormal rates or growth rates 1 month after CI between first- and second-side CI-implanted children, indicating that unilateral and sequential bilateral CI have similar effects on vestibular functions. However, before CI, second-side CI-implanted children showed higher abnormal rates compared with first-side CI-implanted children as revealed by the VEMP test. In the present study, the second-side CI-implanted children received bilateral CI sequentially with a mean inter-implant interval of 4 years. Therefore, the vestibular dysfunction caused by unilateral (first) CI may last for a long time. The higher baseline (pre-implantation abnormal rate) in second-side CI-implanted children may possibly explain the smaller change from pre- to post-implantation (lower growth rate, not significant) compared with first-side CI-implanted children. Inconsistent with the VEMP findings, the caloric test showed no significant difference of abnormal rates not only between first- and second-side CI-implanted children before CI but also from pre- to post-implantation in the second-side CI-implanted children, suggesting that the caloric test results tend to normalize over time. Previous findings also suggest that CI may cause certain damage to the function of the saccule and utricle, revealed by cVEMP and oVEMP, respectively, and this damage can last for a long time (23). It has been further reported that the saccule, which is close to the cochlea, is the structure most vulnerable to damage from CI as most patients with CI have reduced saccular function measured by cVEMP (27, 28). The next most vulnerable structure is the utricle because of its distance from the cochlea (29). The vestibular functions are greatly damaged by both unilateral and sequential bilateral CI.

The vertigo questionnaires demonstrated no significant difference of DHI and PVSQ scores between pre- and post-implantation for unilateral CI in both adults and children. In children with bilateral CI, PVSQ scores increased significantly at day 3 post-implantation but significantly decreased at day 30, which implies that the changes may be some acute reaction to anesthesia or to middle/inner ear trauma after the surgery. These subjective performances are quite different from the objective assessment outcomes from the caloric and VEMP tests. Abouzayd et al. also showed a poor correlation between the objective vestibular outcomes and subjective symptoms (30). Katsiari et al. found that dizziness rarely persisted beyond 1 month after CI (31). Therefore, accurate diagnosis and treatment of vestibular dysfunction only by objective questionnaires is a great challenge, especially for children. A new meta-analysis showed that only 1.7% of children in contrast to 31.3% of adults had post-operative vertigo (7). The incidence of post-operative vertigo in children is far lower than that in adults, possibly related to children's poor ability to express themselves. It is difficult for children to accurately and clearly describe the symptoms of vertigo. Therefore, it is necessary to make a comprehensive and systematic assessment for vestibular functions by combining objective with subjective methods. In our study, we found a significantly positive correlation between the DHI score and the results of the caloric test at day 30 after implantation in first-side CI-implanted adults but not in children. This finding implies that, compared with children, adults with vestibular dysfunction may suffer more from postoperative vertigo. Long-term impacts on vestibular function from CI surgery, as well as the chronic electrical stimulation to the cochlea, are still to be investigated.

CONCLUSIONS

In this study, we observed that vestibular function improved in the short term from day 3 to day 30 post-implantation. Increased abnormal rates from pre- to post-implantation in caloric and VEMP tests but not in vHIT suggest that otolith and low-frequency SCC are more vulnerable. No significant

difference of abnormal rates after CI between first-side CI-implanted adults and children or between first- and second-side CI-implanted children, further indicating that alterations of vestibular function resulting from CI surgery may be independent of age at CI and CI approach (unilateral or sequential bilateral).

DATA AVAILABILITY STATEMENT

The raw data supporting the conclusions of this article will be made available by the authors, without undue reservation.

ETHICS STATEMENT

The studies involving human participants were reviewed and approved by Anhui Provincial Hospital Ethics Committee. Written informed consent to participate in this study was provided by the participants' legal guardian/next of kin.

AUTHOR CONTRIBUTIONS

RG, JinS, XG, and JiaS conceived and designed the experiments. RG, YW, SW, BZ, and XG recruited participants and performed data acquisition. RG, YW, JinS, XG, and JiaS analyzed the data. All authors wrote the paper and approved the final article.

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REFERENCES

1. Michelson RP. Electrical stimulation of the human cochlea. A preliminary report. *Arch Otolaryngol*. (1971) 93:317–23. doi: 10.1001/archotol.1971.00770060455016
2. Terry B, Kelt RE, Jeyakumar A. Delayed complications after cochlear implantation. *JAMA Otolaryngol Head Neck Surg*. (2015) 141:1012–7. doi: 10.1001/jamaoto.2015.2154
3. Sokolov M, Gordon KA, Polonenko M, Blaser SI, Papsin BC, Cushing SL. Vestibular and balance function is often impaired in children with profound unilateral sensorineural hearing loss. *Hear Res*. (2019) 372:52–61. doi: 10.1016/j.heares.2018.03.032
4. Buchman CA, Joy J, Hodges A, Telischi FF, Balkany TJ. Vestibular effects of cochlear implantation. *Laryngoscope*. (2004) 114(10 Pt 2 Suppl 103):1–22. doi: 10.1097/00005537-200410001-00001
5. Devroede B, Pauwels I, Le Bon SD, Monstrey J, Mansbach AL. Interest of vestibular evaluation in sequentially implanted children: preliminary results. *Eur Ann Otorhinolaryngol Head Neck Dis*. (2016) 133(Suppl. 1):S7–11. doi: 10.1016/j.anorl.2016.04.012
6. Cheng LJ, Soon SS, Wu DB, Ju H, Ng K. Cost-effectiveness analysis of bilateral cochlear implants for children with severe-to-profound sensorineural hearing loss in both ears in Singapore. *PLoS ONE*. (2019) 14:e0220439. doi: 10.1371/journal.pone.0220439
7. Hansel T, Gauger U, Bernhard N, Behzadi N, Romo Ventura ME, Hofmann V, et al. Meta-analysis of subjective complaints of vertigo and vestibular tests after cochlear implantation. *Laryngoscope*. (2018) 128:2110–23. doi: 10.1002/lary.27071
8. Murray D, Viani L, Garvan J, Murphy A, Vance R, Simoes-Franklin C, et al. Balance, gait and dizziness in adult cochlear implant users: a cross sectional study. *Cochlear Implants Int*. (2020) 21:46–52. doi: 10.1080/14670100.2019.1662978
9. Shepard NT, Jacobson GP. The caloric irrigation test. *Handb Clin Neurol*. (2016) 137:119–31. doi: 10.1016/B978-0-444-63437-5.00009-1
10. Imai T, Okumura T, Ohta Y, Oshima K, Sato T, Kamakura T, et al. Effects of cochlear implants on otolith function as evaluated by vestibulo-ocular reflex and vestibular evoked myogenic potentials. *Auris Nasus Larynx*. (2019) 46:836–43. doi: 10.1016/j.anl.2019.03.011
11. Dagkiran M, Tuncer U, Surmelioglu O, Tarkan O, Ozdemir S, Cetik F, et al. How does cochlear implantation affect five vestibular end-organ functions and dizziness? *Auris Nasus Larynx*. (2019) 46:178–85. doi: 10.1016/j.anl.2018.07.004
12. Pavlou M, Whitney S, Alkathiry AA, Huett M, Luxon LM, Raglan E, et al. The pediatric vestibular symptom questionnaire: a validation study. *J Pediatr*. (2016) 168:171–7 e1. doi: 10.1016/j.jpeds.2015.09.075
13. Piker EG, Riska K, Garrison D, Kaylie DM. Vestibular function after cochlear implantation: a test battery and case-by-case approach. *Laryngoscope Investig Otolaryngol*. (2020) 5:560–71. doi: 10.1002/lio2.413
14. Handzel O, Burgess BJ, Nadol JB Jr. Histopathology of the peripheral vestibular system after cochlear implantation in the human. *Otol Neurotol*. (2006) 27:57–64. doi: 10.1097/01.mao.0000188658.36327.8f
15. Stultiens JJA, Kieft HW, Mylanus EAM, Pennings RJE, Terwoert L, Beynon AJ. Impact of cochlear implantation on the function of the three semicircular canals. *Int J Audiol*. (2020) 59:843–9. doi: 10.1080/14992027.2020.1768310
16. Proctor LR, Dix RC. New approach to caloric stimulation of the vestibular receptor. *Ann Otol Rhinol Laryngol*. (1975) 84(5 Pt 1):683–94. doi: 10.1177/000348947508400520
17. Ibrahim I, da Silva SD, Segal B, Zeitouni A. Effect of cochlear implant surgery on vestibular function: meta-analysis study. *J Otolaryngol Head Neck Surg*. (2017) 46:44. doi: 10.1186/s40463-017-0224-0
18. Jutila T, Aalto H, Hirvonen TP. Cochlear implantation rarely alters horizontal vestibulo-ocular reflex in motorized head impulse test. *Otol Neurotol*. (2013) 34:48–52. doi: 10.1097/MAO.0b013e318277a430
19. Tsuji K, Velazquez-Villasenor L, Rauch SD, Glynn RJ, Wall C 3rd, Merchant SN. Temporal bone studies of the human peripheral vestibular system. Meniere's disease. *Ann Otol Rhinol Laryngol Suppl*. (2000) 181:26–31. doi: 10.1177/00034894001090S505
20. Kuang H, Haversat HH, Michaelides EM. Impairment of Caloric Function After Cochlear Implantation. *J Speech Lang Hear Res*. (2015) 58:1387–95. doi: 10.1044/2015_JSLHR-H-15-0010
21. Tseng CL, Chou CH, Young YH. Aging effect on the ocular vestibular-evoked myogenic potentials. *Otol Neurotol*. (2010) 31:959–63. doi: 10.1097/MAO.0b013e3181e8fb1a
22. Louza J, Mertes L, Braun T, Gurkov R, Krause E. Influence of insertion depth in cochlear implantation on vertigo symptoms and vestibular function. *Am J Otolaryngol*. (2015) 36:254–8. doi: 10.1016/j.amjoto.2014.11.007

23. Xu XD, Zhang XT, Zhang Q, Hu J, Chen YF, Xu M. Ocular and cervical vestibular-evoked myogenic potentials in children with cochlear implant. *Clin Neurophysiol*. (2015) 126:1624–31. doi: 10.1016/j.clinph.2014.10.216
24. West N, Sass H, Klokker M, Caye-Thomasen P. Functional loss after meningitis-evaluation of vestibular function in patients with postmeningitic hearing loss. *Front Neurol*. (2020) 11:681. doi: 10.3389/fneur.2020.00681
25. Yu H, Li H. Vestibular dysfunctions in sudden sensorineural hearing loss: a systematic review and meta-analysis. *Front Neurol*. (2018) 9:45. doi: 10.3389/fneur.2018.00045
26. Meli A, Aud BM, Aud ST, Aud RG, Cristofari E. Vestibular function after cochlear implant surgery. *Cochlear Implants Int*. (2016) 17:151–7. doi: 10.1179/1754762815Y.0000000014
27. Krause E, Louza JP, Wechtenbruch J, Hempel JM, Rader T, Gurkov R. Incidence and quality of vertigo symptoms after cochlear implantation. *J Laryngol Otol*. (2009) 123:278–82. doi: 10.1017/S002221510800296X
28. Obeidat FS, Bell SL, Julie E. An exploration of vestibular function pre and post unilateral cochlear implantation. *Cochlear Implants Int*. (2020) 21:281–91. doi: 10.1080/14670100.2020.1774716
29. Krause E, Louza JP, Wechtenbruch J, Gurkov R. Influence of cochlear implantation on peripheral vestibular receptor function. *Otolaryngol Head Neck Surg*. (2010) 142:809–13. doi: 10.1016/j.otohns.2010.01.017
30. Abouzayd M, Smith PF, Moreau S, Hitier M. What vestibular tests to choose in symptomatic patients after a cochlear implant? A systematic review and meta-analysis. *Eur Arch Otorhinolaryngol*. (2017) 274:53–63. doi: 10.1007/s00405-016-4007-4
31. Kubo T, Yamamoto K, Iwaki T, Doi K, Tamura M. Different forms of dizziness occurring after cochlear implant. *Eur Arch Otorhinolaryngol*. (2001) 258:9–12. doi: 10.1007/PL00007519

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Vestibular Function After Cochlear Implantation in Partial Deafness Treatment

Magdalena Sosna-Duranowska[1], Grazyna Tacikowska[1], Elzbieta Gos[1], Anna Krupa[1], Piotr Henryk Skarzynski[1,2] and Henryk Skarzynski[1]*

[1] Institute of Physiology and Pathology of Hearing, Warsaw, Poland, [2] Medical University of Warsaw, Warsaw, Poland

Introduction: Cochlear implantation is a fully accepted method of treating individuals with profound hearing loss. Since the indications for cochlear implantation have broadened and include patients with low-frequency residual hearing, single-sided deafness, or an already implanted ear (meaning bilateral cochlear implantation), the emphasis now needs to be on vestibular protection.

Materials and Methods: The research group was made up of 107 patients operated on in the otorhinolaryngosurgery department: 59 females and 48 males, aged 10.4–80.2 years (M = 44.4; SD = 18.4) with hearing loss lasting from 1.4 to 56 years (M = 22.7; SD = 13.5). The patients underwent cVEMP, oVEMP, a caloric test, and vHIT assessment preoperatively, and, postoperatively, cVEMP and oVEMP at 1–3 months and a caloric test and vHIT at 4–6 months.

Results: After cochlear implantation, there was postoperative loss of cVEMP in 19.2% of the patients, oVEMP in 17.4%, reduction of caloric response in 11.6%, and postoperative destruction of the lateral, anterior, and posterior semicircular canal as measured with vHIT in 7.1, 3.9, and 4% respectively.

Conclusions: Hearing preservation techniques in cochlear implantation are connected with vestibular protection, but the risk of vestibular damage in never totally eliminated. The vestibular preservation is associated with hearing preservation and the relation is statistically significant. Informed consent for cochlear implantation must include information about possible vestibular damage. Since the risk of vestibular damage is appreciable, preoperative otoneurological diagnostics need to be conducted in the following situations: qualification for a second implant, after otosurgery (especially if the opposite ear is to be implanted), having a history of vestibular complaints, and when there are no strict audiological or anatomical indications on which side to operate.

Keywords: cochlear implantation, vestibular evoked miogenic potentials, round window approach, video head impulse test, caloric test

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****Correspondence:***
Magdalena Sosna-Duranowska
magda.sosna@gmail.com

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INTRODUCTION

Cochlear implantation (CI) is a well-known method of treating individuals with profound hearing loss. Despite its great effect in restoring hearing, after a CI procedure there is the risk of traumatization of the inner ear causing residual hearing loss or vestibular damage (1–4). Previously, vestibular damage was usually supposed to be negligible, due to the operation of central compensation mechanisms, and was rarely thought to cause persistent disability.

With recent advances in technology, in otosurgical techniques, and in our understanding of hearing electrophysiology, the population eligible for cochlear implantation has been broadened. Not only patients with bilateral profound sensorineural hearing loss but also those with unilateral deafness (5) or partial deafness (6) or the elderly (7) can profit from cochlear implantation. In addition, bilateral implantation in order to achieve better speech discrimination and sound localization is becoming more common (8). This brings new opportunities but also new risks to cochlear implant surgery.

Patients with low-frequency residual hearing (partial deafness) achieve statistically better preoperative results in vestibular tests than do standard implantees, but their vestibular performance may be compromised after a CI procedure (9). Elderly patients are more likely to have comorbidities affecting central compensation mechanisms, for example neurological, orthopedic, psychiatric, or ophthalmological dysfunction. If bilateral vestibular damage should occur, the prognosis is rather poor compared to unilateral dysfunction (10). All these considerations prompt a change of mind toward vestibular preservation and make it important to maintain the labyrinth and vestibulum after a CI procedure.

In the 1990s and into this century, the first steps toward "soft surgery" in cochlear implantation began to be implemented (6, 11, 12). Now the use of soft electrodes, a round window approach (RWA), reduced insertion angles, and use of perioperative steroids has become widespread and has proven to be effective in preserving the cochlear structure (13–15). However, the question of how protective these measures are on the vestibule still remains unanswered.

Many papers have assessed vestibular function following cochlear implantation done via cochleostomy or the round window approach. However, they show a big discrepancy in the incidence of postoperative vestibular deterioration: for cochleostomy, the figures are 31–86% for cervical Vestibular Evoked Myogenic Potentials (cVEMPs), 6–50% for caloric tests, and 4–9% for video Head Impulse Test (vHIT); for the round window approach, the comparable figures are 0–76% for cVEMPs, 5–37% for ocular Vestibular Evoked Myogenic Potentials (oVEMPs), and 0–93% for caloric tests (16–28). Moreover, the effect of electrode type and length on vestibular function remains unclear.

The aim of this study was to assess the safety of cochlear implantation in partial deafness in terms of vestibular preservation, with hearing preservation (HP) techniques and range of electrode types.

Figure 1 shows the diversity of audiograms categorized as partial deafness. According to the treatment strategy used, the following groups can be distinguished: electro-natural stimulation (PDT-ENS)—patients with normal or only slightly elevated thresholds in the low- and mid-frequency bands, who need electrical complementation with a very short electrode (16–19 mm); electrical complement (PDT-EC)—patients with normal or only slightly elevated thresholds at low frequencies, who need electrical complementation with short electrodes (20–25 mm) and no amplification at the apex; electro-acoustic stimulation (PDT–EAS)—patients with low- and mid-frequency residual hearing who need amplification from a hearing aid for low frequencies and electrical stimulation from implanted electrode (25–28 mm) for mid and high frequencies; and electrical stimulation (PDT-ES)—patients with non-functional residual hearing who rely fully on electrical stimulation (28–31 mm length electrode) but in whom preservation of cochlear structures is still desirable (6, 29, 30).

MATERIALS AND METHODS

In total, 149 patients qualified for PDT-EAS, PDT-EC, or PDT-ES cochlear implantation (**Figure 1**) were enrolled in this study. Of the 149, there were 13 patients who already had a CI and received a second implant, and four who were implanted twice during the study (they received a CI on both sides sequentially), so that finally 153 ears were operated on.

The exclusion criteria included reimplantation cases and the presence of complete vestibular damage prior to implantation—demonstrated by the absence of cVEMP and oVEMP, areflexia in a caloric test with a slow-component velocity (SCV) $<12°/s$, or covert or overt saccades in all three planes of the vHIT. Additionally, cVEMP and oVEMP were not performed if there were superior semicircular canal dehiscence syndrome (SSCD), inner ear malformation (including large aqueductus vestibule syndrome LVAS), retrocochlear pathology, central nervous system (CNS) pathology affecting the reflex arc (neurodegenerative disease, demyelinating disease, cerebellar pathology), conductive hearing loss, or highly probable conductive hearing loss. Caloric tests were not done if there was a history of canal wall down tympanoplasty, tympanic membrane perforation, inner ear malformation, or cerebellar pathology. The RWA implantation was carried out according to a six-step procedure for Partial Deafness Treatment (PDT): (1) antrotomy; (2) posterior tympanotomy to allow for visualization of the round window niche; (3) puncture of the round window membrane; (4) insertion of the electrode array, approaching the scala tympani directly through the round window membrane; (5) electrode fixation in the round window niche with fibrin glue (with the membrane partially uncovered to preserve its mobility); and (6) fixation of the device in a well-created in the temporal bone (6). We use soft lateral wall electrodes. Exceptionally, in some non-functional residual hearing (PDT-ES) or borderline PDT-EAS and PDT-ES cases, we may choose the perimodiolar electrode. The study protocol and the informed consent form were approved by

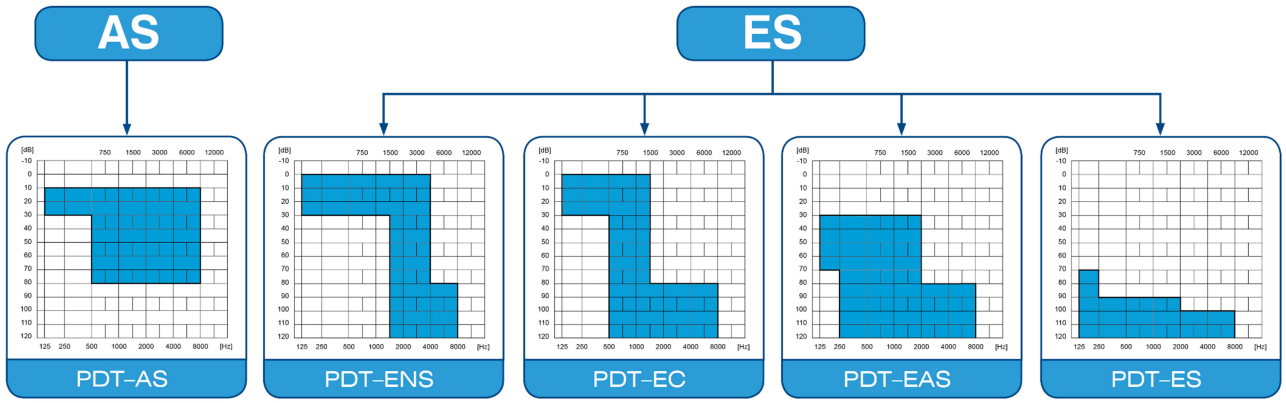

FIGURE 1 | Four categories of partial hearing loss (6, 29, 30).

the Institutional Bioethics Committee (IFPS:/KB/15/2014). All participants gave their written informed consent for participating in the study and publication of the results with maintained anonymity according to General Data Protection Regulations. The study has been conducted in accordance with the World Medical Association's Declaration of Helsinki from 1964.

VEMP

Candidates participated in presurgery cVEMP and oVEMP assessment and were retested 1–3 months later with the CI switched off. Both tests were performed on Eclipse software (Interacoustics A/S, Denmark). The patients were stimulated with a 500-Hz tone burst 2:2:2 at 97 dB nHL using an insert tip (31, 32). The impedance at each electrode was <2.5 Ω, and other parameters were a stimulus rate of 5.1 per second and a 10–1,000-Hz bandpass filter.

In cVEMP, patients were asked to turn their head 45° away from the examined ear and to tension the sternocleidomastoid muscle (SCM) at a contraction level of 50–150 μV with the assistance of visual feedback from the software. The right and left electrodes were placed at the midpoint between the termination of the muscle at the mastoid and its origin at the sternum on the right and left sides, respectively, with the vertex electrode situated between the sternoclavicular joints, the ground electrode at the forehead. Averaging of 200 stimulus repetitions was done, and two repeated wave patterns were accepted as a positive response. Results were determined based on the amplitude asymmetry ratio (norm <36%) (33), response latencies (P1, N1), and amplitudes (P1–N1) corrected by dividing by the prestimulus sternocleidomastoid muscle (SCM) contraction level.

Following oVEMP standards, the recording electrodes were placed infraorbitally in the midline of the contralateral eye to the side they refer to, with the ground electrode at the forehead and the vertex on the chin. Signal averaging was increased to 500. The patient was instructed to fix their gaze at a point 35° upward (34). The response was regarded as present if two repeatable patterns were recorded. The results were analyzed based on the latency (N1, P1), amplitude (N1–P1), and interaural amplitude ratio (norm <34%) (35).

Caloric Tests

During the examination, the patient lay recumbent with the head elevated by 30°. Bilateral caloric stimulation used water at 30°C and 44°C for 30 s into the ear canal with each trial preceded by an 8-min break (VisualEyes BNG of Micromedical Technologies). Unilateral weakness (UW) and slow component velocity (SCV) on both sides before and after cochlear implantation were compared. The degree of canal paresis (UW) was calculated based on Jongkees' formula. A difference of UW > 25% between pre- and postoperative measurements toward the implanted ear was judged as a weakened response. The examination was carried out 4–6 months after the operation.

Video Head Impulse Test

vHIT was performed using an ICS Impulse type 1085 (GN Otometrics). The patient was seated and asked to focus on a spot 1.5 m away. Then abrupt, unpredictable, small-angle (10–20°) head movements were done in three planes: horizontal, LARP (left anterior–right posterior), and RALP (right anterior–left posterior). In each case, 20 impulses were delivered with a minimum peak head velocity of 150°/s. Normal gain (the quotient of head movement speed and eye movement speed) ranged from 0.6 to 1.2. A gain below 0.6 or the appearance of covert or overt saccades was considered as damage to the particular semicircular canal. The test was conducted preoperatively and 4–6 months postoperatively.

Hearing Preservation

We measured the hearing preservation 3 and 6 months after cochlear implantation using the following formula (36): HP = [1–(PTApost–PTApre)/(PTAmax–PTApre)]*100%, where PTApre is the pure tone average measured preoperatively, PTApost is the pure tone average measured postoperatively, and PTAmax is the maximum level generated by the audiometer. The HP (hearing preservation) values were divided into total loss

of hearing (no detectable hearing), minimal HP (range 1–25%), partial HP (26–75%), and complete HP (>75%) (36).

Statistical Analysis

Statistical analysis was performed using IBM SPSS Statistics v.24. A Mann–Whitney *U*-test was used to examine the relationship between age and postoperative vestibular preservation as well as between hearing preservation (in percent) and vestibular preservation. A Chi-square test was used to investigate the relation between sex, type of electrode, its length, and the postoperative test results and the relation between the postoperative affiliation of the HP group and postoperative vestibular function. A paired-sample *t*-test was applied to assess the latency of the VEMP before and after cochlear implantation. In all cases, $p < 0.05$ was considered statistically significant.

RESULTS

From the initially enrolled group of 149 patients (153 ears), 32 patients (34 ears) were excluded due to complete damage of the vestibulum before implantation according to the criteria described in "Material and methods." The study did not include people who had inner ear malformation (bilateral large vestibular aqueduct syndrome, LVAS, $n = 1$; or an incomplete partition, $n = 1$) or those with other factors affecting the postoperative function of the labyrinth: recurrent vertigo attacks due to possible delayed Meniere's disease within 9 months after cochlear implantation, $n = 1$; the need for reimplantation due to inflammation of the implant bed, $n = 1$; head injury within a few months after cochlear implantation, $n = 1$; the need for reimplantation due to failure of the internal part of the implant, $n = 1$; and Meniere's disease on the implanted side existing preoperatively and active postoperatively, $n = 1$. Additionally, subjects were excluded after a non-standard course of the CI procedure: traumatic electrode insertion ($n = 2$), with the need to apply a trial electrode in one patient, and a narrow round window niche demanding an extended round window approach ($n = 2$).

The final group included 107 patients operated on in the otorhinolaryngosurgery department: 59 females, 48 males, 10.4–80.2 y.o. (M = 44.4, SD = 18.4) with hearing loss lasting from 1.42 to 56 years (M = 22.7; SD = 13.5). The implanted ear was right in 56 cases and left in 51.

Of the 107 patients, 103 were implanted with soft lateral wall electrodes and four with precurved electrodes. Among the 103 patients implanted with soft electrodes, 80 were implanted with ultrasoft Flex electrodes. That is, in terms of inserted electrodes, there were three groups: precurved ($n = 4$), soft/straight ($n = 23$), and ultrasoft ($n = 80$). The range of inserted electrodes included Advanced Bionics HiRes 90k Advantage Mid-scala ($n = 4$), Cochlear Nucleus CI422 ($n = 5$), Cochlear Nucleus CI522 ($n = 4$), Med-El Sonata Standard ($n = 6$), Advanced Bionics HiRes Hi Focus Slim J ($n = 1$), Med-El Sonata Medium ($n = 3$), Med-El Concerto Medium ($n = 3$), Med-El Sonata Form24 ($n = 1$), Med-El Concerto Form24 ($n = 1$), Med-El Sonata Compressed ($n = 1$), Med-El Sonata Flex soft ($n = 10$), Med-El Concerto Flex soft ($n = 2$), Med-El Concerto Flex28 ($n = 8$), Med-El Sonata Flex28 ($n = 20$), Med-El Synchrony Flex28 ($n = 3$), Med-El Sonata$_{Ti100}$ Flex28 ($n = 1$), Med-El Concerto Flex24 ($n = 8$), Med-El Sonata Flex24 ($n = 17$), Med-El Synchrony Flex24 ($n = 2$), Med-El Concerto Flex20 ($n = 5$), and Med-El Sonata Flex20 ($n = 2$).

The tests performed included cVEMP ($n = 103$), oVEMP ($n = 69$), caloric test ($n = 43$), vHIT horizontal semicircular canal ($n = 28$), vHIT anterior semicircular canal ($n = 26$), and vHIT posterior semicircular canal ($n = 25$).

cVEMP

Of the 103 people who underwent a preoperative examination, responses were recorded in 73 cases. We found a postoperative loss of cVEMPs in 14 of 73 patients (19.2%). The preoperative and postoperative latency of P1 and N1 peak did not differ significantly ($p = 0.410$ and $p = 0.157$, respectively). The rate of saccular loss was not affected by sex ($p = 0.554$). However, it depended on age (Mann–Whitney *U*-test: $U = 230$; $p = 0.010$). A preserved cVEMP response was present in 31 women and 28 men aged 10.4 to 68.2 y.o. (M = 36.2, SD = 17.0) and a lost cVEMP response by nine women and five men aged 30–67.3 years (M = 48.6, SD = 11.4). The causes of hearing loss in patients with an abnormal cVEMP response postoperatively were head injuries ($n = 1$; 1.4%), autoimmune inner ear disease ($n = 1$; 1.4%), sudden idiopathic deafness ($n = 3$; 4.1%), viral infection ($n = 2$; 2.7%), and unknown origin ($n = 7$; 9.6%). The etiology of hearing loss in patients with a preserved VEMP response was much wider: acoustic trauma ($n = 1$; 1.4%) cholesteatoma ($n = 1$; 1.4%), TORCH infection ($n = 2$; 2.7%), genetic mutation ($n = 2$; 2.7%), head injury ($n = 1$; 1.4%), effect of ototoxic drugs ($n = 4$; 5.5%), prematurity ($n = 4$; 5.5%), barotrauma ($n = 1$; 1.4%), sudden idiopathic deafness ($n = 6$; 8.2%), unknown origin ($n = 35$; 48.0%), and viral infection ($n = 2$; 2.7%). Due to the wide diversity of hearing loss causes, no statistical analysis of its effect on test results was undertaken. No statistically significant differences were found regarding the effect of electrode type on postoperative vestibular function (perimodiolar vs. straight vs. ultrasoft, $p = 0.097$), although the incidence of saccular damage was lowest in the group of ultrasoft electrodes. In the three groups implanted with the ultraflex, straight, and precurved electrodes, elicitable cVEMPs were found postoperatively in 49 of 57 patients (86.0%), 9 of 14 patients (64.3%), and 1 of 2 patients (50%), respectively. In a further analysis of the effect of electrode length on postoperative cVEMP responses, two patients with incomplete electrode insertion were excluded. Maintenance of saccular responses was seen in 4/6 (66.7%) using 20-mm electrodes, 23/27 (85.2%) using 24-mm electrodes (Flex 24, Form, Medium), 18/20 (90%) using 28-mm electrodes, and 8/11 (72.7%) using 31-mm electrodes (Flex soft, Standard). A similar analysis restricted to the four subgroups of the Flex group (Flex 20, Flex 24, Flex 28, and Flex soft) showed retained cVEMP in 4/6 patients (66.7%), 19/21 patients (90.5%), 18/20 patients (90%), and 6/8 patients (75%), respectively. There was no significant effect of electrode length either by analyzing within the Flex electrodes ($p = 0.367$) or by pairing different types of lateral wall electrodes into groups of the same length

TABLE 1 | Postoperative cVEMP results.

cVEMP test result		Present	Absent
Demographic information	Sex (female:male ratio)	31:28	9:5
	Average age (std. deviation)	36.15 (SD = 17.01)	48.57 (SD = 11.35)
Type of electrode	Perimodiolar	1 (50)	1 (50)
	Straight/soft	9 (64.3)	5 (35.7)
	Ultrasoft	49 (86)	8 (14)
Length of electrode*	Flex 20	4 (66.7)	2 (33.3)
	Flex 24, Form 24, Medium	23 (85.2)	4 (14.8)
	Flex 28	18 (90)	2 (10)
	Flex Soft, Standard	8 (72.7)	3 (27.3)

Figures in brackets for the type and length of electrode are percentages.
**Two patients with incomplete electrode insertion were excluded.*

($p = 0.437$). All the postoperative cVEMP results are summarized in **Table 1**.

oVEMP

Among the 69 oVEMP tests performed on the patients preoperatively, positive responses were recorded in 46 of them. Of the 46 patients, postoperative losses were found in 8 (17.4%). The difference between preoperative and postoperative N1 and P1 latency was not statistically significant ($p = 0.066$ and $p = 0.074$, correspondingly). The loss of response was not influenced by gender ($p = 0.999$) or age ($U = 114.00$; $p = 0.271$), although the mean age of people with oVEMP loss was higher than the mean age of people with preserved oVEMP responses, and the youngest person with loss of utricular function was 34 years old.

oVEMP responses were preserved in 21 women and 17 men, while no response was recorded in four women and four men. The age of the patients with retained oVEMPs ranged from 11.08 to 68.17 y.o. (M = 40.29, SD = 17.52), and the age of those with newly postoperative absent oVEMPs ranged from 34.50 to 64.25 y.o. (M = 48.91, SD = 10.09). Among patients with oVEMP loss, the etiology of hearing loss was unknown ($n = 5$, 14.9%), head injury ($n = 1$; 2.2%), idiopathic sudden deafness ($n = 1$; 2.2%), and autoimmune inner ear disease ($n = 1$; 2.2%). Patients with recorded postoperative utricular responses had the following hearing loss etiology: acoustic trauma ($n = 1$; 2.2%), cholesteatoma ($n = 3$; 6.5%), TORCH infection ($n = 1$; 2.2%), genetic defect ($n = 1$; 2.2%), ototoxic drugs ($n = 1$; 2.2%), post labyrinthitis ($n = 1$; 2.2%), sudden idiopathic deafness ($n = 7$; 13.0%), viral infection ($n = 2$; 4.4%), and unknown ($n = 21$; 45.7%). Due to the multiplicity of etiological factors, their effect on oVEMP responses after CI was not analyzed.

In terms of the impact of electrode type (precurved, straight, ultrasoft) on postoperative oVEMPs, we found retained responses in one of two (50.0%), eight of nine (88.9%), and 29 of 35 (82.9%), respectively. There was no significant correlation between the frequency of oVEMP loss and the type of electrode ($p = 0.421$). When considering the effect of electrode length on the maintenance of oVEMP responses, two patients with incomplete electrode insertion were excluded from the calculations. The results for preserved oVEMPs after CI were 3 out of 4 (75%) for 20 mm, 18 out of 20 (90%) for 24 mm, 9 out of 12 for 28 mm (75%), and 5 out of 5 (100%) for the 31-mm electrode length recipients. If one only takes into consideration electrode length within the Flex group, the percentage of postoperatively recorded oVEMPs was 75% (3 out of 4) for the Flex 20, 86.7% (13 out of 15) for the Flex 24, 75% (9 out of 12) for the Flex 28, and 100% (3 out of 3) for the Flex soft group. Similarly to the cVEMP responses, no statistically significant relationship was found between electrode length and the risk of possible postoperative oVEMP loss, either for the Flex electrodes alone ($p = 0.698$) or when comparing groups of electrodes of the same length ($p = 0.462$). The postoperative prevalence of oVEMPs is shown in **Table 2**.

cVEMP vs. oVEMP

Altogether, 43 patients elicited both cVEMP and oVEMP responses preoperatively.

Of the 34 subjects with a preserved cVEMP response postoperatively, all presented oVEMP responses within the normal range. Of the nine with a lost cVEMP response after CI, six lost the oVEMP response and three retained it. However, in two of three people with a preserved oVEMP response, there was a significant change in the amplitude asymmetry ratio (by 0.58 and 0.47) with the weakness on the implanted side, and in one other there was only a slight change in this index (0.19) with a correct value in the postoperative examination (0.30 with a predominance of the implanted side). Among 37 subjects with a preserved oVEMP response after CI, 34 presented cVEMP responses simultaneously and 3 patients lost cVEMPs. All six subjects with postoperative oVEMP loss did present cVEMP loss. In summary, maintenance of the cVEMP response (an indicator of saccule function) was always associated with a preserved oVEMP response (which assesses utricle function), whereas loss of oVEMP response was always associated with a loss of cVEMP response.

Caloric Test

The caloric test was performed pre- and postoperatively in 43 patients, five of whom (11.6%) had a postoperative change in unilateral weakness UW >25% toward the implanted ear.

TABLE 2 | Postoperative oVEMP results.

oVEMP test result		Present	Absent
Demographic information	Sex (female:male ratio)	21:17	4:4
	Average age (std. deviation)	40.29 (SD = 17.52)	48.91 (SD = 10.09)
Type of electrode	Perimodiolar	1 (50.0)	1 (50.0)
	Soft	8 (88.9)	1 (11.1)
	Ultrasoft	29 (82.9)	6 (17.1)
Length of electrode*	Flex 20	3 (75.0)	1 (25)
	Flex 24, Form 24, Medium	18 (90.0)	2 (20.0)
	Flex 28	9 (75.0)	3 (25.0)
	Flex Soft, Standard	5 (100)	0 (0)

Numbers in brackets for the type and length of electrode are in percentage.
**Two patients with incomplete electrode insertion were excluded.*

The group with maintained caloric response consisted of 20 females and 18 males aged 12.3–80.2 years (M = 49.5, SD = 17.8), and those with a weakened response after CI were represented by three females and two males aged 26.0 to 74.8 years (M = 55.4, SD = 18.6). The results were not affected by the age of the patients according to a Mann–Whitney *U*-test ($U = 75$, $p = 0.449$). Due to the small size of the group with weakened responses in the caloric sample, no further statistical analysis was undertaken. The CI recipients with weakened caloric response were implanted with Flex28 ($n = 2$), Flex28 ($n = 1$), Flex soft ($n = 1$), and Medium ($n = 1$), and their hearing losses were caused by ototoxic drugs ($n = 1$), Meniere's disease ($n = 1$), viral infection ($n = 1$), sudden idiopathic deafness ($n = 1$), and unknown factor ($n = 1$). Patients with preserved caloric responses received the following electrodes: CI 422 ($n = 2$; 4.7%), CI 522 ($n = 1$; 2.3%), Compressed ($n = 1$; 2.3%), Flex 20 ($n = 4$; 9.3%), Flex 24 ($n = 8$; 18.6%), Flex 28 ($n = 12$; 27.9%), Form 24 ($n = 1$; 2.3%), Medium ($n = 2$; 4.7%), Mid-scala ($n = 4$; 9.3%), Standard ($n = 2$; 4.7%), and SlimJ ($n = 1$; 2.3%). Their hearing loss etiology was as follows: idiopathic sudden deafness ($n = 3$; 4.7%), acoustic trauma ($n = 2$; 2.3%), cholesteatoma ($n = 1$; 2.3%), genetic ($n = 1$; 2.3%), head trauma ($n = 1$; 2.3%), otosclerosis ($n = 3$; 7.0%), postinflammatory ($n = 2$, 4.7%), Meniere's disease ($n = 1$; 2.3%), autoimmune inner ear disease ($n = 1$; 2.3%), and unknown ($n = 22$; 51.2%).

Among five subjects with weakened caloric responses postoperatively, two of them also showed a loss of cVEMP response, in two cVEMPs were not done, and one patient had a preserved response (with a change in the amplitude asymmetry index by 0.36 with weakness of the implanted ear). oVEMP response in the group with weakened caloric response was as follows: absent in one patient postoperatively, absent in one patient already preoperatively, preserved in one patient (with a change in the amplitude asymmetry index of 0.59 showing weakness of the implanted side), and two patients not tested. The results of caloric tests after CI are shown in **Table 3**.

TABLE 3 | Caloric test postoperative results.

Caloric test result		Normal	Weakness
Demographic information	Sex (female:male ratio)	20:18	3:2
	Average age (std. deviation)	49 (SD = 17.8)	55 (SD = 18.6)
Type of electrode	Perimodiolar	4 (100)	0 (0)
	Soft	10 (90.9)	1 (9.1)
	Ultrasoft	24 (85.71)	4 (14.3)

vHIT

Postoperative damage to the lateral semicircular canal was found in 2 of 28 patients (7.1%), the anterior semicircular canal in 1 of 26 (3.9%), and the posterior semicircular canal in 1 of 25 (4.0%) patients. One of the patients had damage to all semicircular canals (64.8 y.o. male, RWA, Flex 28). The second patient lost function in the lateral canal, while the anterior and posterior canals presented responses within the normal range (61.7 y.o. female, RWA, Flex soft).

vHIT was preserved in 15 women and 11 men, aged 12.3 to 77.3 years (M = 49.8, SD = 17.7).

Hearing Preservation

Hearing preservation (HP) was assessed 3 and 6 months postoperatively in 79 CI recipients who had significant preoperative low-frequency residual hearing and so had undergone PDT-EC and PDT-EAS cochlear implantation. cVEMP and oVEMP results were compared with HP at 3 months and with the caloric test, and vHIT results were compared with HP at 6 months after CI, matching the timeline of vestibular tests. Of 10 patients who had postoperative loss of cVEMP responses, hearing preservation ranged from 0 to 100% (M = 48.1%, SD = 42.9) and was described as complete HP ($n = 3$; 30%), partial HP ($n = 3$; 30%), or total hearing loss ($n = 4$; 40%). There were 49 patients with retained cVEMPs who presented HP of 31–100% (M = 79.9%, SD = 19.9) and were classified as partial HP ($n = 17$; 34.7%) or complete HP ($n = 32$; 65.3%). The difference in HP between both groups (lost vs. maintained cVEMPs) was statistically significant in both percentage of preserved hearing ($U = 146$; $p = 0.042$) and affiliation to the particular group

($p = 0.001$). There were six people who lost oVEMPs after CI who had preserved hearing postoperatively consisting of two patients (33.3%) with complete HP, one patient (16.7%) with partial HP, and three patients (50%) with hearing loss (M = 43.9%, SD = 47.4%). Maintained postoperative oVEMP responses ($n = 33$) together with hearing preservation ranged from 31 to 100% (M = 82.7%, SD = 20.5%), and there were 25 CI recipients (75.8%) with complete HP and eight (24.2%) with partial HP. The difference in HP between the patients with and without maintained oVEMPs postoperatively was on the border of statistical significance ($U = 50.5$, $p = 0.054$) and statistical significance ($p < 0.001$) if one considers the percentage and affiliation to each group, respectively. In case of the caloric tests, three patients with weakened responses after CI achieved hearing preservation (0, 55.8, and 60%) 6 months postoperatively (M = 38.6%, SD = 33.5%) and were consequently classified as partial HP ($n = 2$; 66.7%) or total hearing loss ($n = 1$; 33.3%). In contrast, among 25 people with maintained postoperatively caloric responses, hearing preservation was 0 to 100% (M = 72.7%, SD = 26.1%), and so 10 patients (41.7%) were classified as having complete HP, 12 patients (50%) with partial HP, and two patients (8.4%) with total hearing loss. Due to the small numbers, a statistical analysis was not undertaken.

In one case of lateral, anterior, and posterior semicircular canal loss in vHIT, hearing loss of 0% was measured. However, in the group of 16 patients with correct vHIT in the horizontal plane after CI, it was found that seven (43.8%) had complete HP, five (31.3%) had partial HP, and four (25.0%) had total hearing loss (HP ranged from 0 to 100% with M = 58.3 and SD = 36.1). Similarly, in 15 cases of preserved vHIT for the anterior semicircular canal after CI, HP ranged from 0 to 100% (M = 62.2, SD = 33.8) with three patients (20.0%) having total hearing loss, seven (46.7%) with complete HP, and five (33.3%) with partial HP. Finally, the group with correct postoperative vHIT responses for the posterior semicircular canal ($n = 14$) was characterized by HP of 0 to 100% (M = 63.5%, SD = 34.7) and their group affiliations were eight complete HP (57.1%), four partial HP (28.6%), and three total hearing loss (21.4%).

DISCUSSION

Much research has been done on assessing vestibular function after cochlear implantation surgery, looking for differences in surgical techniques and approaches (in particular, cochleostomy vs. the round window approach) (16–28). A review of the literature does not actually give a clear answer to which access route is better in terms of vestibular preservation. Even trying to define the incidence of vestibular damage after cochlear implantation encounters problems.

In addressing the problem of vestibular damage after a CI, there is first a need to define the criteria of how to analyze and compare otoneurological tests (cVEMP, oVEMP, caloric response, and vHIT) pre- and postoperatively, since there is a definite lack of uniformity in the literature. These criteria should specify which change in response represents definite vestibular damage rather than just say that the test is within or beyond norms.

In the case of the caloric test, the slow component velocity (SCV) may depend on many factors such as the patient's alertness or small differences in performing the exam. It is possible that day-to-day changes in this parameter can be observed even when there are no vestibular changes. UW (unilateral weakness) is a much more reliable parameter to compare. Nevertheless, only specifying a change between categories (normal vs. hyporeflexia vs. areflexia) may falsely lead one to say that there is vestibular damage among patients with borderline Unilateral Weakness (UW), even though the UW change is not significant. Proctor et al. and Piker et al. investigated the minimum detectable change in UW in test–retest exams and found that it was 24% (37) and 23% (38), respectively. It therefore seems reasonable to take a change of UW $\geq$25% as a marker of lateral semicircular canal damage.

Interpreting vHIT exams is more clear-cut, and detecting new overt or covert saccades in the postoperative period, or drop in the gain of head movement/eye movement to <0.6, should be recognized as vestibular damage. However, the sensitivity of vHIT is a matter for further research and many papers indicate that, among patients with vestibular neuritis or other symptoms suggestive of impairment, a lower percentage have vestibular damage detected by vHIT than by the caloric test (39–41). The same discrepancy was observed in our study. Despite its high specificity, vHIT may not be ideal for identifying minor changes within the vestibule after a CI.

cVEMP and oVEMP are thought to be the most sensitive tools to detect post-CI changes in the vestibulum as they represent the most fragile organs, the saccule and the utricle. The loss of cVEMPs or oVEMPs should be treated as vestibular damage unless there is conductive hearing loss. However, vestibular damage may lead not only to total loss but also to a decrease in amplitude, making analysis more complicated. Comparing the corrected P1–N1 amplitude in cVEMPs, or N1–P1 amplitude in oVEMPs, between pre- and postoperative exams may be erroneous, although some good test–retest reliability has been reported (42). No strict threshold for vestibular damage has yet been identified in terms of change in amplitude or amplitude asymmetry ratio. Elevated thresholds for eliciting VEMPs after a CI procedure may be a good marker of otolith hypofunction. It is worth mentioning that measuring a VEMP threshold extends recording time and necessitates stimulating the ear with multiple high-intensity sounds.

Our study has shown that, based on a wide range of electrodes, partial deafness treatment is protective in terms of vestibular preservation. However, the risk of postoperative vestibular damage is not eliminated. It gives a rate of saccular damage of 19.2% and utricular damage of 17.4% measured by VEMP loss. A reduction in horizontal semicircular canal response was noticed in 11.6% if measured by the caloric response, and damage to the horizontal, anterior, and posterior semicircular canals, as measured by vHIT,

of 7.1, 3.9, and 4%, respectively. Hearing preservation was associated with maintenance of vestibular function, and the relation was statistically significant. Patients with elicitable VEMP responses after a CI had at least partially preserved hearing, but never total hearing loss. Weakened caloric tests postoperatively were always associated with at least partial hearing loss.

To properly discuss the counseling of CI candidates, certain facts about central compensation of the unilateral and bilateral vestibular damage need to be recalled. Unilateral vestibular damage can be treated with vestibular rehabilitation including Cawthorne–Cooksey exercises, optokinetic training, virtual reality games, or posturographic training. Such exercises are effective and end with full recovery unless additional comorbidities exist (neurological, psychiatric, orthopedic, ophthalmologic). With bilateral vestibular damage, many functions are affected: postural stability, visual stability during head movements, autonomic cardiovascular reaction of the lower part of the body while standing, cognitive abilities like spatial orientation, navigation abilities, and impairment in dual tasking (10, 42). Only 50% of patients with bilateral hypofunction profit from vestibular rehabilitation (10). In addition, balance may get worse with age and sudden falls may occur. Some symptoms can be easily relieved by rehabilitation exercises like postural stability on an even ground and autonomic vessel reactions in an upright position. Others, like the vestibulo-ocular reflex, can only be partly compensated for by the cervico-ocular reflex or predictive saccades, with handicaps remaining in response to abrupt, unpredictable head movements (43–45). For these reasons, it is reasonable to recommend caution and to consider the potential audiological benefits when deciding to give a second implant in the only-functioning or better vestibulum. The increasing interest in a vestibular prosthesis (46, 47) and vestibulocochlear implants (48) may change our attitude toward bilateral loss of vestibular input. However, as long as such efforts are still under development, and restricted to single clinics and small groups of patients (46–49), we should avoid bilateral vestibular loss.

Our PDT implantation strategy involves applying "soft surgery": the use of a round window approach via scala tympani which lowers the risk of misinsertion, the administration of postoperative steroids, micropuncture of the round window membrane, insertion of soft electrodes, and reduced insertion angles.

Histological studies have found that vestibular damage is significantly reduced when the electrode is inserted into scala tympani (3, 49). Temporal bone studies indicate that the scala height at the central and lateral portions of scala tympani decreases with increasing distance from the round window (with significant reduction after 450°), whereas the height of the modiolar area remains nearly constant. This increases the risk of unwanted contact of the electrode with the basilar membrane, spiral ligament, or the osseous spiral lamina and consequently the risk of intracochlear trauma. Also, the mechanical properties of the basilar membrane are different depending on the distance from the round window, while the thickness of this structure decreases toward the apex (50–52).

To avoid intracochlear trauma by deep electrode insertion, a flex electrode is used. It has special features such as the five most apical electrode contacts being single, whereas the basal seven electrodes are paired, reducing the diameter of the electrode tip.

Despite the above anatomical facts, we did not find any strong relationship between either electrode type or length and postoperative vestibular function. However, the multiple types of electrodes used restrict the statistical power of being able to see the effect of electrode type on the incidence of vestibular damage. This also agrees with other reports. Nordfalk et al. (22) measured a loss of VEMP responses in five of 14 patients (35.7%) and weakened caloric responses in four out of 10 patients (40%) implanted with a Flex 28 electrode via a round window approach, but, due to the small number of patients, they did not discuss the results of inserting shorter electrodes. Louza and colleagues (25) did not find any statistically significant relationship between postoperative vestibular function and the insertion depth of the electrode (276–707°).

CONCLUSIONS

Hearing preservation techniques in cochlear implantation are connected with vestibular protection, but the risk of vestibular damage is never totally eliminated. The vestibular preservation is associated with hearing preservation, and the relation is statistically significant. Special care and counseling are recommended when qualifying a patient for implantation when that ear has the only (or better) vestibulum, since there is then the risk of bilateral hypofunction or areflexia. Similarly, caution is needed for a patient with comorbidities affecting central nervous system compensation. Therefore, preoperative otoneurological diagnostics are necessary in the following situations: qualification for a second implant, after otosurgery (especially if the opposite ear is to be implanted), with a history of vestibular complaints, with comorbidities that may result in impairment of central compensation mechanisms, and in those who do not have any strict audiological and anatomical indication about which side to operate.

DATA AVAILABILITY STATEMENT

The datasets generated for this article are not readily available because the patients did not agree to share their data publicly. The datasets are stored on an internal server and are only available to co-workers. All data related to people in the European Union (EU) is protected by law of the General Data Protection Regulation (GDPR). Requests to access the datasets should be directed to m.sosna@ifps.org.pl.

ETHICS STATEMENT

The studies involving human participants were reviewed and approved by Institutional board's ethics committee–Institute of Physiology and Pathology of Hearing, Warsaw, Poland. Written informed consent to participate in this study was provided by each participant or the participants' legal guardian (Only by legal quardian, not next of kin).

AUTHOR CONTRIBUTIONS

MS-D: study design, data collection, data interpretation, preparation of manuscript, literature analysis. GT: data interpretation, preparation of manuscript. EG: data analysis/statistics. AK: data collection, preparation of manuscript. PS and HS: study design, data collection. All authors contributed to the article and approved the submitted version.

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REFERENCES

1. Fina M, Skinner M, Goebel JA, Piccirillo JF, Neely JG. Vestibular dysfunction after cochlear implantation. *Otol Neurotol*. (2003) 24:234–42. doi: 10.1097/00129492-200303000-00018
2. Kubo T, Yamamoto K, Iwaki T, Doi K, Tamura M. Different forms of dizziness occurring after cochlear implant. *Eur Arch Otorhinolaryngol*. (2001) 258:9–12. doi: 10.1007/PL00007519
3. Tien H-C, Linthicum FH. Histopathologic changes in the vestibule after cochlear implantation. *Otolaryngol Head Neck Surgery*. (2002) 127:260–64. doi: 10.1067/mhn.2002.128555
4. Eshragi AA, Lang DM, Roell J, Van de Water TR, Garnham C, Rodrigues H, et al. Mechanismis of programmed cell death signaling in hair cells and support cells post-electrode insertion trauma. *Acta Otolaryngol*. (2015) 135:328–34. doi: 10.3109/00016489.2015.1012276
5. Finke M, Bönitz H, Lyxell B, Illg A. Cochlear implant effective-ness in postlingual single-sided deaf individuals: what's the point? *Int J Audiol*. (2017) 56:417–23. doi: 10.1080/14992027.2017.1296595
6. Skarzynski H, Lorens A, Piotrowska A, Anderson I. Preservation of low frequency hearing in partial deafness CI (PDCI) using the round window surgical approach. *Acta Otolaryngol*. (2007) 127:41–8. doi: 10.1080/00016480500488917
7. Ghiselli S, Nedic S, Montino S, Astolfi L, Bovo R. Cochlear implantation in post-lingually deafened adults and elderly patients: analysis of audiometric and speech perception outcomes during the first year of use. *Acta Otorhinolaryngol Italy*. (2016) 36:513–19. doi: 10.14639/0392-100X-1222
8. Moeller MP, Stille LJ, Hughes ML, Lusk RP. Perceived improvements and challenges following sequential bilateral cochlear implantation in children and adults. *Cochlear Implants Int*. (2018) 19:72–87. doi: 10.1080/14670100.2017.1414021
9. Sosna M, Tacikowska G, Pietrasik K, Skarzynski H, Skarzynski PH. Vestibular status in partial deafness. *Braz J Otorhinolaryngol*. (2019) 20: S1808-8694(19)30143-0. doi: 10.1016/j.bjorl.2019.09.012
10. Gillespie MB, Minor LB. Prognosis in bilateral vestibular hypofunction. *Laryngoscope*. (1999) 109:35–41. doi: 10.1097/00005537-199901000-00008
11. Lehnhardt E. Intracochlear placement of cochlear implant electrodes in soft surgery technique. *HNO*. (1993) 41:356–9
12. Gstoettner W, Kiefer J, Baumgartner WD, Pok S, Peters S, Adunka O. Hearing preservation in cochlear implantation for electric acoustic stimulation. *Acta Otolaryngol*. (2004) 124:348–52. doi: 10.1080/00016480410016432
13. Skarzynski H, Lorens A. Partial deafness treatment. *Cochlear Implants Int*. (2010) 11:29–41. doi: 10.1179/146701010X12671178390799
14. O'Connell BP, Hunter JB, Haynes DS, Holder JT, Dedmon MM, Noble JH, et al. Insertion depth impacts speech perception and hearing preservation for lateral wall elec-trodes. *Laryngoscope*. (2017) 127:2352–7. doi: 10.1002/lary.26467
15. Lo J, Campbell L, Sale P, Chambers S, Hampson A, Eastwood H, et al. The role of preoperative steroids in atraumatic cochlear implantation surgery. *Otol Neurotol*. (2017) 38:1118–24. doi: 10.1097/MAO.0000000000001505
16. Krause E, Louza JPR, Wechtenbruch J, Gürkov R. Influence of cochlear implantation on peripheral vestibular receptor function. *Otolaryngol Head Neck Surg*. (2010) 142:809–13. doi: 10.1016/j.otohns.2010.01.017
17. Migliaccio AA, Della Santina CC, Carey JP, Niparko JK, Minor LB. The vestibulo-ocular reflex response to head impulses rarely decreases after cochlear implantation. *Otol Neurotol*. (2005) 26:655–60. doi: 10.1097/01.mao.0000178125.20741.27
18. Todt I, Basta D, Ernst A. Does the surgical approach in cochlear implantation influence the occurrence of postopera-tive vertigo? *Otolaryngol Head Neck Surg*. (2008) 138:8–12. doi: 10.1016/j.otohns.2007.09.003
19. Rah YC, Park JH, Park JH, Choi BY, Koo JW. Dizziness and vestibular function before and after cochlear implantation. *Eur Arch Otorhinolaryngol*. (2016) 273:3615–21. doi: 10.1007/s00405-016-3988-3
20. Melvin T-AN, Della Santina CC, Carey JP, Migliaccio AA. The effects of cochlear implantation on vestibular function. *Otol Neurotol*. (2009) 30:87–94. doi: 10.1097/MAO.0b013e31818d1cba
21. Chen X, Chen X, Zhang F, Qin Z. Influence of cochlear implantation on vestibular function. *Acta Otolaryngol*. (2016) 136:655–9. doi: 10.3109/00016489.2016.1154186
22. Nordfalk KF, Rasmussen K, Hopp E, Bunne M, Silvola JT, Jablonski GE. Insertion depth in cochlear implantation and outcome in residual hearing and vestibular function. *Ear Hear*. (2016) 37:129–37. doi: 10.1097/AUD.0000000000000241
23. Meli A, Aud BM, Aud ST, Aud RG, Cristofari E. Vestibular function after cochlear implant surgery. *Cochlear Implants Int*. (2016) 17:151–7. doi: 10.1179/1754762815Y.0000000014
24. Robard L, Hitier M, Lebas C, Moreau S. Vestibular func-tion and cochlear implant. *Eur Arch Otorhinolaryngol*. (2015) 272:523–30. doi: 10.1007/s00405-014-3040-4
25. Louza J, Mertes L, Braun T, Gürkov R, Krause E. Influence of insertion depth in cochlear implantation on vertigo symptoms and ves-tibular function. *Am J Otolaryngol*. (2015) 36:254–8. o.2014.11.007 doi: 10.1016/j.amjoto.2014.11.007
26. Tsukada K, Moteki H, Fukuoka H, Iwasaki S, Usami SI. Effects of EAS cochlear implantation surgery on vestibular function. *Acta Otolaryngol*. (2013) 133:1128–32. doi: 10.3109/00016489.2013.824110
27. Dagkiran M, Tuncer U, Surmelioglu O, Tarkan O, Ozdemir S, Cetik F, et al. How does cochlear implantation affect five vestibular end-organ functions and dizziness? *Auris Nasus Larynx*. (2018) 46 :P178–85. doi: 10.1016/j.anl.2018.07.004
28. Stultiens JJA, Kieft HW, Mylanus EAM, Pennings RJE, Terwoert L, Beynon AJ. Impact of cochlear implantation on the function of the three semicircular canals. *Int J Audiol Nov*. (2020) 59:843–9. doi: 10.1080/14992027.2020.1768310
29. Podskarbi-Fayette R, Pilka A, Skarzynski H. Electric stimu-lation complements functional residual hearing in partial deafness. *Acta Otolaryngol*. (2010) 130:888–96. doi: 10.3109/00016480903567189
30. Skarzynski H, Lorens A, Dziendziel B, Skarzynski PH. Expanding pediatric cochlear implant candidacy: a case study of electro-natural stimulation (ENS) in partial deafness treatment. *Int J Pediatr Otorhinolaryngol*. (2015) 79:1896–900. doi: 10.1016/j.ijporl.2015.08.040
31. Akin FW, Murnane OD, Proffitt TM. The effects of click and tone-burst stimulus parameters on the vestibular evoked myogenic potential (VEMP). *J Am Acad Audiol*. (2003) 14:500–9. doi: 10.3766/jaaa.14.9.5
32. Takahashi K, Tanaka O, Kudo Y, Sugawara E, Johkura K. Effects of stimulus conditions on vestibular evoked myogenic potentials in healthy subjects. *Acta Otolaryngol*. (2019) 139:500–4. doi: 10.1080/00016489.2019.1592224
33. Yi-Ho Y, Chen-Chi W, Chih-Hsiu W. Augmentation of vestibular evoked myogenic potentials: an indication for distended saccular hydrops. *Laryngoscope*. (2009) 112:509–12. doi: 10.1097/00005537-200203000-00019
34. Kantner C, Gürkov R. The effects of commonly used upward gaze angles on ocular vestibular evoked myogenic potentials. *Otol Neurotol*. (2014) 35:289–93. doi: 10.1097/MAO.0b013e318299a812

35. Piker EG, Jacobson GP, McCaslin DL, Hood LJ. Normal characteristics of the ocular vestibular evoked myogenic potential. *J Am Acad Audiol*. (2011) 22:222–30. doi: 10.3766/jaaa.22.4.5
36. Skarzynski H, van de Heyning P, Agrawal S, Arauz SL, Atlas M, Baumgartner W, et al. Towards a consensus on a hearing preservation classification system. *Acta Otolaryngol Suppl*. (2013) 564:3–13. doi: 10.3109/00016489.2013.869059
37. Proctor L, Glackin R, Shimizu H, Smith C, Lietman P. Reference values for serial vestibular testing. *Ann Otol Rhinol Laryngol*. (1986) 95:83–90. doi: 10.1177/000348948609500118
38. Piker EG. Minimal detectable change in caloric test. In: *Podium Presentation at the Annual Meeting of the American Balance Society*. Scottsdale, AZ. (March 2018).
39. Bell LS, Barker F, Heselton H, MacKenzie E, Dewhurst D, Sanderson A. A study of the relationship between the video head impulse test and air calorics. *Eur Arch Otorhinolaringol*. (2015) 272:1287–94. doi: 10.1007/s00405-014-3397-4
40. Mezzalira R, Bittar RSM, Bilecki-Stipsky MM, Brugnera C, Grasel SS. Sensitivity of caloric test and video head impulse as screening test for chronic vestibular complaints. *Clinics (Saõ Paulo)*. (2017) 72: 469–73. doi: 10.6061/clinics/2017(08)03
41. McCaslin DL, Jacobson GP, Bennett ML, Gruenwald JM, Green AP. Predictive properties of the video head impulse test: measures of caloric symmetry and self-report dizziness handicap. *Ear Hear*. (2014) 35:e185–91. doi: 10.1097/AUD.0000000000000047
42. Nguyen KD, Welgampola MS, Carey JP. Test-retest reliability and age-related characteristics of the ocular and cervical vestibular evoked myogenic potential tests. *Otol Neurotol*. (2010) 31:793–802. doi: 10.1097/MAO.0b013e3181e3d60e
43. McCall A, Yates B. Compensation following bilateral vestibular damage. *Front Neurol*. (2011) 2: 88. doi: 10.3389/fneur.2011.00088
44. Herdmann SJ, Schubert MC, Tusa RJ. Role of central preprogramming in dynamic visual acuity with vestibular loss. *Arch Otolaryngol Head Neck Surg*. (2001) 127 :1205–10. doi: 10.1001/archotol.127.10.1205
45. Mac Dougall HG, Curthoys IS. Plasticity during vestibular compensation: the role of saccades. *Front Neurol*. (2012) 3:21. doi: 10.3389/fneur.2012.00021
46. Della S.antina CC, Migliaccio AA, Hayden R, Melvin TA, Fridman GY, Chiang B, et al. Current and future managment of bilateral loss of vestibular sensation – an update of John Hopkins Multichannel Prosthesis Project. *Cochlear Implants Int*. (2010) 11 (Suppl. 2):2–11. doi: 10.1179/146701010X12726366068454
47. Rubinstein J, Bierer S, Kaneko Ch, Ling L, Nie K, Oxford T, et al. Implantation of the semicircular canals with preservation of hearing and rotational sensitivity: a vestibular neurostimulator suitable for clinical research. *Otol Neurotol Jul*. (2012) 33(5):789–96. doi: 10.1097/MAO.0b013e318254ec24
48. Fornos AP, Cavuscens S, Ranieri M, van de Berg R, Stokroos R, Kingma H, et al. The vestibular implant: a probe in orbit around the human balance system. *J Vestib Res*. (2017) 27:51–61. doi: 10.3233/VES-170604
49. Handzel O, Burgess BJ, Nadol JB. Histopathology of the peripheral vestibular system after cochlear implantation in the human. *Otol Neurotol*. (2006) 27:57–64 doi: 10.1097/01.mao.0000188658.36327.8f
50. Avci E, Nauwelaers T, Lenarz T, Hamacher V, Kral A. Variations in microanatomy of the human cochlea. *J Comp Neurol*. (2014) 522:3245–61. doi: 10.1002/cne.23594
51. Biedron S, Prescher A, Ilgner J, Westhofen M. The internal dimensions of the cochlear scalae with special reference to cochlear electrode insertion trauma. *Otol Neurotol*. (2010) 31:731–7 doi: 10.1097/MAO.0b013e3181d27b5e
52. Ishii T, Takayama M, Takahashi Y. Mechanical properties of human round window, basilar and Reissner's membranes. *Acta Otolaryngol Suppl*. (1995) 519:78–82. doi: 10.3109/00016489509121875

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Differences in Vestibular-Evoked Myogenic Potential Responses by Using Cochlear Implant and Otolith Organ Direct Stimulation

Isaura Rodriguez Montesdeoca[1†], *Angel Ramos de Miguel*[2*†], *Juan Carlos Falcon González*[1†], *Silvia Borkoski Barreiro*[1†], *Nicolás Pérez Fernández*[3], *Robby Vanspauwen*[4] and *Angel Ramos-Macias*[1,2†]

[1] Department of Otolaryngology, Head and Neck Surgery, Complejo Hospitalario Universitario Insular Materno Infantil de Gran Canaria, Las Palmas, Spain, [2] Hearing and Balance Laboratory, Las Palmas de Gran Canaria University (SIANI), Las Palmas, Spain, [3] Otorhinolaryngology Department, Clinica Universidad de Navarra, Pamplona, Spain, [4] European Institute for Otorhinolaryngology Head and Neck Surgery, Gasthuiszusters Antwerpen Hospitals Antwerp, Wilrijk, Belgium

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***Correspondence:**
Angel Ramos de Miguel
aramos.gcc@gmail.com

[†]These authors have contributed equally to this work and share first authorship

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Objective: Several studies have demonstrated the possibility to obtain vestibular potentials elicited with electrical stimulation from cochlear and vestibular implants. The objective of this study is to analyze the vestibular-evoked myogenic potentials (VEMPs) obtained from patients implanted with cochlear and vestibulo-cochlear implant.

Material and Methods: We compared two groups: in the first group, four cochlear implant (CI) recipients with present acoustic cVEMPs before CI surgery were included. In the second group, three patients with bilaterally absent cVEMPs and bilateral vestibular dysfunction were selected. The latter group received a unilateral cochleo-vestibular implant. We analyze the electrically elicited cVEMPs in all patients after stimulation with cochlear and vestibular electrode array stimulation.

Results: We present the results obtained post-operatively in both groups. All patients (100%) with direct electrical vestibular stimulation *via* the vestibular electrode array had present cVEMPs. The P1 and N1 latencies were 11.33–13.6 ms and 18.3–21 ms, respectively. In CI patients, electrical cVEMPs were present only in one of the four subjects (25%) with cochlear implant ("cross") stimulation, and P1 and N1 latencies were 9.67 and 16.33, respectively. In these patients, the responses present shorter latencies than those observed acoustically.

Conclusions: Electrically evoked cVEMPs can be present after cochlear and vestibular stimulation and suggest stimulation of vestibular elements, although clinical effect must be further studied.

Keywords: electrical stimulation, vestibular implant, balance, bilateral vestibulopathy, vestibulo-collic reflex, CVEMPs

INTRODUCTION

Vestibular system is essential for the sense of balance. It contributes to gaze stabilization through the action of the vestibulo-ocular reflex (VOR) and head stabilization in space through the activation of the neck musculature and control of posture through the vestibulocollic reflex (VCR) and the related cervicocollic reflex (CCR) complementing the VOR (1).

In bilateral vestibulopathy (BVP), patients' susceptibility for falling increases, with a higher risk of accidental injury or even death (2). Thus, for this kind of patients, therapeutic management becomes complicated because there is no effective treatment able to restore vestibular function (3–5). Vestibular rehabilitation and galvanic stimulation have been used and have a positive functional impact for these patients (6–8). In view of the foregoing, the vestibular implant represents a new vestibular rehabilitation tool with promising results (9).

Vestibular implants are based on electrical stimulation principles that were described for the first time by Suzuki and Cohen, pioneers in the electrical stimulation of the vestibular nerve branches (10). As indicated in previous studies, there are several ways of vestibular electrical stimulation that are under investigation. In our present research, we will analyze two of them: vestibular cross-stimulation using a cochlear implant (CI) and direct vestibular stimulation using a vestibular implant.

In the case of costimulation, it has been observed that the effects on the vestibular portion of the inner ear remain unclear. Histopathological studies of cadaveric temporal bones after CI demonstrated vestibular damage. Fibrosis of the vestibule and distortion of the saccular membrane have been observed (11). On the other side, reports of improved balance function after cochlear implant activation suggest that CI also have a positive impact on the vestibular system. There are also evidence that suggest that peripheral vestibular afferents are preserved after CI, even after end organ trauma (12). As stimulation current can widely spread from an intracochlear electrode array to the facial nerve, the possibility of a vestibular cross-stimulation must be also considered (13). Vestibular-evoked myogenic potentials (VEMPs) first reported by Colebatch and Halmagyi (14) are electromyographic responses from the vestibule evoked by sound, vibration, or electrical stimulation. In our study, we will reach conclusions largely based on this test results that analyze the otolith organs. Saccule and utricle constitute the otolith organs, which are sensors of linear acceleration and related reflex pathways.

On the other hand, direct electrical stimulation by vestibular implant has aimed to restore vestibular function as a whole; until now, the research has focused mainly on the restoration of the vestibulo-ocular reflex. However, recent studies have begun to evaluate the effect in the vestibulocollic and vestibulospinal reflexes (15, 16).

Abbreviations: BVP, bilateral vestibulopathy; CCR, cervicocollic reflex; cVEMP, cervical-vestibular evoked myogenic potentials; DVA, dynamic visual acuity; EcVEMPs, electrical cervical vestibular-evoked myogenic potentials; CI, cochlear implant; SHV, subjective visual horizontal; SVV, subjective visual vertical; VCR, vestibulocollic reflex; VI, vestibular implant; VEMPs, vestibular-evoked myogenic potentials; VHIT, vestibular head impulse test; VOR, vestibulo-ocular reflex.

The objective of our study is to verify if the vestibulocollic reflex (VCR) may be evoked by electrical stimulation through a cochlear and vestibular implant. For this purpose, the EcVEMPs of the patients after implantation were analyzed.

MATERIALS AND METHODS

Prospective, Observational, and Descriptive Study

Seven patients were included in this study between May 2019 and December 2019, divided in two groups: the cochlear implant group and the vestibular implant group. In the cochlear implant group, four patients presented severe hearing loss. In all cases, acoustic VEMP responses were present before cochlear implant implantation. In the vestibular implant group, three patients had bilateral vestibular dysfunction (BVD) and met the inclusion criteria for vestibular implantation research, which have been described in detail in a previous study (17). All three of these patients also had severe hearing loss. All patients were selected and implanted by the same surgical team (**Table 1**).

Cochlear Implant Group (Four Patients)

Two patients received a CI532® implant (perimodiolar) (one case unilateral CI and one case bilateral CI). One of those cases preserved residual hearing after surgery. One case received a CI512® (straight electrode array). The surgical technique was standardized including electrode round window approach in all cases (**Table 2**).

Vestibular Implant Group (Three Patients)

Three patients with BVL received a new research vestibular implant (VI). The VI is a custom-modified cochlear implant with a full-band straight electrode, CI24RE (ST), from Cochlear Ltd (Lane Cove, NSW, Australia) with three active electrodes for VI stimulation (17). Full-band electrodes were selected to assure that the electrodes were facing the closest area of neural tissue related to the saccular area. For the cochlear stimulation, a Cochlear CI532® perimodiolar electrode array (Cochlear Ltd., Sydney, NSW, Australia) was used in all of them (**Table 2**).

VEMP Testing

All patients underwent cVEMP recordings, before and after surgery. In order to obtain EcVEMP recordings after surgery, a second test using Cochlear's Custom Sound Evoked Potential Software tool (version 5.2) was used. In this study, cervical vestibular-evoked myogenic potentials were obtained by using Eclipse EP 15/EP25/VEMPs (Interacoustics AS, Assens, Denmark system). In order to determine the accuracy of the calibration method, the active electromyogram (EMG) electrode was placed over on the upper third to midpoint of the sternocleidomastoid (SCM) muscle; a reference electrode was placed on the sternum, and the ground electrode was placed on the forehead. The sitting patients were instructed to turn the head >45° to the contralateral side, in order to achieve the maximum sternocleidomastoid contraction, to generate a constant tonic tension of the SCM during the recording.

TABLE 1 | Clinical data of both vestibular and cochlear implanted patients (group 1: cochleo-vestibular implant; group 2: cochlear implant).

Subject	Age of implantation	Etiology	Implantation (year)	Implanted side	Onset	Sex	DHI Pre	DHI Post	VHIT Post	PTA Pre	PTA Post (1 year follow-up)
Group 1											
VI/CI1	46	Meningitis	2018	OI	45 (2017)	Male	80	20	–	–	–
VI/CI2	41	Meningitis	2018	OI	29 (2006)	Male	28	2	–	–	–
VI/CI3	53	Meningitis	2019	OD	52 (2018)	Male	20	16	–	–	–
Group 2											
C1	43	Otosclerosis	2018	OI	(30) 2005	Female	6	8	N	Residual hearing	–
C2	56	Otosclerosis	2018	OI	(26) 1990	Female	0	0	N	Residual hearing	Residual hearing
C3	51	Unknown	2017	OD	(5) 1971	Female	36	34	N	Residual hearing	–
C4	54	Unknown	2020	OI	(5) 1971	Female	34	78	N	Residual hearing	–

TABLE 2 | Characteristic of cervical VEMPs pre-operative and evoked by electrical stimulation after surgery in both groups.

Subject	Electrode type	N–P amplitude (μV) pre	P1 latency (ms) pre	N1 latency (ms) pre	N–P amplitude (μV) post	P1 latency(ms) post	N1 latency(ms) post
C1V1	CI532®/Cochlear 24RE ST	–	–	–	25.8	12.6	18.6
C2V2	CI532®/Cochlear 24RE ST	–	–	–	47.3	13.6	21
C3V3	CI532®/Cochlear 24RE ST	–	–	–	38.6	11.33	18.33
C1	IC 512	47.5	18.33	25.33	–	–	–
C2	IC 532	58.5	16.3	24.3	72.69	9.67	16.3
C3	IC532	36	18	25	–	–	–
C4	IC 532	37	15	23	–	–	–

The cVEMP (in response to acoustic stimulation) and EcVEMP (in response to electrical stimulation) waveform, respectively, were recorded on the ipsilateral SCM of the ear being tested. Impedance was kept below 5 kΩ. EMG signals were bandpass filtered (1–3,000 Hz) and recorded in a 25–50-ms window relative to stimulus onset. No online artifact rejection was used. For all VEMP tests, at least three trials (100 sweeps each) were conducted. We considered EcVEMPs as present when the first positive P1 peak and negative N1 peak were visible and reproducible with a peak-to-peak amplitude >20 μv (13). We established absent VEMPs if we did not obtain recognizable waveforms. When such responses were not identified after two trials, testing was ended. All registries were made at least 1 year after implantation to assess long-term responses.

Acoustic Stimulus

Myogenic responses were elicited by 500-Hz tone bursts (2:2:2) at a repetition frequency of 5.1/s with an intensity at 95 and 100 dB HL, delivered through calibrated headphones. The analysis time was 100 ms; the electromyographic signal was bandpass filtered from 10 to 750 Hz. Every set of 150 stimuli was averaged and repeated twice to verify the reproducibility of the response. Acoustic stimulus was used in order to analyze the possible differences between acoustic and direct electrical stimulation.

Electrical Stimulus

The EcVEMPs were analyzed in the cochlear implant group with the Nucleus Freedom processor (Cochlear Corp., Sydney, Australia), which delivered an electrical stimulus directly to the participant's cochlear implant, using Custom Sound EP software (Cochlear Corp.), by using a trigger system in all CI patients. Electrical stimulus was monopolar, and the base parameters are presented in **Table 3**.

The EcVEMPs in the vestibular implant group were analyzed with the processor CP910 Nucleus® 6 (Cochlear Corp., Sydney, Australia), which delivered an electrical stimulus directly to the participant's cochlear implant, using Custom Sound EP software V.6.0 (Cochlear Corp.). The EcVEMP tests were first conducted by using electrode 1 and then were repeated by using the other inserted electrodes 2 and 3 of the vestibular implant array (pulse, 50; measurement windows, 1,600 μs). All cochlear electrodes were switched off during the registry in the case of patients with

TABLE 3 | Parameters used in vestibular cross stimulation with cochlear implant.

Type	Current level	Stimulus pulse width (μs)	Stimulus interphase gap (μs)	Stimulus NR pulse per burst (μs)	Stimulus duration (μs)	Stimulus repetition rate (Hz)	Number of sweeps
Cross-stimulation							
MP1	180	25	7	1	57	35	1,200

TABLE 4 | Characteristics of the dynamic range of each of the patients in group 1 (vestibular implant).

Patient	Dynamic range	Stimulus pulse width (μs)	C level	T level	Maxima	Canal frequency (Hz)
Direct stimulation						
C1V1	1	25	139	138	8	900
C2V2	1	25	192	191	8	900
C3V3	1	25	196	195	8	900

vestibular implants. Monopolar stimulation (MP) MP1 + MP2 was used with trigger system, and the stimulus characteristics in every patient are explained in the next table (**Table 4**).

The setup consists of a lap computer, cochlear POD interface, Nucleus Chronic Electrical Stimulation of the Otolith Organ Freedom processor (Cochlear Corp., Sydney, NSW, Australia), and CI24RE (ST).

We also measured horizontal angular VOR gain by vestibular head impulse test (VHIT) (ICS Impulse type 1085 from GN Otometrics A/S).

This study was conducted in accordance with the guidelines contained in the Declaration of Helsinki on Ethical Principles for Medical Research Involving Human Subjects. This work was approved by the Provincial Ethic Committee of our hospital (Id:CEIm-CHUIMI-2017/956).

RESULTS

The results were carried out 1 year after surgery in both patient groups: group 1, vestibular implant and group 2, cochlear implant. Six adults participated, three male and three female, age ranging from 41 to 56 years, with five unilateral implanted and one CI bilateral implanted. The hearing loss etiology was heterogeneous (**Table 1**). One of the implanted patient underwent her second implant 3 years after the first surgery, so we studied the two ears independently (C3–C4).

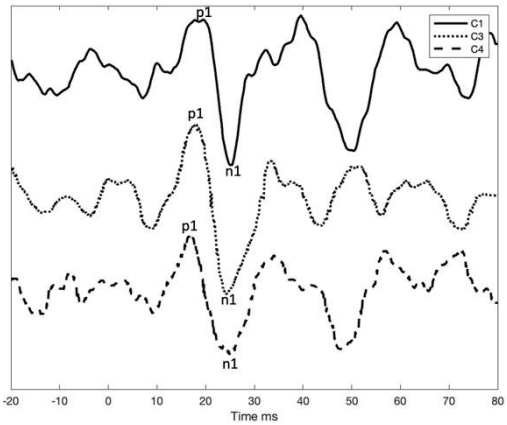
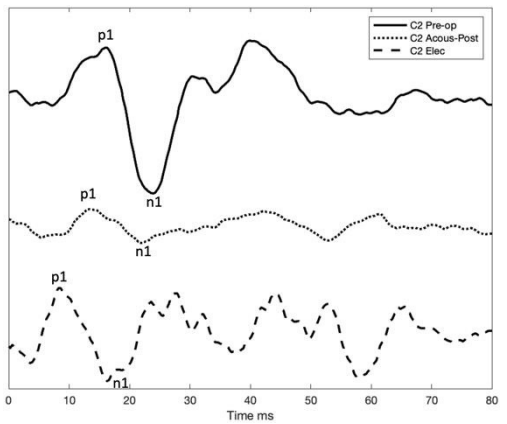
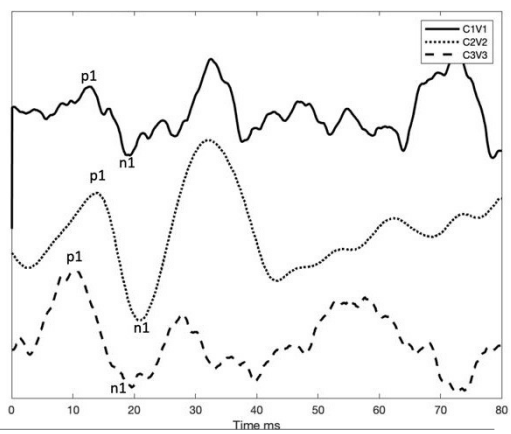
In the cochlear implant group, acoustic cVEMPs latencies before surgery were P1 from 15 to 18.33 ms and N1 from 23 to 25.33 ms, respectively. After surgery, acoustic cVEMPs were obtained in only one of the ear tested acoustic VEMPS, patient "C2" with P1–N1 latencies of 13.7 and 21 ms, respectively. It must also be mentioned that this patient preserved some residual hearing in low frequency hearing [$PTA_{(0.125-0.5\,kHz)} \leq 70$ dB HL].

In the cochlear implant group, electrical cVEMPs were obtained in the same patient (C2) with latencies P1 9.67 and N1 16.33 ms and only present in basal and medium stimulation of the electrode array. Patients did not report vestibular dysfunctions during the registration. However, in one of these patients, there was a transitory worsening in balance with cochlear implant use (C2). A second cochlear implant patient (C4) presented a severe handicap after surgery, which was partially restored. We must take into account that, in this case, the patient underwent bilateral cochlear implant, and the worsening in balance appeared after the second cochlear implantation.

In our three BVD patients, acoustic cVEMPs were absent before surgery, and electrical cVEMPs were obtained in the implanted side after VI surgery. P1 and N1 latencies were 11.33–13.6 and 18.33–21 ms, respectively. These results were present 12 months after implantation, representing the activation of the vestibulocollic reflex and, consequently, of the otolith organ activation (17). We consider it interesting to note that in patients with vestibular implants, fast saturation occurs after generating a greater intensity above the threshold used in their daily use. EcVEMPs are similar to acoustic ones, and we consider not to take into account amplitude differences between electrically and acoustically evoked responses since they depend on muscle contraction (**Table 5**).

VHIT analysis was performed before and after the intervention in all the subjects in the six canals. In the group of cochlear implant, VOR gain thresholds were normal (defined as >0.8), without alterations after surgery that shows persistence of the vestibular function corresponding to the semicircular canals. In BVL patients, VOR gains <0.66, before and after surgery, were found without changes in all subjects (**Table 6**).

TABLE 5 | Waveforms of cervical VEMPs (cVEMPs) in response to acoustic (left) and electrical stimulation (right).

cVEMPS acoustical pre-operative (C1, C3, C4)	
cVEMPS acoustical pre-operative and cVEMPS acoustical post-operative and ecVEMPs post-operative C2	
ecVEMPs post-operative C1V1, C2V2, C3V3	

VEMPs, vestibular evoked myogenic potentials.
VEMP test findings for case 3. The figures indicate the cVEMP data obtained on the side of cochlear (C1–C4) and vestibular (C1V1–C3V3) implantation (mean values).

DISCUSSION

Cochlear Implant

One of the objectives of this research was to analyze the costimulation effect by cochlear implant, in patients with no previous vestibular damage. One of our aims in this study was to verify if saccular function persists, taking into account the possible risk of cochlear damage and also the possible "cross" activation, by electrical stimulation with cochlear implant.

According to previous studies, the incidence of potential vestibular damage after intervention varies between 39 and 74% (18) due to trauma caused by insertion that provokes loss of perilymph (19), labyrinthitis because of foreign body reaction (20), perilymph fistula (21), and endolymphatic hydrops (22). Electrode insertion by round window cochlear implant approach has been proposed to reduce trauma to the cochlea (23–25).

Our results in the cochlear implant group show that only in one case (with some residual hearing) acoustic VEMPs were preserved. Additionally, it is confirmed that such a damage occurs in three out of four ears since acoustical cVEMPs were absent (26). Tien and Linthicum reported that 75% of the temporal bones evaluated with saccular damage coincided with damage to the basal turn of the cochlea (11). For this reason, the reduction in cochlear damage during surgery would foreseeably suppose greater preservation of hearing and saccular function, observing minor changes in post-operative VEMPS.

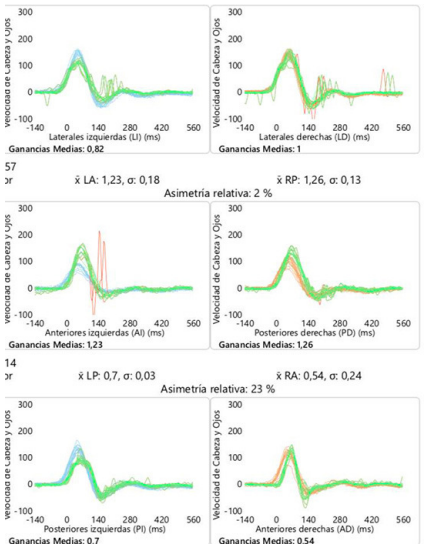
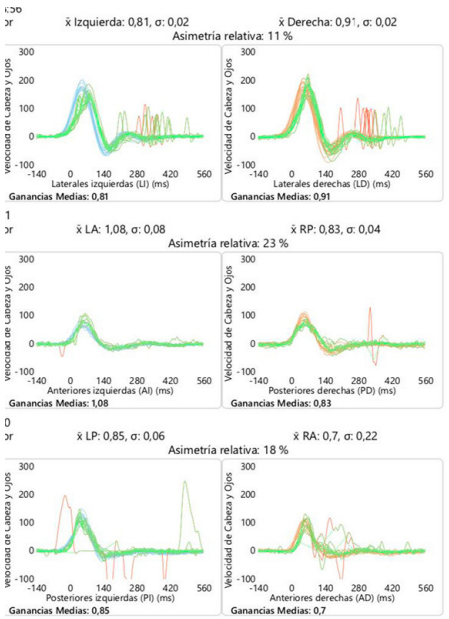
Furthermore, this damage was severe enough not to be reversed by costimulation of the cochlear implant stimulation. However, semicircular canals functioning remained stable in these patients, so there is no evidence of imbalance observed in the subject C3–C4 related to semicircular canals. This has also been described by Shute et al. (27) during early post-operative situation, and we observe the same situation after 1 year follow-up. In contrast, other studies show an involvement of the horizontal semicircular canal with a functional deficit in 44% of patients (18). These results also show the importance of the otolithic organs in the severity of bilateral vestibular dysfunction, which, up to now, is not included within the criteria of this clinical situation (28).

The costimulation effect has an anatomical proof/justification that has been exposed in previous studies. Current spread to the vestibular system is likely due to the effect that membranous labyrinths of the auditory and vestibular systems are connected through the fluid-filled ductus reuniens (29). In fact, vestibular and balance function can improve after CI activation in some cases (13, 30, 31).

Until now, it is unknown where the vestibular activation occurs, although due to the shortening of latencies, direct stimulation to the afferents may occur. This situation is comparable to cochlear implant stimulation of the cochlear nerve; electric current was seemingly able to bypass dysfunctional otoliths to more directly stimulate the vestibular neural/afferent elements. These observations would explain that the EcVEMPs were faster in the onset than in acoustically evoked VEMPs and comparable to the responses obtained with direct promontory stimulation (13, 17). Although there is a variability in the response, we should also take into account the influence of deafness etiology or the specific environment surrounding the electrode.

As previously described, vestibular costimulation may help to restore damaged vestibular function (17, 32) but may not be considered for all situations in cochlear implant recipients

TABLE 6 | An example of VOR gain in six canals (VHIT) before and after cochlear implant group (example of C1 patient).

Subject	VHIT Pre	VHIT Post
C1		

and may be related to end organ preservation after CI. Parkes et al. describe that 48% of the 96 ears studied in their study presented EcVEMPs, and in 27% of these, even without acoustic responses. Previous studies have analyzed VEMPs in children and young adults (13), but with adult samples, like the present study (>41 years old), age must be taken into account as a possible risk factor (18). For this reason, in the cochlear implant group, only patients with VEMPs prior to the intervention were chosen. However, we could not probe if age itself is decisive in costimulation. Therefore, it is necessary to obtain a greater number of cases to establish more conclusive results. The next studies should be aimed at defining what factors could be correlated with these findings: etiology, age, residual hearing, or the type of stimulation used.

Vestibular

Electrical stimulation induces myogenic responses in the vestibulocollic pathway as has already been established before (15). We observe that otolith organ electrical stimulation can restore the vestibulocollic reflex in patients with BVD and vestibular implant, in all cases in this study, with an important effect on the clinical situation and BVD symptoms restoration (17).

The shape of the EcVEMP was similar to the conventional acoustically elicited cVEMP. However, the latencies were shorter, similar to previous observations in studies comparing galvanic stimulation (33) and electrical stimulation by cochlear implant (13). We hypothesize whether the latency variation of the response in different studies could be explained because of different circumstances: vestibular implant location, implant design, and differences in the stimulation profile and vestibular etiology, which could explain the differences found.

We found an increase in amplitude in a very short range of increasing intensity, observing a quick saturation in the response. Our findings are not directly comparable with other groups (15). The differences could be related to the kind of stimulus or semicircular canal contribution in this reflex during the semicircular canal stimulation. It is suggested that convergent neurons may receive both canal and otolith stimulation that contribute to the vestibulocollic reflex, but this circumstance is reduced in the VOR (34). This supports the idea that the selective reflexes can be elicited from different end organs (35, 36). Other options that must be under consideration is the etiology of these dysfunctions, since in our three patients, meningitis was the etiology; other groups included traumatic or genetic origin (DFNA9).

The stimulus used to evoke EcVEMPs were not perceived by the cochlear group tested; however, in the second group, they perceived an immediate stability sensation without unpleasant sensation, which implies an improvement in their clinical situation. This soft sensation must be considered, as the vestibulocollic pathway shows a low threshold of stimulation than other pathways such as the vestibulo-ocular reflex. In our case, we are not able to obtain an improvement in VOR gain by VHIT, so it might imply that there is a selective stimulation of vestibular afferents and different vestibular pathways have different activation profiles (37). However, we are not able to explain how this inputs are "processed" by the central system.

In functional conditions, our BVD patients recovered a good quality of life, with improvement in their stability, and activities in their daily life remained stable during chronic implant use for more than a year, as it has been presented previously (17). Aside from VEMPs being anticipated in future articles, there are other objective responses in vestibular implant sample such as subjective visual vertical (SVV), subjective visual horizontal (SHV), and dynamic visual acuity (DVA), which justify the restoration of vestibular function.

This results can be explained or discussed in light of an otolith selective response, given the shortening of latencies, or this can be also explained by a current spread or central convergence of the primary vestibular afferents on the second-order vestibular nuclei neurons as has been theorized in other studies (32, 38–41).

Although we have observed in this study shortened latencies in both stimuli, we did not observe a constant response due to costimulation in all patients. In these cases, vestibular activation seems to be present only when residual hearing is preserved (less iatrogenic damage) and in patients who previously presented vestibular function. Although in this study the number of patients is very small, we may assume that costimulation would be possible if the saccular damage is not severe. However, in the case of direct stimulation, we can evoke responses in previously areflexic patients; therefore, it should be considered in severe cases.

Given the small number of previous studies on chronic electrical stimulation, future challenge to obtain the maximum benefit for patients should be aimed to:

(1) define the involvement of the otolith organs and semicircular canals in the vestibulocollic reflex;
(2) analyze if new parameters in the electrical stimulation and vestibular prothesis design would obtain a selective activation of different reflexes;
(3) achieve better EcVEMPs understanding through a larger sample of patients implanted with vestibular prostheses;
(4) define effects, incidence, and possible risk factors of otolith function damage after cochlear implant and the underestimated presence of vestibular cross-stimulation.

Weakness

This study had some limitations. First of all is the very small sample that did not allow us to provide statistical analyses (in this phase of the research, only a very limited number of patients can be included in this research). Second, it is difficult to make comparisons in the electrical response, since it is the first vestibular implant with the otolithic organs chronic stimulation used in humans.

Conclusion

Electrically cVEMPs may be present after 12 months of follow-up of chronic vestibular stimulation mainly in patients with vestibular implant and a small number of patients with cochlear implant. This suggest that stimulation of vestibular elements is feasible, although the clinical effects must be further studied.

DATA AVAILABILITY STATEMENT

The raw data supporting the conclusions of this article will be made available by the authors, without undue reservation.

ETHICS STATEMENT

The studies involving human participants were reviewed and approved by Comite etico—Complejo Hospitalario Universitario Insular Materno Infantil. The patients/participants provided their written informed consent to participate in this study.

AUTHOR CONTRIBUTIONS

IR: data acquisition and manuscript writing. AR: manuscript writing and graphics. JG: data acquisition and patients fitting. SB: manuscript. NP and RV: verification of VEMPS recordings. AR-M: original idea, manuscript, and verification. All authors contributed to the article and approved the submitted version.

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REFERENCES

1. Mitchell DE, Dai C, Rahman MA, Ahn JH, Della Santina CC, Cullen KE. Head movements evoked in alert rhesus monkey by vestibular prosthesis stimulation: implications for postural and gaze stabilization. *PLoS ONE*. (2013) 8:e78767. doi: 10.1371/journal.pone.0078767
2. Herdman SJ, Blatt P, Schubert MC, Tusa RJ. Falls in patients with vestibular deficits. *Am J Otol*. (2000) 21:847–51.
3. Zingler VC, Weintz E, Jahn K, Mike A, Huppert D, Rettinger N, et al. Follow-up of vestibular function in bilateral vestibulopathy. *J Neurol Neurosurg Psychiatry*. (2008) 79:284–8. doi: 10.1136/jnnp.2007.122952
4. Guinand N, Boselie F, Guyot JP, Kingma H. Quality of life of patients with bilateral vestibulopathy. *Ann Otol Rhinol Laryngol*. (2012) 121:471–7. doi: 10.1177/000348941212100708
5. Sun D, Ward BK, Semenov Y, Carey J, Della Santina CC. Bilateral vestibular deficiency: quality of life and economic implications. *JAMA Otolaryngol Head Neck Surg*. (2014) 140:527–34. doi: 10.1001/jamaoto.2014.490
6. Krebs DE, Gill-Body KM, Parker SW, Ramirez JV, Wernick- Robinson M. Vestibular rehabilitation: useful but not universally so. *Otolaryngol Head Neck Surg*. (2003) 128:240–50. doi: 10.1067/mhn.2003.72
7. Gimmon Y, Migliaccio AA, Kim KJ, Schubert MC. VOR adaptation training and retention in a patient with profound bilateral vestibular hypofunction. *Laryngoscope*. (2019) 129:2568–73. doi: 10.1002/lary.27838
8. Wuehr M, Nusser E, Decker J, Krafczyk S, Straube A, Brandt T, et al. Noisy vestibular stimulation improves dynamic walking stability in bilateral vestibulopathy. *Neurology*. (2016) 86:2196–202. doi: 10.1212/WNL.0000000000002748
9. Guyot JP, Perez Fornos A. Milestones in the development of a vestibular implant. *Curr Opin Neurol*. (2019) 32:145–53. doi: 10.1097/WCO.0000000000000639
10. Suzuki JI, Cohen B. Head, eye, body and limb movements from semicircular canal nerves. *Exp Neurol*. (1964) 10:393–405. doi: 10.1016/0014-4886(64)90031-7

11. Tien HC, Linthicum FH, Jr. Histopathologic changes in the vestibule after cochlear implantation. *Otolaryngol Head Neck Surg.* (2002) 127:260–4. doi: 10.1067/mhn.2002.128555
12. Handzel O, Burgess BJ, Nadol JB, Jr. Histopathology of the peripheral vestibular system after cochlear implantation in the human. *Otol Neurotol.* (2006) 27:57–64. doi: 10.1097/01.mao.0000188658.36327.8f
13. Parkes WJ, Gnanasegaram JJ, Cushing SL, McKnight CL, Papsin BC, Gordon KA. Vestibular evoked myogenic potential testing as an objective measure of vestibular stimulation with cochlear implants. *Laryngoscope.* (2017) 127:E75–81. doi: 10.1002/lary.26037
14. Colebatch J, Halmagyi G. Vestibular evoked potentials in human neck muscles before and after unilateral vestibular deafferentation. *Neurology.* (1992) 42:1635–6. doi: 10.1212/WNL.42.8.1635
15. Fornos AP, van de Berg R, Armand S, Cavuscens S, Ranieri M, Crétallaz C, et al. Cervical myogenic potentials and controlled postural responses elicited by a prototype vestibular implant. *J Neurol.* (2019) 266(Suppl. 1):33–41. doi: 10.1007/s00415-019-09491-x
16. Phillips C, Defrancisci C, Ling L, Nie K, Nowack A, Phillips JO, et al. Postural responses to electrical stimulation of the vestibular end organs in human subjects. *Exp Brain Res.* (2013) 229:181–95. doi: 10.1007/s00221-013-3604-3
17. Ramos A, Ramos de Miguel A, Rodriguez I, Borkoski S, Falcon JC. Chronic electrical stimulation of the otolith organ: preliminary results in humans with bilateral vestibulopathy and sensorineural hearing loss. *Audiol Neurootol.* (2020) 25:79–90. doi: 10.1159/000503600
18. Meli A, Aud BM, Aud ST, Aud RG, Cristofari E. Vestibular function after cochlear implant surgery. *Cochlear Implants Int.* (2016) 17:151–7. doi: 10.1179/1754762815Y.0000000014
19. Adunka O, Teagle H, Zdanski C, Buchman C. Influence of an intraoperative perilymph gusher on cochlear implant performance in children with labyrinthine malformations. *Otol Neurotol.* (2012) 33:1489. doi: 10.1097/MAO.0b013e31826a50a0
20. Lim H, Lee E, Park H, Park K, Choung Y. Foreign body reaction after cochlear implantation. *Int J Pediatr Otorhinolaryngol.* (2011) 75:1455–8. doi: 10.1016/j.ijporl.2011.08.004
21. Kusuma S, Liou S, Haynes D. Disequilibrium after cochlear implantation caused by a perilymph fistula. *Laryngoscope.* (2005) 115:25–6. doi: 10.1097/01.mlg.0000150680.68355.cc
22. Smeds H, Eastwood H, Hampson A, Sale P, Campbell L, Arhatari B, et al. Endolymphatic hydrops is prevalent in the first weeks following cochlear implantation. *Hear Res.* (2015) 327:48–57. doi: 10.1016/j.heares.2015.04.017
23. Ishiyama A, Doherty J, Ishiyama G, Quesnel A, Lopez I, Linthicum F. Post hybrid cochlear implant hearing loss and endolymphatic Hydrops. *Otol Neurotol.* (2016) 37:1516–21. doi: 10.1097/MAO.0000000000001199
24. Adunka O, Dillon M, Adunka M, King E, Pillsbury H, Buchman C. Cochleostomy versus round window insertions: influence on functional outcomes in electric-acoustic stimulation of the auditory system. *Otol Neurotol.* (2014) 35:613–8. doi: 10.1097/MAO.0000000000000269
25. Burghard A, Lenarz T, Kral A, Paasche G. Insertion site and sealing technique affect residual hearing and tissue formation after cochlear implantation. *Hear Res.* (2014) 312:21–7. doi: 10.1016/j.heares.2014.02.002
26. Xu XD, Zhang XT, Zhang Q, Hu J, Chen YF, Xu M. Ocular and cervical vestibular-evoked myogenic potentials in children with cochlear implant. *Clin Neurophysiol.* (2015) 126:1624–31. doi: 10.1016/j.clinph.2014.10.216
27. Shute WG, McOwan B, O'Leary SJ, Szmulewicz D. The early postoperative effects of cochlear implantation on horizontal semicircular canal function. *Otol Neurotol.* (2018) 39:e524–31. doi: 10.1097/MAO.0000000000001840
28. Strupp M, Kim JS, Murofushi T, Straumann D, Jen JC, Rosengren SM, et al. Bilateral vestibulopathy: diagnostic criteria consensus document of the classification committee of the bárány society. *J Vestib Res.* (2017) 27:177–89. doi: 10.3233/VES-170619
29. Rubinstein D, Sandberg EJ, Cajade-Law AG. Anatomy of the facial and vestibulocochlear nerves in the internal auditory canal. *AJNR Am J Neuroradiol.* (1996) 17:1099–105.
30. Eisenberg LS, Nelson JR, House WF. Effects of the single-electrode cochlear implant on the vestibular system of the profoundly deaf adult. *Ann Otol Rhinol Laryngol Suppl.* (1982) 91:47–54.
31. Basta D, Todt I, Goepel F, Ernst A. Loss of saccular function after cochlear implantation: the diagnostic impact of intracochlear electrically elicited vestibular evoked myogenic potentials. *Audiol Neurootol.* (2008) 13:187–92. doi: 10.1159/000113509
32. Sluydts M, Curthoys I, Vanspauwen R, Papsin BC, Cushing SL, Ramos A, et al. Electrical vestibular stimulation in humans: a narrative review. *Audiol Neurootol.* (2020) 25:6–24. doi: 10.1159/000502407
33. Watson SR, Colebatch JG. Vestibulocollic reflexes evoked by short-duration galvanic stimulation in man. *J Physiol.* (1998) 513:587–97. doi: 10.1111/j.1469-7793.1998.587bb.x
34. Uchino Y, Sasaki M, Sato H, Bai R, Kawamoto E. Otolith and canal integration on single vestibular neurons in cats. *Exp Brain Res.* (2005) 164:271–85. doi: 10.1007/s00221-005-2341-7
35. Curthoys IS, Markham CH. Convergence of labyrinthine influences on units in the vestibular nuclei of the cat. I. Natural stimulation. *Brain Res.* (1971) 35:469–90. doi: 10.1016/0006-8993(71)90489-6
36. Kushiro K, Zakir M, Sato H, Ono S, Ogawa Y, Meng H, et al. Saccular and utricular inputs to single vestibular neurons in cats. *Exp Brain Res.* (2000) 131:406–15. doi: 10.1007/s002219900312
37. Perez Fornos A, Cavuscens S, Ranieri M, van de Berg R, Stokroos R, Kingma H, et al. The vestibular implant: A probe in orbit around the human balance system. *J Vestib Res.* (2017) 27:51–61. doi: 10.3233/VES-170604
38. Golub JS, Ling L, Nie K, Nowack A, Shepherd SJ, Bierer SM, et al. Prosthetic implantation of the human vestibular system. *Otol Neurotol.* (2014) 35:136–47. doi: 10.1097/MAO.0000000000000003
39. Guinand N, van de Berg R, Cavuscens S, Stokroos RJ, Ranieri M, Pelizzone M, et al. Vestibular implants: 8 years of experience with electrical stimulation of the vestibular nerve in 11 patients with bilateral vestibular loss. *ORL.* (2015) 77:227–40. doi: 10.1159/000433554
40. Boutros PJ, Schoo DP, Rahman M, Valentin NS, Chow MR, Ayiotis AI, et al. Continuous vestibular implant stimulation partially restores eye-stabilizing reflexes. *JCI Insight.* (2019) 4:e128397. doi: 10.1172/jci.insight.128397
41. Goldberg JM, Cullen KE. Vestibular control of the head: possible functions of the vestibulocollic reflex. *Exp Brain Res.* (2011) 210:331–45. doi: 10.1007/s00221-011-2611-5

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PERSPECTIVE
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Perspectives: Evaluation of Older Adult Cochlear Implant Candidates for Fall Risk in a Developing Country Setting

*Christine Rogers**

Department of Health and Rehabilitation Sciences, Faculty of Health Sciences, University of Cape Town, Cape Town, South Africa

Dizziness, vertigo, and falls are common in older adults. Data suggest that cochlear implant candidates are no different and could be argued to be at elevated risk due to the presence of hearing loss and likely vestibular involvement. *Perspectives* contextualizes current testing and screening paradigms for vestibular deficits and fall risk and suggests a protocol suitable for use in developing country settings.

Keywords: cochlear implants, developing countries, falls, older adults, vestibular deficits

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***Correspondence:**
Christine Rogers
Christine.Rogers@uct.ac.za

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INTRODUCTION

Falls are common events in older adults with one in four falling each year (1). There is little reason to suspect the narrative is any different in emerging regions and, in fact, could be worse as "old age" and its attendant health-related problems may start as early as the end of the reproductive years (2). While more than 400 risk factors for falls exist (3), usually intrinsic and extrinsic factors combine with disease and aging to make falls and their adverse sequelae a reality for many. One important risk factor for falls is the presence of dizziness and vertigo, which are common complaints in older adults (4) and, along with subjective imbalance, increase the odds ratio 12-fold (5). Abundant studies describe the anatomical and physiological impact of the aging vestibular system although gaps in the literature exist. Scanty literature discusses the functional impact of vestibular impairment on daily living (6) as well as the delineation of the exact relationship between vestibular impairment, aging, and falls (7). Furthermore, review of the literature concerning falls is confounded by operational and methodological issues, for example, how a fall is defined. Differences in definitions for falls obfuscate the generalizability of clinical trials, treatment strategies, and outcome evaluation, including meta-analyses (8, 9). Researchers are urged to use a standardized definition of falls, such as the one promulgated by the Prevention of Falls Network Europe (PRoFaNE), which has been widely adopted by the scientific community (10, 11). Thus, when considering protocols for evaluation of patient groups, the definition shown in **Figure 1** is recommended for researchers and clinicians alike. The definition concurs with recommendations from the American and British Geriatric Societies, the World Health Organization, and the UK National Institute for Clinical Excellence (NICE) (13).

A fall describes an individual unintentionally and involuntarily moving towards the ground or other lower level, which is not the result of a major intrinsic event or hazard.*

FIGURE 1 | Suggested definition for a fall.
*Intrinsic fall risk factors are idiosyncratic health-related issues, such as visual acuity or balance deficits and may include age, sex, and ethnicity (12). Loss of consciousness due to syncope or stroke is an example of a major intrinsic event excluded from this definition of a fall (13, 14). The definition excludes major extrinsic events such as pedestrian traffic accidents (15).

Hearing loss is another risk factor identified as strongly correlated with fall events. One meta-analysis demonstrates that the presence of audiometrically proven hearing loss resulted in an almost seven-fold increased risk of falling (16). Further correlates of hearing impairment in older adults relevant to fall risk include sedentary behavior, slower gait speed, social isolation and withdrawal, and cognitive decline, itself a risk factor for falls (17–19). Cochlear implant (CI) candidates tend to have severe-to-profound hearing loss, which is likely to increase risk fall risk further. CI candidates may well have associated vestibular loss as the etiology of the loss could have affected both cochlear and vestibular apparatus. Around half of CI recipients are thought to have abnormal vestibular function prior to implantation although the procedure itself may cause temporary or permanent damage (20).

It is reasonable to assume that vestibular lesions before and after implantation extend to elevated fall risk. For example, one small study (20 participants, mean age 52 years, range 27–78 years) suggests impaired postural control in individuals' pre-implant assessments and cites a higher risk of falling (21). Participants underwent a battery of tests that evaluated sway using a mobile posturograph. Many of the tests resembled functional activities of daily living, such as walking with added head movements, short walks, and transitioning from sitting to standing. Participants' scores were compared with sex and age-matched normative data. Using the Vertiguard equipment, fall risk is regarded as scores of $\geq$40%. Preimplantation, fall risk in the CI group had a mean of 51% (range 24–80%) compared with normative data of 0–40% risk. The comparatively low mean age of the CI candidates is notable. Although this was an underpowered study using equipment not in common use, the strength is the choice of static and dynamic balance activities that were challenging for CI candidates. At the very least the study signals a need to consider fall risk in adult CI recipients. Rather than using a form of posturography, Stevens and coworkers (2014) (22) used the modified Clinical Test of Sensory Integration of Balance (m-CTSIB) (see later in this article) to assess their patients before and two weeks after CI. Nine of the 16 participants experienced a statistically significant decline (signaling poorer balance performance) in m-CTSIB scores post-operatively. Although the controversy regarding the links between vestibular function and deficits on the m-CTSIB must be acknowledged (22, 23), nevertheless, individuals over 60 years of age had a relative risk for falls of 2.1, more than their younger counterparts.

Another small study (24) evaluated the presence of vertigo in CI candidates pre-and postoperatively. Prior to implantation, half the participants had vertigo with abnormality in instrumented tests, including calorics and VEMP (see later in this article). More than one in three (36%) patients reported balance impairment postoperatively. Of pertinence to this *Perspectives* article, older adults, especially those over 75 years of age, were more likely to have long-term impaired vestibular function, which the authors (24) suggest was a sign of fragility and risk of falls. Interestingly, Colin et al. (24) and Louza et al. (21), and Amin et al. (25), suggest either an overall improvement in balance in some patients post-CI or, at least, no increase in the rate of injurious falls.

Falls have a detrimental and long-term impact on quality of life (26, 27) and are life-changing events for older adults (28). There is compelling evidence that the health status of adults who fall, in terms of physical, cognitive, and mental function, is fundamentally different from older adults who do not fall (29). Moreover, mortality linked to injurious falls is a serious concern. Evidence suggests that death rates from falls have risen precipitously in the last decade (30, 31). The WHO estimated 646,000 fall-related adult deaths each year; 80% of which occur in low- and middle-income countries (32). Older adults are particularly susceptible with most fall-related deaths recorded in individuals over 65 years of age (32). Frequently, survivors of the immediate postfall period have guarded outcomes in terms of both morbidity and mortality. Older adults are at increased risk for head, neck, and pelvis injuries compared with their younger counterparts (33). For example, falls are the leading cause of traumatic brain injury and are heavily implicated in hip fractures in older individuals (34, 35). It is not possible to overstate the devastating effects of an injurious fall for an older adult or the cost to public health budgets (36, 37). These concerns raise questions that all clinicians and researchers should be considering when dealing with CI programs. The studies discussed in this section should, at least, prompt consideration of obligations to older adults regarding potentially undesirable changes to vestibular and balance status post-implant. Is the patient at risk for falls? What is the best way to identify and manage that fall risk? What should comprise the minimum fall risk assessment, counseling, and safety precautions before and after an invasive procedure that may impair vestibular function at least temporarily? Implementation and evaluation of a protocol to explore vestibular deficits and fall risk requires further research.

Contributors to vestibular lesions pre- and post-implantation and, thus, elevated fall risk in CI candidates are briefly discussed next.

Vestibular Lesions Pre- and Post-implantation

CI candidates are not a homogenous group, and causes of hearing loss may well be associated with progressive vestibular deficits. Examples include Ménière's disease, vestibulotoxicity,

and ossification of the labyrinth post-meningitis. Older adults may have presbyvestibulopathy in addition to their cause for hearing loss. Presbyvestibulopathy is a chronic vestibular syndrome characterized by unsteadiness; impaired gait; falls; and mild, bilateral vestibular deficits on specialized investigation (38). The term "presbyvestibulopathy" supercedes others, such as presbyvertigo, presbyastasis, and presbyataxia (39). Ibrahim et al. (40) describe several potential mechanisms for vestibular deficits linked to the CI surgery itself. Mechanisms include trauma induced by electrode insertion, serous labyrinthitis due to the cochleostomy, a foreign body reaction labyrinthitis, endolymphatic hydrops, and finally electrical stimulation from the implant itself (40).

Symptoms associated with implantation may be episodic, delayed, or permanent and are thought to arise from the damage caused by CI, alteration of the vestibular receptors, and/or possible effects on the central nervous system (41). Postoperative complaints of vertigo are thought to be common although the incidence appears to vary widely (41). Clinicians who only question patients regarding vertigo *per se* may miss reports of unsteadiness, imbalance, instability, and dysequilibrium as well as falls. A meta-analysis by Hänsel et al. (41) suggests that vertigo was found in 16.8% of adult patients post CI, and as expected, a marked age effect was demonstrated. Age at implant was a significant risk factor with an age threshold of 59 years thought to herald increased risk, a finding supported by other authors. Again, variability in the incidence of postoperative symptoms is noted with results from Ibrahim et al. (40) suggesting approximately one third of recipients reported dizziness post-implantation. Importantly in terms of fall risk, the time for recovery, and possibility for incomplete recovery (compensation) increases for individuals over the age of 70 years (42).

SPECIALIZED EQUIPMENT-BASED ASSESSMENT OF VESTIBULAR FUNCTION IN OLDER ADULT CI CANDIDATES

Over the last two decades, more extensive testing of the vestibular pathway has become more available in the clinic, leading to greater diagnostic accuracy (43). All five of the vestibular end organs can be evaluated given the appropriate equipment. However, specialized equipment is less available in under-resourced settings, so alternative screening strategies are suggested later in this *Perspectives* article. Despite flourishing CI programs in some emerging regions and the likelihood of these being located in at least secondary or tertiary level facilities, the specialized equipment and testing discussed in the following section could be out of reach. For example, in the Western Cape of South Africa, which has approximately seven million citizens [83% of all South Africans are reliant on state healthcare services (44)], only one tertiary facility has limited objective tests (VNG, VEMP, vHIT) available. The center at which most CIs are performed has no equipment. Another province has three implant centers and no vestibular apparatus whatsoever. South African Cochlear Implant Group guidelines suggest the use of the Dizziness Handicap Inventory and mentions calorics, vHIT, and C-VEMP (all discussed later in this section) as being suggested by the literature and in clinical use for bilateral or sequential CI procedures, but they stop short of mandating these measures (45).

Formal testing of vestibular function might guide decisions as to which ear to implant rather than solely relying on audiologic criteria (20). The ear with the vestibular deficit is likely the ear selected for implantation (46). Very little research reports preimplantation vestibular function screening, nor is there consensus as to the protocol for screening and management of the challenges associated with conducting assessments in CI patients (46). Furthermore, each test described in this section has distinct advantages and disadvantages in a CI population and may be influenced by non-vestibular issues including cooperation and alertness. Aging effects themselves are thought to have widespread but variable impact on the instrumented tests (47) described here. Hearing loss associated with visual impairment presents specific concerns in terms of vestibular assessment as do cognitive issues that may impact understanding instructions. Testing might be done with fixation abolished or in reduced lighting conditions, meaning that patients are unable to speech read or hear instructions to improve the quality of the results.

Caloric testing, usually as part of a videonystagmography (VNG) test battery, has been extensively researched (48) and is a mainstay of testing horizontal, semicircular canal function. VNG can also inform regarding the status of central vestibular and oculo-motor pathways, making identification of lesions therein possible (49). VNG offers advantages and disadvantages when applied in an older population. First, age has been linked to mild, progressive oculo-motor decline, which would show on the relevant subset of tests on VNG (47). Although central causes are thought to be present in around 25% of vertiginous patients in specialized facilities (50), oculo-motor deficits found on VNG should not result in exclusion from CI candidacy.

Caloric testing is not without its challenges. First, information regarding vestibular function is limited in that the stimulus is directed primarily at the horizontal semicircular canal (48). Although the calorics subtest is most useful to identify an asymmetry in responses between the two ears (5) as noted previously, presbyvestibulopathy may result in mild, bilateral loss of function to which calorics are relatively insensitive. However, in clear cases of asymmetry, guidance toward which ear to implant is possible. There are few studies on the impact of age on calorics, and age-related decline has not been empirically proven (47).

Patient-related concerns also have bearing on the results. Calorics may be uncomfortable and can induce symptoms of vertigo, nausea, and even vomiting. Symptoms may be so severe the patient declines further testing, leaving the battery of caloric tests incomplete. However, any temporary discomfort during testing is worth tolerating when compared with the risk of damaging the only ear with vestibular function during surgery. Furthermore, the impact of medication might influence the excitability of the responses and should be considered in an older population who often consume significant amounts of medication. Vestibular sedatives, in particular, might have a

negative influence on results although opinion differs, and there is a lack of firm evidence (51). Finally, VNG is time-consuming, and post-VNG morbidity is a factor (52). An interesting point raised by Piker et al. (53) is that caloric testing may be influenced by changes in temporal bone anatomy post-CI and, thus, is not suitable for evaluating postoperative vestibular status. However, postoperatively, the focus should be on functional recovery.

Video head impulse testing (vHIT) is a newer addition to the armamentarium and is capable of assessing all three semicircular canals. vHIT assesses the gain of the vestibulo-ocular reflex. Vestibular gain is the ratio of slow-phase compensatory eye velocity to head impulse velocity (54). Abnormal responses suggest reduced gain in the canal under test (20), and a major advantage of the test is that each canal can be investigated separately. High specificity (which can be up to 100% depending on the extent of the lesion) (54) allows the potential "target" canals vulnerable to iatrogenic damage to be evaluated, obviating some of the issues with calorics restricted to testing the horizontal semicircular canal. vHIT is quick and easy to administer and well-tolerated (54). It takes time to practice the appropriate technique to optimize results, so the equipment cannot be regarded as "plug and play" (55). Patient-related factors that might make vHIT difficult to administer include those with a loss of facial skin tone, making the goggles too loose and issues affecting neck/head mobility (5, 46), such as arthritis. Systems with external cameras might be better for older populations with more appropriate management of artifacts and ill-fitting goggles. Changes with aging, which include reduced gain, still yield results within normal limits, making the test desirable (48). There are few studies that examine the impact of age on vHIT, but it appears that gain is stable up to the age of 70 years and then decreases and is most marked after the age of 79 (47). The portable nature of vHIT equipment (laptop and lightweight glasses with high-resolution cameras attached) makes vHIT intuitively appealing. Due to the inherent advantages of vHIT, which include ease of administration, acceptability to patients, and space and cost constraints, if only one piece of equipment were possible, then vHIT is a logical choice for under-resourced settings. Moreover, for CI centers with pediatric services, vHIT is far more acceptable to very young children (from 3 months) for whom calorics are not possible until the age of about 8 years (56). Therefore, combined with the results of bedside testing (oculo-motor tests, use of Frenzel lenses, and others) described in the next section, vHIT would feature strongly in a battery approach as a pass/fail criterion to identify CI candidates who require further evaluation and referral.

The final equipment-based test discussed here evaluates utricular and saccular function, viz., vestibular evoked myogenic potential testing (VEMP). VEMPs assess otolith function and the neural pathways (48). Two important patient-related variables are relevant for older adult CI assessments. Aging is a concern. The variability of the VEMP response increases with age to the point that the range is so variable and the yield so poor that certain authors suggest that there is little to be gained from conducting VEMPS in populations over the age of 70 years (38, 48). For example, the series by Piker et al. (57) demonstrates that, in participants with otherwise normal hearing and vestibular function, c-VEMPS were six times more likely to be absent in adults aged in their 50 and 60s, rising to 22 times more likely for adults over 70 years of age. Current practice guidelines (58) support the use of VEMP to diagnose semicircular canal dehiscence syndrome. Expert consensus holds that VEMP can be used to evaluate the extent of vestibular nerve involvement in vestibular deficits, but meta-analysis notes insufficient data for the efficacy of diagnosis of several specific vestibular disorders, including Ménière's disease (58). Standardization is required to increase the effective use of VEMP along with facilities developing their own data sets for both young and older patient cohorts (58). Therefore, at this time, the likely disadvantages of VEMP in older CI candidates outweigh advantages, such as speed and ease of administration.

Having discussed equipment-based tests, which might not be available in developing country contexts, a strategy for office-based clinical evaluation of CI candidates' vestibular and balance function is presented next.

LOW-TECH ASSESSMENT OF VESTIBULAR FUNCTION AND FALL RISK SUITABLE FOR EMERGING COUNTRIES

In developing regions, some consideration of either an office-based screening protocol or a system to select patients who should be referred for objective testing is necessary. Computerized testing for vestibular lesions, although more objective, is often costly, time-consuming, and demanding of space (59). Therefore, a more pragmatic approach is required that highlights the most sensitive and specific screening tests, which can be applied easily without the use of sophisticated and often expensive equipment. Selected tests should demonstrate clinical utility (ease and efficiency of use, resulting in relevant and clinically meaningful information) (60) and preferably be responsive so the effect of therapeutic interventions may be evaluated. The nature of screening tests implies that they could be conducted by several different cadres of staff, including audiologists, as part of the workup prior to CI. Mention must be made include the proliferation of tests available using fairly simple technology, such as laptops and smartphones, which is relatively inexpensive and required for a CI program in any case. Instrumented versions of tests such as Dynamic Visual Acuity are available for download to computers and in a virtual reality format. Mobile apps of the Subjective Visual Vertical test have been released at very little cost and are being evaluated for sensitivity and specificity (61–64). Commercially available interactive exergaming technology, such as the Wii Fit, is shown to give valuable and accurate information regarding balance control (65) and can be used for pre-habilitation and rehabilitation post-implantation.

A SUGGESTED PROTOCOL FOR VESTIBULAR AND BALANCE SCREENING OF OLDER ADULT CI CANDIDATES

The proposed protocol encompasses testing different constructs of vestibular and balance function. First, self-assessment scales or questionnaires are suggested. These instruments are often free

from copyright and cost and can be completed at home, saving the clinician valuable time. Domains such as dizziness handicap, impact of symptoms on daily living, balance confidence, benefit from vestibular rehabilitation, and fall risk are explored in numerous well-constructed and validated scales, many of which are translated into major languages. An excellent resource is the Rehabilitation Measures database (https://www.sralab.org/rehabilitation-measures#our-database), which is a repository of measures commonly used in vestibular assessment and rehabilitation. Normative data and reviews of tests' psychometric properties are provided for many measures.

Key aspects of the case history are discussed next, followed by bedside tests. As the sensitivity and specificity of each clinical test varies, a test battery is helpful rather than singling out one or two tests. Finally, as discussed, aging increases the risk of falls, and vestibular deficits are a known risk factor for falls. However, vestibular inputs are just one source of information supporting the sense of balance. Balance requires the integration of signals from several systems, including vision and proprioception. Therefore, it is important to move the assessment beyond evaluation of vestibular end-organ function and to examine overall function and balance capacity along with fall risk (48).

Self-Assessment Scales/Questionnaires

Two questionnaires are suggested: The first should evaluate the presence of symptoms of vestibular disorder, such as the short dizziness questionnaire from Roland et al. (66) or the Dizziness Symptom Profile (67). Colin et al. (24) propose a very simple, seven-item questionnaire for their CI series of patients, focused on the presence of vertigo and imbalance, quality of and associated symptoms, and timing. The brevity of the simplified Colin et al. assessment questionnaire is most appealing. As falls are such a concern in older adults, fear of falling and balance confidence should be assessed. The two most used scales, both of which have validated translations into many languages, are the Falls Efficacy Scale International (FES-I) and the Activities-Specific Balance Confidence (ABC). Generally, however, screening tools for falls perform poorly and are best used in conjunction with clinical judgement (68) and direct questioning regarding fall events, including slips, trips, and near misses. Of interest is the new fall risk calculator used for research, the FRAT-Up, into which patients' individual data can be entered, and a fall risk estimate is given on a dashboard (http://ffrat.farseeingresearch.eu/). The FRAT-Up correlates well with a history of falls (69). If the responses from the chosen questionnaires do not raise any concerns, potential CI candidates could exit the vestibular and falls assessment protocol at this point. Presence of a fall (whether injurious or not) within the last year should prompt further implementation of the suggested protocol.

Case History

Case history is crucial! Although specialized and clinical testing may point to the site of a lesion, it should be acknowledged that there is little relationship between objective signs and the presence of symptoms due to central compensation processes. Thus, a case history is essential as is an assessment of self-perceived levels of handicap. The latter may indicate patients at risk for a poor prognosis in terms of functional recovery (70). Triggers and the temporal pattern of dizziness should be probed as these descriptions are more reliable than the type of dizziness described (71). The presence of associated symptoms may signal otological or neurological involvement. Routine medications should be reviewed and managed for their contributions to dizziness and fall risk, particularly instances of polypharmacy, which is increasingly frequent in older adults (72). Other causes for dizziness, particularly central causes, should be excluded. Patients whose history suggests progressive vestibular disorders, such as Ménière's disease, should be flagged for referral to a center with objective testing.

Clinical Vestibular Screening Tests

Clinical tests of the vestibulo-ocular reflex include head thrust (also known as head impulse) testing, head shake, dynamic visual acuity, and hyperventilation. Using a test battery of screening vestibular tests enhances constructing a picture of unilateral or bilateral vestibular hypofunction and, thus, is recommended. As supported by vHIT, clinical screening for mild-to-moderate unilateral vestibular hypofunction is somewhat insensitive, so the head thrust test has limited usefulness for screening (73). However, the test is useful for identification of bilateral vestibular hypofunction (73) and is, thus, worthwhile conducting in a CI population. As with the instrumented test, technique is important (73). Patients identified with a positive head thrust should be referred for further testing, particularly if there is no acute cause for vertigo on the day of the test. Head shake performs more poorly than head thrust in terms of sensitivity but has good specificity (73). The test is commonly used despite poor evidence to support it, and of course, in patients with bilateral lesions, the test is even less helpful. Results are enhanced for tests such as head shake and hyperventilation if fixation is abolished, and cheap versions of Frenzel-type lenses are readily available.

The Subjective Visual Vertical (SVV) test can be done in an analog form or digitally using a mobile phone app, both in a bucket (64). Vestibular lesions are known to influence the perception of gravitational vertical. The test is quick and easy to administer, and the equipment can be assembled with little cost. Results are resistant to changes with age, making SVV appealing for an older adult population. Of interest for older CI candidates, some researchers suggest that the SVV can be helpful in the chronic phase of Ménière's disease (64) although, as with all the screening tests in this section, there have been questions regarding SVV's sensitivity and specificity (73). A recent meta-analysis has gone some way to refine the role of SVV in patients with peripheral vestibular disorder, and pooled results recommend SVV for the evaluation of vestibular function in patients undergoing vestibular surgery, such as vestibular schwannoma removal (74). Moreover, as discussed, VEMPs are not practical in an older and hearing-impaired population, so at least the clinical SVV gives some information regarding the otolith-ocular reflex.

As benign paroxysmal positional vertigo (BPPV) is so common, routine testing with a Dix-Hallpike maneuver and tests

of the horizontal canal are highly recommended (73) along with appropriate treatment. CI candidates with a history of BPPV or new onset positionally induced symptoms should be screened after surgery to ensure that the condition has not arisen.

Screening tests might assist with lateralizing the side of lesion along with identifying possible bilateral lesions, and so can help refine the necessity for further testing in resource-constrained settings. Bedside evaluation may quickly answer questions as to which side to implant in unilateral recipients, but the role of vestibular compensation could influence the likelihood of positive findings. Finally, testing may help to identify patients who may need to be referred for vestibular rehabilitation therapy either before or after implantation. It is suggested that the following results, either in isolation or combination should trigger a referral for further testing: presence of spontaneous or gaze nystagmus, uni- or bilateral saccade/s on head thrust, abnormal SVV, nystagmus on headshake. Any BPPV should be treated and the patient reevaluated prior to further referral decisions.

Exclude Another Common Condition: Orthostatic Hypotension

Orthostatic hypotension, with its associated dizziness and faintness on standing, can impair quality of life as well as reduce the ability to conduct the activities of daily living, making it potentially disabling (75). As orthostatic hypotension is linked to both dizziness and falls, clinicians working with older adults should be aware of the problem and the new diagnostic criteria from the Bárány Society (76) among others. Studies concerning the prevalence of orthostatic hypotension cite varying prevalence, likely linked to varying techniques for diagnosing the condition; however, a meta-analysis suggests that around 22.2% of older adults have the condition (75). This one in five prevalence makes a case for measuring blood pressure in supine and standing conditions in older adults.

Tests of Static and Dynamic Balance

Tests of static and dynamic balance shift the focus from evaluation of the vestibular end-organs. Good balance is crucial for maintaining independence and competence in the activities of daily living along with preventing falls. Different components of balance are involved in maintaining either static (standing quietly) or dynamic (moving) balance, and it is important to test both aspects of postural control. Vestibular deficits are shown to increase the likelihood of falling during performance of simple dynamic balance tasks, such as transitioning from sitting to standing or changing body position (77). A plethora of tests exist across different age groups and medical conditions. One static and one dynamic test of balance is suggested for screening older adult CI candidates in emerging regions. Both tests are simple, in common use, and require minimal training. Should the results be abnormal, more focused tests should be considered (e.g., MiniBESTest) along with strategies to evaluate and manage fall risk. The Clinical Test of Sensory Integration of Balance (now referred to as the modified or m-CTSIB) is superior to the Romberg tests of old and can be used to evaluate the different inputs to balance (vision, vestibular, proprioception), giving important information for a therapeutic focus. The m-CTSIB is reliable and uses minimum equipment (78). Normative data for different age groups have been published recently (73). The test should be done with shoes removed and may be conducted with the feet together or apart (78).

Dynamic gait tests assess mobility walking and transitioning and are suitable to assess the functional status of older adults (79) along with fall risk. Specific to the older adult population, tests including transfers from sitting to standing are suggested. One of the most popular is the Timed-Up-and-Go (TUG), which is frequently used in both research and clinical contexts, including primary care in developed countries. Controversy exists regarding the cutoff at which fall risk can be reliably identified. The Centers for Disease Control's recommendation of 12 s (80) should be adopted. Normative data are available, which clearly show the relationship between sex and age with slowing of scores (81). Enhancements involving dual tasking (manual and cognitive conditions) help sharpen the test. Although a cognitive version has shown significant correlations with fall events (82), the dual-tasking mode of walking and counting might be challenging for patients with limited numeracy skills.

NEXT STEPS

With a dearth of reports on screening protocols for older CI candidates, formal research is required to evaluate protocols' efficiency and clinical utility for vestibular and fall risk assessments. The simple nature of the screening assessments suggested in this *Perspectives* article has inherent appeal. Should one piece of equipment be considered, vHIT makes the most prudent choice. The proposed protocol lends itself to be adopted by a variety of professionals in different contexts. The author calls for audiologists in particular to embrace their role assessing and indeed managing vestibular disorders in older adults in general as well as CI candidates, which should include judicious application of vestibular rehabilitation therapy and fall risk–reduction strategies.

DATA AVAILABILITY STATEMENT

The original contributions presented in the study are included in the article/supplementary material, further inquiries can be directed to the corresponding author.

AUTHOR CONTRIBUTIONS

The author confirms being the sole contributor of this work and has approved it for publication.

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REFERENCES

1. Cuevas-Trisan R. Balance problems and fall risks in the elderly. *Phys Med Rehabil Clin.* (2017) 28:727–37. doi: 10.1016/j.pmr.2017.06.006
2. Gorman M. Development and rights of older people. In: Randal TG, Ewing D, editors. *The Ageing and Development Report.* 1st ed. London: Routlege (2017) p. 21–39. doi: 10.4324/9781315071541-2
3. Masud T, Morris RO. Epidemiology of falls. *Age Ageing.* (2001) 30:3–7. doi: 10.1093/ageing/30.suppl_4.3
4. Jahn K. The aging vestibular system: dizziness and imbalance in the elderly. *Adv Otorhinolaryngol.* (2019) 82:143–9. doi: 10.1159/000490283
5. Agrawal Y, Merfeld DM, Horak FB, Redfern MS, Manor B, Westlake KP, et al. Aging, vestibular function, and balance: proceedings of a national institute on aging/National institute on deafness and other communication disorders workshop. *J Gerontol.* (2020) 75:2471–80. doi: 10.1093/gerona/glaa097
6. Anson E, Jeka J. Perspectives on aging vestibular function. *Front Neurol.* (2016) 6:269. doi: 10.3389/fneur.2015.00269
7. Agrawal Y. Age-related vestibular loss: current understanding and future research directions. *Front Neurol.* (2017) 8:443. doi: 10.3389/fneur.2017.00443
8. Ambrose AF, Paul G, Hausdorff JM. Risk factors for falls among older adults: a review of the literature. *Maturitas.* (2013) 75:51–61. doi: 10.1016/j.maturitas.2013.02.009
9. Frith J, Davison J. Falls. *Rev Clin Gerontol.* (2013) 23:101–7. doi: 10.1017/S0959259813000026
10. Skelton DA, Hauer K, Lamb S. Re: "falls definition validation." *Age Ageing.* (2007) 36:111–2. doi: 10.1093/ageing/afl138
11. Copsey B, Hopewell S, Becker C, Cameron ID, Lamb SE. Appraising the uptake and use of recommendations for a common outcome data set for clinical trials: a case study in fall injury prevention. *Trials.* (2016) 17:131. doi: 10.1186/s13063-016-1259-7
12. Kosma M. An expanded framework to determine physical activity and falls risks among diverse older adults. *Res Aging.* (2014) 36:95–114. doi: 10.1177/0164027512469215
13. Kenny RA, Romero-Ortuno R, Kumar P. Falls in older adults. *Medicine.* (2017) 45:28–33. doi: 10.1016/j.mpmed.2016.10.007
14. Avin KG, Hanke TA, Kirk-Sanchez N, McDonough CM, Shubert TE, Hardage J, et al. Management of falls in community-dwelling older adults: clinical guidance statement from the academy of geriatric physical therapy of the American physical therapy association. *Phys Ther.* (2015) 95:815–34. doi: 10.2522/ptj.20140415
15. Kiely DK, Kim DH, Gross AL, Habtemariam DA, Leveille SG, Li W, et al. Fall risk is not black and white. *J Health Dispar Res Prac.* (2015) 8:72–84.
16. Jiam NTL, Li C, Agrawal Y. Hearing loss and falls: a systematic review and meta-analysis. *Laryngoscope.* (2016) 126:2587–96. doi: 10.1002/lary.25927
17. Shayman CS, Earhart GM, Hullar TE. Improvements in gait with hearing aids and cochlear implants. *Otol Neurotol.* (2017) 38:484–6. doi: 10.1097/MAO.0000000000001360
18. Criter RE, Honaker JA. Falls in the audiology clinic: a pilot study. *J Am Acad Audiol.* (2013) 24:1001–5. doi: 10.3766/jaaa.24.10.11
19. Rutherford BR, Brewster K, Golub JS, Kim AH, Roose SP. Sensation and psychiatry: linking age-related hearing loss to late-life depression and cognitive decline. *Am J Psychiatry.* (2017) 175:215–24. doi: 10.1176/appi.ajp.2017.17040423
20. Bittar RSM, Sato ES, Ribeiro DJS, Tsuji RK. Preoperative vestibular assessment protocol of cochlear implant surgery: an analytical descriptive study. *Braz J Otorhinolaryngol.* (2017) 83:530–5. doi: 10.1016/j.bjorl.2016.06.014
21. Louza J, Klappert CL, Ledderose G, Gürkov R, Krause E. Cochlear implant surgery and the risk of falls in an adult population. *Otol Neurotol.* (2018) 39:e74–9. doi: 10.1097/MAO.0000000000001656
22. Stevens MN, Baudhuin JE, Hullar TE, Group WUCIS. Short-term risk of falling after cochlear implantation. *Audiol Neurotol.* (2014) 19:370–7. doi: 10.1159/000363214
23. Jacobson GP, McCaslin DL, Piker EG, Gruenwald J, Grantham S, Tegel L. Insensitivity of the "Romberg test of standing balance on firm and compliant support surfaces" to the results of caloric and VEMP tests. *Ear Hear.* (2011) 32:e1–5. doi: 10.1097/AUD.0b013e31822802bb
24. Colin V, Bertholon P, Roy S, Karkas A. Impact of cochlear implantation on peripheral vestibular function in adults. *Eur Ann Otorhinolaryngol Head Neck Dis.* (2018) 135:417–20. doi: 10.1016/j.anorl.2018.10.007
25. Amin N, Wong G, Nunn T, Jiang D, Pai I. The outcomes of cochlear implantation in elderly patients: a single United Kingdom center experience. *Ear Nose Throat J.* (2020) 99:0145561320910662. doi: 10.1177/0145561320910662
26. Gibson W, Hunter KF, Camicioli R, Booth J, Skelton DA, Dumoulin C, et al. The association between lower urinary tract symptoms and falls: forming a theoretical model for a research agenda. *Neurourol Urodyn.* (2017) 37:501–9. doi: 10.1002/nau.23295
27. Rose D. Predicting the risk of falls and promoting balance in older adults. *Ann Rheum Dis.* (2017) 76:30. doi: 10.1136/annrheumdis-2017-eular.7244
28. Larson EB. Evidence supports action to prevent injurious falls in older adults. *JAMA.* (2017) 318:1659–60. doi: 10.1001/jama.2017.15098
29. O'Connell M, Kenny RA, Donoghue O. *Measures of Health and Function That Predict Future Falls.* Dublin: Trinity College (2017). doi: 10.38018/TildaRe.2017-01.c6
30. Sri-On J, Tirrell GP, Bean JF, Lipsitz LA, Liu SW. Revisit, subsequent hospitalization, recurrent fall, and death within 6 months after a fall among elderly emergency department patients. *Ann Emerg Med.* (2017) 70:521.e2. doi: 10.1016/j.annemergmed.2017.05.023
31. Li F, Eckstrom E, Harmer P, Fitzgerald K, Voit J, Cameron KA. Exercise and fall prevention: narrowing the research-to-practice gap and enhancing integration of clinical and community practice. *J Am Geriatr Soc.* (2016) 64:425–31. doi: 10.1111/jgs.13925
32. Organisation WH. *Falls Fact Sheet*. WHO (2017).
33. Siracuse JJ, Odell DD, Gondek SP, Odom SR, Kasper EM, Hauser CJ, et al. Health care and socioeconomic impact of falls in the elderly. *Am J Surg.* (2012) 203:335–8. doi: 10.1016/j.amjsurg.2011.09.018
34. Fu WW, Fu TS, Jing R, McFaull SR, Cusimano MD. Predictors of falls and mortality among elderly adults with traumatic brain injury: a nationwide, population-based study. *PLoS ONE.* (2017) 12:e0175868. doi: 10.1371/journal.pone.0175868
35. Albrecht JS, Al Kibria G, Gruber-Baldini A, Magaziner J. Risk of mortality in individuals with hip fracture and traumatic brain injury. *J Am Geriatr Soc.* (2019) 67:124–7. doi: 10.1111/jgs.15661
36. Fernandez MA, Griffin XL, Costa ML. Management of hip fracture. *Br Med Bull.* (2015) 115:165–72. doi: 10.1093/bmb/ldv036
37. Zanker J, Duque G. Rapid geriatric assessment of hip fracture. *Clin Geriatr Med.* (2017) 33:369–82. doi: 10.1016/j.cger.2017.03.003
38. Agrawal Y, Van de Berg R, Wuyts F, Walther L, Magnusson M, Oh E, et al. Presbyvestibulopathy: diagnostic criteria consensus document of the classification committee of the barany society. *J Vestib Res.* (2019) 29:161–70. doi: 10.3233/VES-190672
39. Rogers C. Presbyastasis: a multifactorial cause of balance problems in the elderly. *South Afr Fam Pract.* (2010) 52:431–4. doi: 10.1080/20786204.2010.10874018
40. Ibrahim I, da Silva SD, Segal B, Zeitouni A. Effect of cochlear implant surgery on vestibular function: meta-analysis study. *J Otolaryngol Head Neck Surg.* (2017) 46:1–10. doi: 10.1186/s40463-017-0224-0
41. Hänsel T, Gauger U, Bernhard N, Behzadi N, Romo Ventura ME, Hofmann V, et al. Meta-analysis of subjective complaints of vertigo and vestibular tests after cochlear implantation. *Laryngoscope.* (2018) 128:2110–23. doi: 10.1002/lary.27071
42. Rohloff K, Koopmann M, Wei D, Rudack C, Savvas E. Cochlear implantation in the elderly: does age matter? *Otol Neurotol.* (2017) 38:54–9. doi: 10.1097/MAO.0000000000001262
43. van de Berg R, Rosengren S, Kingma H. Laboratory examinations for the vestibular system. *Curr Opin Neurol.* (2018) 31:111–6. doi: 10.1097/WCO.0000000000000526
44. Ngobeni V, Breitenbach MC, Aye GC. Technical efficiency of provincial public healthcare in South Africa. *Cost Eff Resour Allocation.* (2020) 18:3. doi: 10.1186/s12962-020-0199-y
45. South African Cochlear Implant Group (2020). *Appendix F. Guidelines for Pre- and Post-operative Audiological Assessment of Adults and Children and Long-Term Management*. Available online at: http://www.sacig.org.za/wp-content/

uploads/2020/01/APPENDIX-F-AUDIOLOGICAL-ASSSESSMENT-AND-MANAGEMENT.pdf (accessed March 21, 2021).
46. West N, Klokker M, Cayé-Thomasen P. Vestibular screening before cochlear implantation: clinical implications and challenges in 409 cochlear implant recipients. *Otol Neurotol.* (2021) 42:e137–44. doi: 10.1097/MAO.0000000000002898
47. Zalewski CK. Aging of the human vestibular system. *Semin Hear.* (2015) 36:175–96. doi: 10.1055/s-0035-1555120
48. Krager R. Assessment of vestibular function in elderly patients. *Curr Opin Otolaryngol Head Neck Surg.* (2018) 26:302–6. doi: 10.1097/MOO.0000000000000476
49. Tarnutzer AA, Straumann D. Nystagmus. *Curr Opin Neurol.* (2018) 31:74–80. doi: 10.1097/WCO.0000000000000517
50. Brandt T, Dieterich M. The dizzy patient: don't forget disorders of the central vestibular system. *Nat Rev Neurol.* (2017) 13:352–62. doi: 10.1038/nrneurol.2017.58
51. McCaslin DL. Stopping medications before vestibular testing: evidence-bnsed or neuromythology? *J Am Acad Audiol.* (2018) 29:566–7. doi: 10.3766/jaaa.29.7.1
52. Kelly EA, Stocker C, Kempton CM, Dierking DM, Fehlberg HE, Adams ME. Vestibular testing: patient perceptions, morbidity, and opportunity costs. *Otol Neurotol.* (2018) 39:1222–8. doi: 10.1097/MAO.0000000000002025
53. Piker EG, Riska K, Garrison D, Kaylie DM. Vestibular function after cochlear implantation: a test battery and case-by-case approach. *Laryngoscope Investig Otolaryngol.* (2020) 5:560–71. doi: 10.1002/lio2.413
54. Alhabib SF, Saliba I. Video head impulse test: a review of the literature. *Eur Arch Otorhinolaryngol.* (2017) 274:1215–22. doi: 10.1007/s00405-016-4157-4
55. Hougaard DD, Abrahamsen ER. Functional testing of all six semicircular canals with video head impulse test systems. *J Vis Exp.* (2019) 146:1–14. doi: 10.3791/59012
56. Janky KL, Rodriguez AI. Quantitative vestibular function testing in the pediatric population. *Semin Hear.* (2018) 39:257–74. doi: 10.1055/s-0038-1666817
57. Piker EG, Baloh RW, Witsell DL, Garrison DB, Lee WT. Assessment of the clinical utility of cervical and ocular vestibular evoked myogenic potential testing in elderly patients. *Otol Neurotol.* (2015) 36:1238–44. doi: 10.1097/MAO.0000000000000793
58. Fife TD, Colebatch JG, Kerber KA, Brantberg K, Strupp M, Lee H, et al. Practice guideline: cervical and ocular vestibular evoked myogenic potential testing: report of the guideline development, dissemination, and implementation subcommittee of the american academy of neurology. *Neurology.* (2017) 89:2288–96. doi: 10.1212/WNL.0000000000004690
59. Croarkin E, Zampieri C. On the eDGE of task force recommendations: computerized balance assessment. *Rehabil Oncol.* (2021) 39:64–7. doi: 10.1097/01.REO.0000000000000246
60. Smart A. A multi-dimensional model of clinical utility. *Int J Qual Health Care.* (2006) 18:377–82. doi: 10.1093/intqhc/mzl034
61. Marozas M, Marozas V, Stanaitis S, Uloziene I, Ulozas V, Šileikaite M, et al. Virtual reality approach for testing dynamic visual acuity. *Biomed Eng.* (2016) 19:105–10.
62. Riska KM, Hall CD. Reliability and normative data for the dynamic visual acuity test for vestibular screening. *Otol Neurotol.* (2016) 37:545–52. doi: 10.1097/MAO.0000000000001014
63. Wengier A, Ungar OJ, Handzel O, Cavel O, Oron Y. Subjective visual vertical evaluation by a smartphone-based test—taking the phone out of the bucket. *Otol Neurotol.* (2021) 42:455–60. doi: 10.1097/MAO.0000000000002944
64. Zabaneh SI, Voss LJ, Szczepek AJ, Olze H, Stölzel K. Methods for testing the subjective visual vertical during the chronic phase of menière's disease. *Diagnostics.* (2021) 11:249. doi: 10.3390/diagnostics11020249
65. Clark RA, Mentiplay BF, Pua Y-H, Bower KJ. Reliability and validity of the wii balance board for assessment of standing balance: a systematic review. *Gait Posture.* (2018) 61:40–54. doi: 10.1016/j.gaitpost.2017.12.022
66. Roland LT, Kallogjeri D, Sinks BC, Rauch SD, Shepard NT, White JA, et al. Utility of an abbreviated dizziness questionnaire to differentiate between causes of vertigo and guide appropriate referral: a multicenter prospective blinded study. *Otol Neurotol.* (2015) 36:1687–94. doi: 10.1097/MAO.0000000000000884
67. Jacobson GP, Piker EG, Hatton K, Watford KE, Trone T, McCaslin DL, et al. Development and preliminary findings of the dizziness symptom profile. *Ear Hear.* (2019) 40:568–76. doi: 10.1097/AUD.0000000000000628
68. Ruggieri M, Palmisano B, Fratocchi G, Santilli V, Mollica R, Berardi A, et al. Validated fall risk assessment tools for use with older adults: a systematic review. *Phys Occup Ther Geriatr.* (2018) 36:331–53. doi: 10.1080/02703181.2018.1520381
69. Rogers C. *The feasibility and potential effectiveness of a conventional and exergame intervention to alter balance-related outcomes including fall risk: a mixed methods study* (Doctoral). Cape Town South Africa: University of Cape Town (2020).
70. Maarsingh OR, van Vugt VA. Ten vestibular tools for primary care. *Front Neurol.* (2021) 12:642137. doi: 10.3389/fneur.2021.642137
71. Edlow JA, Gurley KL, Newman-Toker DE. A new diagnostic approach to the adult patient with acute dizziness. *J Emerg Med.* (0736-4679). (2018) 54:469–83. doi: 10.1016/j.jemermed.2017.12.024
72. Wastesson JW, Morin L, Tan EC, Johnell K. An update on the clinical consequences of polypharmacy in older adults: a narrative review. *Expert Opin Drug Saf.* (2018) 17:1185–96. doi: 10.1080/14740338.2018.1546841
73. Cohen HS. A review on screening tests for vestibular disorders. *J Neurophysiol.* (2019) 122:81–92. doi: 10.1152/jn.00819.2018
74. Obrero-Gaitán E, Molina F, Montilla-Ibañez MD, Del-Pino-Casado R, Rodriguez-Almagro D, Lomas-Vega R. Misperception of visual vertical in peripheral vestibular disorders. A systematic review with meta-analysis. *Laryngoscope.* (2020) 131:1110–21. doi: 10.1002/lary.29124
75. Saedon NI, Pin Tan M, Frith J. The prevalence of orthostatic hypotension: a systematic review and meta-analysis. *J Gerontol.* (2020) 75:117–22. doi: 10.1093/gerona/gly188
76. Kim HA, Bisdorff A, Bronstein AM, Lempert T, Rossi-Izquierdo M, Staab JP, et al. Hemodynamic orthostatic dizziness/vertigo: diagnostic criteria. *J Vestib Res.* (2019) 29:45–56. doi: 10.3233/VES-190655
77. Dunsky A, Zeev A, Netz Y. Balance performance is task specific in older adults. *BioMed Res Int.* (2017) 2017:6987017. doi: 10.1155/2017/6987017
78. Horn LB, Rice T, Stoskus JL, Lambert KH, Dannenbaum E, Scherer MR. Measurement characteristics and clinical utility of the clinical test of sensory interaction on balance (CTSIB) and modified cTSIB in individuals with vestibular dysfunction. *Arch Phys Med Rehabil.* (2015) 96:1747–8. doi: 10.1016/j.apmr.2015.04.003
79. Dawson N, Dzurino D, Karleskint M, Tucker J. Examining the reliability, correlation, and validity of commonly used assessment tools to measure balance. *Health Sci Rep.* (2018) 1:e98. doi: 10.1002/hsr2.98
80. Ambrose AF, Cruz L, Paul G. Falls and fractures: a systematic approach to screening and prevention. *Maturitas.* (2015) 82:85–93. doi: 10.1016/j.maturitas.2015.06.035
81. Ibrahim A, Singh DKA, Shahar S. "Timed up and go" test: age, gender and cognitive impairment stratified normative values of older adults. *PLoS ONE.* (2017) 12:e0185641. doi: 10.1371/journal.pone.0185641
82. Tong Y, Tian X, Wang Y, Han J, Waddington G, Adams R. Cognitive dual-task timed-up-and-go test as a predictor of falls in the community-dwelling elderly. *J Sci Med Sport.* (2018) 21:S80. doi: 10.1016/j.jsams.2018.09.184

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Alteration of Vestibular Function in Pediatric Cochlear Implant Recipients

*Hajime Koyama[1], Akinori Kashio[1], Chisato Fujimoto[1], Tsukasa Uranaka[1], Yu Matsumoto[1], Teru Kamogashira[1], Makoto Kinoshita[1], Shinichi Iwasaki[2] and Tatsuya Yamasoba[1]**

[1] Department of Otolaryngology and Head and Neck Surgery, Graduate School of Medicine, The University of Tokyo, Tokyo, Japan, [2] Department of Otolaryngology and Head and Neck Surgery, Graduate School of Medical Sciences and Medical School, Nagoya City University, Nagoya, Japan

Background: Vestibular dysfunction is a complication of cochlear implantation (CI). Reports on the evaluation of vestibular function before and after CI are limited, especially in children. We investigated the effect of CI on vestibular function in pediatric patients.

Patients and Methods: We routinely evaluated vestibular function before but not immediately after CI. Therefore, patients who underwent sequential bilateral CI were enrolled in this study. Seventy-three children who underwent sequential CI from 2003 to 2020 at our hospital were included. Since the vestibular function of the first implanted ear was evaluated before the second surgery for the contralateral ear, post-CI evaluation timing differed among the cases. The evaluation included a caloric test, a cervical vestibular-evoked myogenic potential (cVEMP) test, and a damped rotation test. The objective variables included the results of these tests, and the explanatory variables included the age at surgery, cause of hearing loss, electrode type, and surgical approach used. The associations of these tests were analyzed.

Results: cVEMP was the most affected after CI (36.1%), followed by the caloric test (23.6%), and damped rotation test (7.8%). Cochleostomy was significantly more harmful than a round window (RW) approach or an extended RW approach based on the results of the caloric test ($p = 0.035$) and damped rotation test ($p = 0.029$). Perimodiolar electrodes affected the caloric test results greater than straight electrodes ($p = 0.041$). There were no significant associations among these tests' results.

Conclusions: Minimally invasive surgery in children using a round window approach or an extended round window approach with straight electrodes is desirable to preserve vestibular function after CI.

Keywords: cochlear implantation, vestibular dysfunction, caloric test, damped rotation test, perimodiolar electrode

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Hannover Medical School, Germany

***Correspondence:**
Tatsuya Yamasoba
tyamasoba-tky@umin.ac.jp

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INTRODUCTION

Cochlear implantation (CI) is an effective treatment for severe-to-profound sensorineural hearing loss (SNHL). Bilateral CI has been reported to be beneficial for sound localization and for preverbal communication and language development, particularly in pediatric cases (1). However, CI can cause vestibular dysfunction (2–4). The importance of vestibular preservation has been

widely acknowledged because bilateral CI recipients are at an increased risk of bilateral vestibular dysfunction. Previous studies have assessed vestibular function after CI in adults (5, 6) and children (7, 8); however, the incidence of vestibular impairment varies across reports. This variation can be attributed to factors such as patient demographics, differences among electrodes, and insertion approach. Few studies have compared the surgical approach (9, 10) as a risk factor for CI-induced vestibular impairment. Hansel et al. analyzed the risks of cochleostomy in a meta-analysis and found a low incidence of subjective vertigo among children (11), but most of the data in the studies included in their meta-analysis were obtained from adult patients; therefore, the identity of the risk factors for vestibular impairment in children remains unclear. Basic research suggests an age-dependent nature of cochlear damage (12–15), and clarification of the vestibular effects and risk factors after CI is needed not only for adults but particularly for children.

Our hospital routinely performs caloric testing, cervical vestibular-evoked myogenic potential (cVEMP) testing, and damped rotation testing to evaluate vestibular function before CI, even in children. In patients undergoing sequential bilateral CI, identical vestibular tests are performed for both the ears. Using these data, we could compare the vestibular function of the first implanted ear before and after the procedure. This study aimed to estimate the deterioration of vestibular function after CI in pediatric patients who received sequential bilateral CI and identify the risk factors for vestibular dysfunction. By assessing the prognostic factors for CI-induced vestibular dysfunction, we sought to shed light on the best strategy for this procedure in children.

MATERIALS AND METHODS

Participants

A total of 73 children (male: 38, female: 35, mean age: 5 years and 7 months ± 3 years and 6 months) who underwent sequential CI for bilateral, severe-to-profound sensorineural hearing loss from 2003 to 2020 at our hospital were included in this study. The mean age at pre-operative evaluation was 2 years and 8 months (range: 5 months−12 years), and the mean age at post-operative evaluation after the second CI was 5 years and 6 months (range: 1 year 4 months−17 years). The mean interval between the pre-operative and post-operative evaluations was 2 years and 9 months (range: 4 months−13 years).

Informed consent was obtained from the parents of all patients. This study was conducted in compliance with the Declaration of Helsinki. The Institutional Review Board of our institution approved this study (2487).

Vestibular Function Tests

Patients routinely underwent caloric test, cVEMP test, and damped rotation test on both sides before the CI surgery. Post-operative vestibular function in the first implanted ear was measured before the second CI surgery for the contralateral ear. Therefore, we could compare the vestibular function of the first implanted ear before and after CI surgery, and we could measure the change in vestibular function of the non-implanted side during this time without surgery.

We classified the response in each vestibular function test as positive, weak, and negative. We defined the deterioration of vestibular function when the classification changed from positive to weak, positive to negative, or weak to negative, to clearly assess the adverse effect of surgery. Children who were uncooperative or unable to take the test (nine children in caloric test, 17 children in cVEMP test, and 21 children in damped rotation test) could not be assessed, and their data were excluded from the analysis. Those who showed negative responses both pre-operatively and post-operatively (nine children in caloric test, 20 children in cVEMP test, and one child in damped rotation test) were also excluded from the study because we could not accurately evaluate vestibular function alteration caused by surgery. In total, 55, 36, and 51 children were included in caloric test, cVEMP test, and damped rotation test, respectively.

Caloric Test

Two milliliters of cold water (0°C) was injected into the ear of the children, with their head turned by the examiner, and held for 20 s; thereafter, the water was drained by turning the subject's head, and electronystagmography was performed. We employed a caloric test using only ice water because it requires less time and, thus, is considered more convenient for children than the conventional method. A previous report also has revealed that this technique is useful compared with the conventional approach (16). The duration of induced nystagmus was set as the outcome parameter. Because it was difficult to ask children to look at the targets, calibration was not performed. We evaluated the result as previously reported (17). The normal limit of duration was defined as the average value minus two standard deviations at each age (53.3 s for <24 months, 54.3 s for 25–36 months, 52.4 s for 49–60 months, 48.1 s for 61–72 months, and 35.1 s for >72 months). A positive response was defined when the duration was equal to or longer than the normal limit. The response was considered negative when nystagmus could not be confirmed when water was injected into the implanted ear. A weak response was defined when the duration was shorter than the normal limit.

Cervical Vestibular-Evoked Myogenic Potential

cVEMP was performed as described previously (18). In summary, surface electromyographic activity of the sternocleidomastoid muscle in response to short tone bursts of 500 Hz (135 dBSPL, rise/fall time 1 ms, plateau time 2 ms) was recorded, and the positive–negative (p13–n23) complex was assessed. The upper limit of the normal cVEMP asymmetry ratio (AR) was set at 34.0. A positive response was defined when reproducible p13–n23 was found in the implanted ear, and cVEMP AR was normal. A negative response was defined when no reproducible p13–n23 was found. A weak response was defined as when reproducible p13–n23 was found in the implanted ear, and cVEMP AR was greater than the normal upper limit.

Damped Rotation Test

For this test, the children sat on their parent's lap or directly on a chair. The parent restrained the child's head vertically with their arms and hands. The rotation started at 160° per second, and electronystagmography was recorded for 40 s. The chair rotated instantly from this speed toward the non-CI ear, and rotation speed was reduced to zero in 40 s, which indicates that the nystagmus was recorded until the chair stopped. The number of beats was set as the outcome parameter. Calibration was not performed because of similar reasons as that of the caloric test. We evaluated the response as previously reported (17). The normal limit of the number of beats was defined as the average value minus two standard deviations at each age, as was reported by a previous paper for children up to 6 years old (19). For children older than 6 years, the normal limit of number of beats was set as 23, which was based on the number of per-rotatory nystagmus beats in 15 normal children between the ages of 7 and 9 years (31 ± 3.9 beats) recorded in the previous report (17). A positive response was defined when the number of beats was equal to or greater than the normal limit. A response was considered negative when nystagmus could not be confirmed in rotations when the implanted ear was predominantly stimulated. A weak response was defined when the number of beats was less than the normal limit.

Statistical Analysis

Vestibular function deterioration was defined when the patients had a positive or weak response before surgery that dropped to a weak response or no response after surgery in each vestibular test. Correlations between the different test results (caloric test and cVEMP test, caloric test and damped rotation chair test, and cVEMP test and damped rotation chair test) were estimated. The deterioration of vestibular function was determined as an objective variable, and the causes of hearing loss (genetic or otherwise), age at first CI (younger or older than 2 years), type of electrode (straight-type electrode: CI24M, CI24ST, CI24RST, CI422, CI522; or perimodiolar electrode: CI24RCS, CI24RE, CI512), and insertion approaches [cochleostomy, or extended round window (RW) and RW approaches] were selected as explanatory variables. Age threshold was determined based on reports that cochlear implantation under the age of 2 years is more beneficial for the development of receptive and expressive language skills (20, 21), and that there is a growing need to evaluate the risk of the vestibular deterioration after CI in children under 2 years old. We used Fisher's exact test to assess the risk of each independent variable and the differences among each vestibular test. Statistical significance was set to $p < 0.05$.

RESULTS

Patient Demographics

All patients received CI successively. During the follow-up period, no case had any episode of head injury or major complications such as infections that can cause substantial vestibular functional loss after CI.

Table 1 shows the patients' demographics. Genetic mutation was the most frequent cause for SNHL (31/73, 42.4%), followed by viral infection, and syndrome or inner ear malformation. Other causes were neonatal asphyxia and low birth weight. Children were diagnosed with an unknown cause when we were unable to find any genetic mutations, viral infections, other organ diseases, inner ear malformations, or other events that affected hearing function.

TABLE 1 | Patient demographics.

Age at pre-operative evaluation (range)			2 years and 8 months. (5 months–12 years)
Age at post-operative evaluation (range)			5 years and 6 months (1 year and 14 months–17 years)
Side of first CI	Left		17
	Right		56
Etiology	Genetic	*GJB2*	26
		CDH23	3
		OTOF	1
		TMPRSS3	1
	Virus	CMV	9
		Rubella	1
		Mumps	1
	Syndrome	Waardenburg	4
		Usher	1
	Inner ear malformations	CC	1
		IP-1	2
		CH-3	1
		CNC stenosis	1
	Other		2
	Unknown		19
Electrode type	Straight type	CI24M	1
		CI24ST	2
		CI24RST	2
		CI422	8
		CI522	27
	Perimodiolar type	CI24RCS	1
		CI24RE	30
		CI512	1
	Slim modiolar type	CI532	1
Surgical approach	Cochleostomy		35
	Extended RW approach		3
	RW approach		35

CC, common cavity; CMV, cytomegalovirus; CNC, cochlear nerve canal; CH, cochlear hypoplasia; CI, cochlear implantation; RW, round window.

In the electrode selection, CI522 was the most common straight-type electrode used for surgery, while CI24RE was the most common perimodiolar-type electrode used.

Vestibular Function Results

The child's vestibular function was considered to deteriorate when the condition changed from positive preoperatively to

TABLE 2 | Results of vestibular function tests.

Evaluation change from pre to post	Caloric	cVEMP	Damped rotation chair
Positive to weak	6	3	4
Positive to negative	5	10	0
Weak to negative	2	0	0
Number of deteriorations	13	13	4
Total number of patients	55	36	51
Percentage of deterioration	23.6%	36.1%	7.8%

cVEMP, cervical vestibular evoked myogenic potential.

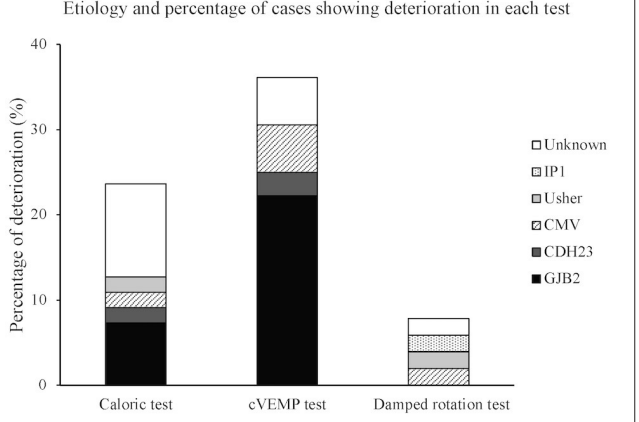

FIGURE 1 | Etiology and percentage of cases showing deterioration in each test. Each bar expresses percentage of deterioration. CMV, cytomegalovirus; IP1, incomplete partition type 1.

weak postoperatively, from positive to negative, or from weak to negative in the three vestibular tests. **Table 2** shows the number of patients displaying the three patterns of deterioration for each test. The numbers indicate the sum total for each test relative to the total number of children who completed the test. Deterioration of test result was most frequently observed in the cVEMP test (36.1%), followed by the caloric test (23.6%), and then the damped rotation test (7.8%). **Figure 1** shows the etiology and percentage of cases that showed deterioration in each test. In the non-CI side, deterioration of test results was observed in only three patients in the caloric test, including one patient who showed the deterioration also in the CI side, four patients in the cVEMP test, including three patients who showed the deterioration in the CI side, and no patient in the damped rotation test.

Associations of the Different Vestibular Function Test Results

Table 3 shows the associations of the different vestibular test results. Comparison between caloric and cVEMP test results indicates that 31 children underwent both tests. When caloric and damped rotation chair tests were compared, a total of 41 children underwent both tests. Finally, between the cVEMP and damped rotation chair tests, a total of 26 children underwent both tests. However, the *p*-values indicate no significant associations among the three vestibular test results.

TABLE 3 | Associations between the vestibular function tests.

		cVEMP test		
		Not deteriorated	**Deteriorated**	***p*-value**
Caloric test	Not deteriorated	17	8	n.s.
	Deteriorated	4	2	
		Damped rotation chair test		
		Not deteriorated	**Deteriorated**	***p*-value**
Caloric test	Not deteriorated	34	2	n.s.
	Deteriorated	3	2	
		Damped rotation chair test		
		Not deteriorated	**Deteriorated**	***p*-value**
cVEMP test	Not deteriorated	15	1	n.s.
	Deteriorated	10	0	

cVEMP, cervical vestibular evoked myogenic potential; n.s., not significant.

Risk Factors Analysis

The deterioration of vestibular function based on each test was compared with age at implantation, surgical approach, electrode type inserted, and existence of genetic mutations (**Table 4**). The number of children categorized with vestibular deterioration, based on each vestibular test result, are shown, and the *p*-values were calculated for comparisons with various parameters. Age and the existence of genetic mutations did not affect any of the vestibular test results. The incidence of reduction in caloric response and damped rotation response was significantly higher ($p = 0.035$ and $p = 0.029$, respectively) among patients in whom an electrode was inserted via a cochleostomy than those who received electrode implantation via a RW or extended RW approach. The patients who received a perimodiolar electrode implantation also showed a significantly higher incidence of reduction in caloric test response ($p = 0.041$) than those who received a straight electrode implantation. However, none of these factors affected the results of the cVEMP test.

DISCUSSION

We evaluated the deterioration of vestibular function in children due to CI using caloric test, cVEMP test, and damped rotation test. In the study population, we observed that 23.6% of the tested patients experienced deterioration in caloric test, 36.1% in cVEMP test, and 7.8% in damped rotation test. Reduction in caloric response and damped rotation response was more frequently observed in patients who underwent cochleostomy, and use of a perimodiolar electrode more frequently caused deterioration of caloric response compared with the use of a straight electrode.

TABLE 4 | Number of deteriorated and non-deteriorated patients in each test and analysis results.

	Caloric test			cVEMP test			Damped rotation test		
	Not deteriorated	deteriorated	*p*-value	Not deteriorated	deteriorated	*p*-value	Not deteriorated	deteriorated	*p*-value
Age at first CI									
≥2	21	7	n.s.	9	7	n.s.	24	2	n.s.
<2	21	6		14	6		23	2	
Surgical approach									
Cochleostomy	15	9	$p = 0.035$	4	5	n.s.	18	4	$p = 0.029$
RW or ExRW	27	4		19	8		29	0	
Electrode type									
Perimodiolar	15	9	$p = 0.041$	5	5	n.s.	18	3	n.s.
Straight	26	4		17	8		28	1	
Genetic mutation									
Yes	19	5	n.s.	13	9	n.s.	22	0	n.s.
No	23	8		10	4		25	4	

CI, cochlear implantation; RW, round window; cVEMP, cervical vestibular evoked myogenic potential; n.s., not significant.

Previous studies have demonstrated that CI has a significant negative effect on the results of caloric and cVEMP test results in adults (5) and children (22). A wide range of rates of negative effects has been reported in caloric test (0–30%) (23, 24) and cVEMP test (20–100%) (25–27), and cochleostomy has also been identified as a risk factor for loss of vestibular function in adults (9). Our results were consistent with those of previous reports, and we also clarified that cochleostomy was a risk factor for vestibular dysfunction in children. We also demonstrated that using a straight electrode reduced the incidence of canal damage.

Several mechanisms have been suggested for vestibular dysfunction due to CI, including traumatic injury, fibrosis, electrical stimulation of the otolithic organs, perilymph fluid leakage, and labyrinthitis due to foreign body reaction (28–30). Histopathological studies have shown that CI insertion affects vestibular function by inducing fibrosis in the vestibule, saccule membrane distortion, and cochlear and vestibular hydrops (31, 32). Compared with the RW approach, cochleostomy has also been suggested to cause fibro-osseous reaction and scala vestibuli fibrosis, resulting in vestibular endolymphatic hydrops more frequently (33, 34). Considering these findings, the RW approach is less likely to cause vestibular damage.

Selection of an electrode type is also important for avoiding inner ear trauma. A previous study reported that a straight electrode is less traumatic to the inner ear than a perimodiolar electrode, which has a higher incidence of translocation from the scala tympani to the scala vestibuli (35). Another histopathology report suggested that scala vestibuli involvement, because of damage to the osseous spiral lamina or basilar membrane in the cochlear basal turn, was highly correlated with vestibular damage (31). Various reports have demonstrated the straight electrode's superiority in cochlear preservation by estimating residual hearing ability (36–38), and a temporal bone study suggested that use of a straight electrode minimized trauma to the intracochlear structures (39). Our results also suggest that a straight electrode is desirable not only for hearing preservation but also for vestibular preservation.

Previous studies have demonstrated that cVEMP is more frequently affected than caloric test or damped rotation chair test (3, 40, 41), as shown in the current study. The saccule may be more susceptible to insertion damage due to its anatomical proximity to the RW. Another reason cVEMP is more frequently affected could be because the packing following implantation may induce conductive hearing loss (42, 43); however, the fascia placed on the RW for packing is very small and may have a limited effect on conduction efficacy. It is noteworthy that the approach of electrode insertion and the electrode type caused a difference in the incidence of CI-induced negative effect on caloric test and rotation test but not on cVEMP. Our results are compatible with previous studies that showed no significant differences in cVEMP between electrode types (44) and between approaches of electrode insertion (22).

It is important to clarify the correlation between the anatomy of the inner ear and the vestibular testing. However, only four cases of inner ear malformation met the criteria of having preoperative and postoperative vestibular testing, and most of them showed a negative response at preoperative evaluation. Because of this limited number of patients, we could not show the correlation between the anatomy of the inner ear and the vestibular testing.

This study has several limitations. First, some children were excluded from this study because they could not be assessed either preoperatively or postoperatively or showed a negative response in vestibular function tests, both preoperatively and postoperatively. Furthermore, when CI was performed on the negative response side, we were unable to detect vestibular function changes. Second, we could not perform a quantitative assessment for either caloric or damped rotation test because we could not complete calibration with the children either preoperative or postoperative condition. Hence, these results contain variability not only at each point but also between these

two time points. Moreover, children are less likely to follow our instructions, which lessens reliability of vestibular test results compared with those of the adults. We attempted to overcome the problem by classifying the test results as previously reported (17, 21). In the current study, deterioration of test results in the non-CI side was observed in only three patients in caloric test, including one who showed the deterioration also in the CI-side, four patients in cVEMP test, including three patients who showed the deterioration in the CI-side, and no patient in damped rotation test. These findings support the high reliability of our test results. Third, electrode type and surgical approach can be correlated, but we were unable to separate the negative effects of these variables. A RW approach is not preferable with a perimodiolar electrode because of anatomical obstacles, namely, the anteroinferior region of the RW bony margin (45). Thus, a straight electrode and RW approach are recommended for vestibular function preservation. As a result, surgeons tend to perform cochleostomy when using a perimodiolar electrode, but an RW approach when using a straight electrode. Fourth, this is a retrospective study, and postoperative evaluation timing differed because the second test was performed just before the second CI, which meant that there was the variety of the intervals. Dysfunctions of the peripheral vestibular receptors could be induced not only by a cochlear implant electrode insertion but also by different mechanisms such as infections or traumatic head injury, and some children with SNHL may experience progressive vestibular dysfunction (46). We could not rule out the effect of these different mechanisms unrelated to the inserted electrode or spontaneous progression of vestibular dysfunction unrelated to CI. In the current study, no patient had experienced head injury after CI or major complications such as infections, which could lessen these effects, and three patients who showed deterioration in the implanted ear showed deterioration of cVEMP in the contralateral non-CI ear, implying that the progressive vestibular dysfunction may not be due to surgery. However, only one patient who showed deterioration on the implanted side showed deterioration on the contralateral side in the caloric test, and no patient showed such deterioration in damped rotation test. A previous report stated that vestibular modifications following the implant were stable (24) and another paper that compared the vestibular test sets performed with different intervals concluded that the differences were not likely a confounder that would influence the results of postoperative decline (10).

In summary, we assessed vestibular function using caloric test, cVEMP test, and damped rotation test before and after CI in children. We evaluated the negative effect of CI on vestibular function based on causes of hearing loss, age at first CI, type of electrode used, and insertion approaches, and concluded that cochleostomy and use of a perimodiolar electrode are risk factors for postoperative deterioration of vestibular function. Although CI is beneficial for children with SNHL, a straight electrode with an RW or extended RW approach would be preferable to preserve vestibular function. Similar results have already been reported in adults, but there were limited number of studies evaluating children. The current study confirms that these findings are also applicable in children. Children with SNHL tend to receive bilateral CI due to bilateral hearing benefit, and the need for preservation of vestibular function is increasing. Therefore, an RW or an extended RW approach with straight electrodes is desirable to preserve vestibular function after CI, especially for children.

DATA AVAILABILITY STATEMENT

The original contributions presented in the study are included in the article/supplementary material, further inquiries can be directed to the corresponding author.

ETHICS STATEMENT

The studies involving human participants were reviewed and approved by Graduate School of Medicine and Faculty of Medicine, The University of Tokyo, Research Ethics Committee. Written informed consent to participate in this study was provided by the participants' legal guardian/next of kin.

AUTHOR CONTRIBUTIONS

HK, AK, CF, and TY contributed to conception and design of the study. HK organized the database, performed the statistical analysis, and wrote the first draft of the manuscript. AK and CF wrote sections of the manuscript. TU, YM, TK, MK, SI, and TY revising it critically for important intellectual content. All authors contributed to manuscript revision, read, and approved the submitted version.

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REFERENCES

1. Lammers MJW, van der Heijden GJMG, Pourier VEC, Grolman W. Bilateral cochlear implantation in children: a systematic review and best-evidence synthesis. *Laryngoscope*. (2014) 124:1694–9. doi: 10.1002/lary.24582
2. Brey RH, Facer GW, Trine MB, Lynn SG, Peterson AM, Suman VJ. Vestibular effects associated with implantation of a multiple channel cochlear prosthesis. *Am J Otol*. (1995) 16:424–30.
3. Buchman CA, Joy J, Hodges A, Telischi FF, Balkany TJ. Vestibular effects of cochlear implantation. *Laryngoscope*. (2004) 114:1–22. doi: 10.1097/00005537-200410001-00001
4. Chiesa Estomba CM, Rivera Schmitz T, Betances Reinoso FA, Dominguez Collado L, Estevez Garcia M, Lorenzo AI. Complications after cochlear implantation in adult patients. 10-year retrospective analysis of a tertiary academic centre. *Auris Nasus Larynx*. (2017) 44:40–5. doi: 10.1016/j.anl.2016.03.012

5. Ibrahim I, Da Silva SD, Segal B, Zeitouni A. Effect of cochlear implant surgery on vestibular function: meta-analysis study. *J Otolaryngol Head Neck Surg*. (2017) 46:44. doi: 10.1186/s40463-017-0224-0
6. Colin V, Bertholon P, Roy S, Karkas A. Impact of cochlear implantation on peripheral vestibular function in adults. *Eur Ann Otorhinolaryngol Head Neck Dis*. (2018) 135:417–20. doi: 10.1016/j.anorl.2018.10.007
7. Yong M, Young E, Lea J, Foggin H, Zaia E, Kozak FK, et al. Subjective and objective vestibular changes that occur following paediatric cochlear implantation: systematic review and meta-analysis. *J Otolaryngol Head Neck Surg*. (2019) 48:22. doi: 10.1186/s40463-019-0341-z
8. Talaat HS, Chedid AIF, Wageih GM, Zein El-Abedein AM. Vestibular function assessment following cochlear implantation using rotatory chair testing. *Eur Arch Oto-Rhino-Laryngol*. (2020). doi: 10.1007/s00405-020-06308-w. [Epub ahead of print].
9. Todt I, Basta D, Ernst A. Does the surgical approach in cochlear implantation influence the occurrence of postoperative vertigo? *Otolaryngol Head Neck Surg*. (2008) 138:8–12. doi: 10.1016/j.otohns.2007.09.003
10. Frodlund J, Harder H, Mäki-Torkko E, Ledin T. Vestibular function after cochlear implantation: a comparison of three types of electrodes. *Otol Neurotol*. (2016) 37:1535–40. doi: 10.1097/MAO.0000000000001229
11. Hansel T, Gauger U, Bernhard N, Behzadi N, Romo Ventura ME, Hofmann V, et al. Meta-analysis of subjective complaints of vertigo and vestibular tests after cochlear implantation. *Laryngoscope*. (2018) 128:2110–23. doi: 10.1002/lary.27071
12. Campo P, Pouyatos B, Lataye R, Morel G. Is the aged rat ear more susceptible to noise or styrene damage than the young ear? *Noise Health*. (2003) 5:1–18.
13. Boettcher FA. Susceptibility to acoustic trauma in young and aged gerbils. *J Acoust Soc Am*. (2002) 112:2948–55. doi: 10.1121/1.1513364
14. Palomar García V, Abdulghani Martínez F, Bodet Agustí E, Andreu Mencía L, Palomar Asenjo V. Drug-induced toxicity: current status. *Acta Otolaryngol*. (2001) 121:569–72. doi: 10.1080/00016480121545
15. Khan HA, Al Deeb S, Al Moutaery K, Tariq M. Influence of age on iminodipropionitrile-induced vestibular and neurobehavioral toxicities in rats. *Exp Toxicol Pathol*. (2003) 55:181–6. doi: 10.1078/0940-2993-00312
16. Schmäl F, Lübben B, Weiberg K, Stoll W. The minimal ice water caloric test compared with established vestibular caloric test procedures. *J Vestib Res*. (2005) 15:215–22.
17. Inoue A, Iwasaki S, Ushio M, Chihara Y, Fujimoto C, Egami N, et al. Effect of vestibular dysfunction on the development of gross motor function in children with profound hearing loss. *Audiol Neurotol*. (2013) 18:143–51. doi: 10.1159/000346344
18. Fujimoto C, Suzuki S, Kinoshita M, Egami N, Sugasawa K, Iwasaki S. Clinical features of otolith organ-specific vestibular dysfunction. *Clin Neurophysiol*. (2018) 129:238–45. doi: 10.1016/j.clinph.2017.11.006
19. Kaga K, Suzuki JI, Marsh RR, Tanaka Y. Influence of labyrinthine hypoactivity on gross motor development of infants. *Ann NY Acad Sci*. (1981) 374:412–20. doi: 10.1111/j.1749-6632.1981.tb30887.x
20. Anderson I, Weichbold V, D'Haese PSC, Szuchnik J, Quevedo MS, Martin J, et al. Cochlear implantation in children under the age of two - What do the outcomes show us? *Int J Pediatr Otorhinolaryngol*. (2004) 68:425–31. doi: 10.1016/j.ijporl.2003.11.013
21. Govaerts PJ, De Beukelaer C, Daemers K, De Ceulaer G, Yperman M, Somers T, et al. Outcome of cochlear implantation at different ages from 0 to 6 years. *Otol Neurotol*. (2002) 23:885–90. doi: 10.1097/00129492-200211000-00013
22. Cozma RS, Hera MC, Cobzeanu MD, Olariu R, Bitere OR, Mârtu C, et al. Saccular function evolution related to cochlear implantation in hearing impaired children. *Rom J Morphol Embryol*. (2020) 1:113–9. doi: 10.47162/RJME.61.1.12
23. Ajalloueyan M, Saeedi M, Sadeghi M, Zamiri Abdollahi F. The effects of cochlear implantation on vestibular function in 1-4 years old children. *Int J Pediatr Otorhinolaryngol*. (2017) 94:100–3. doi: 10.1016/j.ijporl.2017.01.019
24. Jacot E, Van Den Abbeele T, Debre HR, Wiener-Vacher SR. Vestibular impairments pre- and post-cochlear implant in children. *Int J Pediatr Otorhinolaryngol*. (2009) 73:209–17. doi: 10.1016/j.ijporl.2008.10.024
25. Moushey-Bogle J. *The effect of Cochlear implantation on the vestibular evoked myogenic potential response in children and adults*. Speech, Language, and Hearing Services Graduate Theses and Dissertations (2010).
26. Jin Y, Nakamura M, Shinjo Y, Kaga K. Vestibular-evoked myogenic potentials in cochlear implant children. *Acta Otolaryngol*. (2006) 126:164–9. doi: 10.1080/00016480500312562
27. Psillas G, Pavlidou A, Lefkidis N, Vital I, Markou K, Triaridis S, et al. Vestibular evoked myogenic potentials in children after cochlear implantation. *Auris Nasus Larynx*. (2014) 41:432–5. doi: 10.1016/j.anl.2014.05.008
28. Licameli G, Zhou G, Kenna MA. Disturbance of vestibular function attributable to cochlear implantation in children. *Laryngoscope*. (2009) 119:740–5. doi: 10.1002/lary.20121
29. Bance ML, O'Driscoll M, Giles E, Ramsden RT. Vestibular stimulation by multichannel cochlear implants. *Laryngoscope*. (1998) 108:291–4. doi: 10.1097/00005537-199802000-00025
30. O'Leary MJ, Fayad J, House WF, Linthicum FH. Electrode insertion trauma in cochlear implantation. *Ann Otol Rhinol Laryngol*. (1991) 100:695–9. doi: 10.1177/000348949110000901
31. Tien HC and Linthicum FH. Histopathologic changes in the vestibule after cochlear implantation. *Otolaryngol Head Neck Surg*. (2002) 127:260–4. doi: 10.1067/mhn.2002.128555
32. Handzel O, Burgess BJ, Nadol JB. Histopathology of the peripheral vestibular system after cochlear implantation in the human. *Otol Neurotol*. (2006) 27:57–64. doi: 10.1097/01.mao.0000188658.36327.8f
33. Ishiyama A, Doherty J, Ishiyama G, Quesnel AM, Lopez I, Linthicum FH. Post hybrid cochlear implant hearing loss and endolymphatic hydrops. *Otol Neurotol*. (2016) 37:1516–21. doi: 10.1097/MAO.0000000000001199
34. Su-Velez BM, Lopez IA, Ishiyama A, Ishiyama G. Human temporal bone study of vestibular histopathology in cochlear implant patients with cochlear hydrops. *Otol Neurotol*. (2020) 41:e607–14. doi: 10.1097/MAO.0000000000002609
35. Dhanasingh A, Jolly C. An overview of cochlear implant electrode array designs. *Hear Res*. (2017) 356:93–103. doi: 10.1016/j.heares.2017.10.005
36. Skarzynski H, Matusiak M, Lorens A, Furmanek M, Pilka A, Skarzynski PH. Preservation of cochlear structures and hearing when using the Nucleus Slim Straight (CI422) electrode in children. *J Laryngol Otol*. (2016) 130:332–9. doi: 10.1017/S0022215115003436
37. Skarzynski H, Lorens A, Matusiak M, Porowski M, Skarzynski PH, James CJ. Cochlear implantation with the nucleus slim straight electrode in subjects with residual low-frequency hearing. *Ear Hear*. (2014) 35:e33–43. doi: 10.1097/01.aud.0000444781.15858.f1
38. Moran M, Dowell RC, Iseli C, Briggs RJS. Hearing preservation outcomes for 139 cochlear implant recipients using a thin straight electrode array. *Otol Neurotol*. (2017) 38:678–84. doi: 10.1097/MAO.0000000000001374
39. Lenarz T, Stöver T, Buechner A, Paasche G, Briggs R, Risi F, et al. Temporal bone results and hearing preservation with a new straight electrode. *Audiol Neurotol*. (2006) 11:34–41. doi: 10.1159/000095612
40. Basta D, Todt I, Goepel F, Ernst A. Loss of saccular function after cochlear implantation: the diagnostic impact of intracochlear electrically elicited vestibular evoked myogenic potentials. *Audiol Neurotol*. (2008) 13:187–92. doi: 10.1159/000113509
41. Krause E, Louza JPR, Wechtenbruch J, Gürkov R. Influence of cochlear implantation on peripheral vestibular receptor function. *Otolaryngol Head Neck Surg*. (2010) 142:809–13. doi: 10.1016/j.otohns.2010.01.017
42. Melvin TA, Della Santina CC, Carey JP, Migliaccio AA. The effects of cochlear implantation on vestibular function. *Otol Neurotol*. (2009) 30:87–94. doi: 10.1097/MAO.0b013e31818d1cba
43. Merchant GR, Schulz KM, Patterson JN, Fitzpatrick D, Janky KL. Effect of cochlear implantation on vestibular evoked myogenic potentials and wideband acoustic immittance. *Ear Hear*. (2020) 41:1111–24. doi: 10.1097/AUD.0000000000000831
44. Imai T, Okamura T, Ohta Y, Oshima K, Sato T, Kamakura T, et al. Effects of cochlear implants on otolith function as evaluated by vestibulo-ocular reflex and vestibular evoked myogenic potentials. *Auris Nasus Larynx*. (2019) 46:836–43. doi: 10.1016/j.anl.2019.03.011
45. Souter MA, Briggs RJS, Wright CG, Roland PS. Round window insertion of precurved perimodiolar electrode arrays: how successful is it? *Otol Neurotol*. (2011) 32:58–63. doi: 10.1097/MAO.0b013e3182009f52

46. Bernard S, Wiener-Vacher S, Van Den Abbeele T, Teissier N. Vestibular disorders in children with congenital cytomegalovirus infection. *Pediatrics*. (2015) 136:e887–95. doi: 10.1542/peds.2015-0908

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Vertigo Associated With Cochlear Implant Surgery: Correlation With Vertigo Diagnostic Result, Electrode Carrier, and Insertion Angle

Charlotte Weinmann[1], *Uwe Baumann*[2], *Martin Leinung*[1], *Timo Stöver*[1] *and Silke Helbig*[1]*

[1] *Department of Otorhinolaryngology, Goethe-University Frankfurt, Frankfurt, Germany,* [2] *Department of Audiological Acoustics, Goethe-University Frankfurt, Frankfurt, Germany*

Objective: Vertigo is a common side effect of cochlear implant (CI) treatment. This prospective study examines the incidence of postoperative vertigo over time and aims to analyze influencing factors such as electrode design and insertion angle (IA).

Study Design and Setting: This is a prospective study which has been conducted at a tertiary referral center (academic hospital).

Patients: A total of 29 adults were enrolled and received a unilateral CI using one of six different electrode carriers, which were categorized into "structure-preserving" (I), "potentially structure-preserving" (II), and "not structure-preserving" (III).

Intervention: Subjective vertigo was assessed by questionnaires at five different time-points before up to 6 months after surgery. The participants were divided into four groups depending on the time of the presence of vertigo before and after surgery. Preoperatively and at 6 months postoperatively, a comprehensive vertigo diagnosis consisting of Romberg test, Unterberger test, subjective visual vertical, optokinetic test, video head impulse test, and caloric irrigation test was performed. In addition, the IA was determined, and the patients were divided in two groups ($<430°$; $\geq 430°$).

Main Outcome Measures: The incidence of vertigo after CI surgery (group 1) was reported, as well as the correlation of subjective vertigo with electrode array categories (I–III) and IA.

Results: Among the participants, 45.8% experienced new vertigo after implantation. Based on the questionnaire data, a vestibular origin was suspected in 72.7%. The results did not show a significant correlation with subjective vertigo for any of the performed tests. In group 1 with postoperative vertigo, 18% of patients showed conspicuous results in a quantitative analysis of caloric irrigation test despite the fact that the category I or II electrodes were implanted, which are suitable for structure preservation. Average IA was 404° for the overall group and 409° for group 1. There was no statistically significant correlation between IA and perceived vertigo.

Conclusions: Though vertigo after CI surgery seems to be a common complication, the test battery used here could not objectify the symptoms. Further studies should clarify

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Wolfsburg Hospital, Germany
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***Correspondence:**
Silke Helbig
silke.helbig@kgu.de

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whether this is due to the multifactorial cause of vertigo or to the lack of sensitivity of the tests currently in use. The proof of reduced probability for vertigo when using atraumatic electrode carrier was not successful, nor was the proof of a negative influence of the insertion depth.

Keywords: cochlear implant, vestibular function, questionnaire, electrode design, vertigo

INTRODUCTION

Since the beginning of cochlear implant (CI) surgery, vertigo with vestibular origin is known as a typical postoperative side effect and has been described by various authors (1–4). So far, little is known about the factors that increase the risk of vertigo. Within the last decades, the indication criteria for a CI have expanded, and therefore the number of patients who received this neuro-prosthesis increased. Today patients do not have to suffer from complete deafness, and also candidates with low-frequency residual hearing and unilateral hearing loss are eligible for this treatment (5). Surgery in terms of hearing preservation appears to reduce the postoperative risk of vertigo (6). While age is discussed as a potential risk factor in several studies (7, 8), no significant correlation was found regarding gender and etiology of hearing loss (7, 9, 10).

In 2008, Todt et al. were able to show that the insertion of the electrode array through the round window caused less damage to the vestibular organ. Therefore, this approach seems to be the most advantageous and is still favored in "structure-preserving surgery" (11). In addition, electrode arrays were redesigned to be very thin and flexible for insertion without surgically enlarging the round window and therefore helping to maintain the fragile intracochlear structures during insertion. The design and the insertion angle of the electrode carriers seem to influence the occurrence of postoperative vertigo in adult patients (12). However, despite these efforts to preserve the structure of the cochlea, current literature remains to describe that CI surgery carries a likely risk of vertigo. A postoperative pathology of the lateral semicircular canal, measured by caloric testing, as well as a reduced saccular function measured by cVEMPs was demonstrated by different authors (13, 14). However, conspicuous findings of different tests do not always seem to correlate statistically significant with the onset of vertigo. In a review of Krause et al. (15) on vertigo after cochlear implantation, it became evident that only caloric and VEMP test showed significant negative effects. In addition, quality, onset, and duration of perceived vertigo seems to be described differently by patients (1). Therefore, the question remains as to whether all vertigo symptoms originate by vestibular problems and whether factors that increase the risk of postoperative vertigo after CI surgery can be identified. For this reason, this prospective study was initiated to clarify these key questions.

MATERIALS AND METHODS

Subjects

The prospective study presented here was preapproved by the ethics committee at the university hospital Frankfurt/M (no. 524/15). The inclusion criteria were as follows: the patient had to be at least 18 years old, had never received a CI before, and was planned for unilateral implantation. The exclusion criteria were unwillingness to participate in the study, being a minor, and CI re-implantation. Between 2016 and 2018, 32 patients were enrolled; all of them signed an informed consent to participate in the study. Three patients dropped out of the follow-up: one patient could not be implanted due to ossification of the cochlea, and two patients did not show up for follow-up appointments. In total, data obtained from 29 patients was available for evaluation, among them 16 (55%) were women and 13 (45%) were men. The mean age was 58 years (median 57 years, standard deviation $\pm$ 12.5 years). The causes of hearing loss ranged from sudden deafness ($n = 5$), trauma ($n = 1$), apoplexy ($n = 1$), otitis media ($n = 1$), and Ménière's disease ($n = 2$) to congenital deafness due to infection or hypoxia ($n = 4$) and deafness due to unclear etiology ($n = 15$).

It was intended to include a higher number of study participants, but within the observation period of 1.5 years, this could not be achieved. The reasons therefore included a high number of second ear (bilateral) CI surgeries, minority, limiting language barriers, or unwillingness to accept the burdens of vertigo testing without the presence of symptoms.

Surgery

The procedure during surgery is a crucial factor with impact on the delicate intracochlear structures (16). Surgery was performed by three different surgeons and, in all cases, in a standardized manner with a focus on structural preservation within the cochlea. First, mastoidectomy and posterior tympanotomy were performed. Then, a glucocorticoid (triamcinolone) was flushed into the middle ear and left there while drilling the implant bed. Afterwards, the round window was visualized and, if necessary, the overhang was removed with diamond burrs using a reduced rotation speed of 8,000 rpm. Now the implant was placed in its skull bed. After cleaning of the middle ear and punctual opening of the round window, slow insertion of the electrode array was performed. In cases where its diameter did not permit direct insertion, the round window had been extended anterior-laterally according to the required dimensions. After opening the cochlea, suction was avoided.

Electrode Carriers

Patients were provided with different cochlear implants from the following three manufacturers: Cochlear GmbH & Co. KG (Sydney, Australia), MED-EL GmbH (Innsbruck, Austria), and Advanced Bionics AG (Stäfa, Switzerland). Among the electrode carriers used, there were both "structure-preserving" and "not structure-preserving" design forms. The electrodes for which studies have shown that they have a higher probability of residual

TABLE 1 | Implanted devices and electrode designs (for details on the devices and manufacturers, see section "Materials and Methods").

Electrode category	Classification	Device	Electrode design	Number of patients
I	Structure-preserving	CI522	Straight	3 (10%)
I	Structure-preserving	FLEX24	Straight	2 (7%)
II	Potentially structure-preserving	CI532	Preformed perimodiolar	5 (17%)
II	Potentially structure-preserving	FLEX28	Straight	7 (24%)
III	Not structure-preserving	HiFocus Mid-Scala	Preformed perimodiolar	1 (4%)
III	Not structure-preserving	CI512	Preformed perimodiolar	11 (38%)
				$n = 29$ (100%)

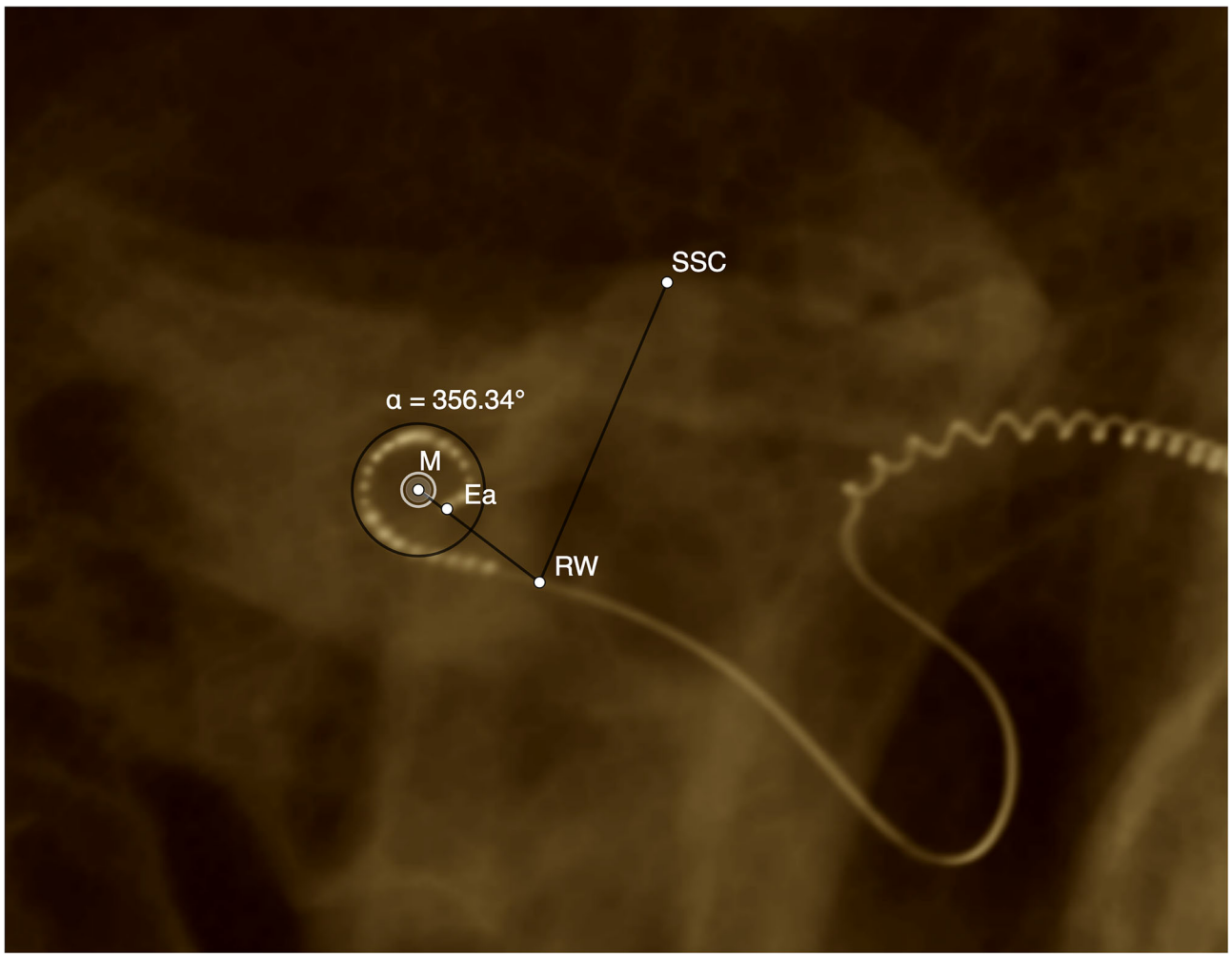

FIGURE 1 | Example DVT reconstruction of CI512 device (left side, patient n20). Determination of insertion angle. M, modiolus; Ea, most apical electrode; RW, round window; SSC, superior semicircular canal; a, insertion angle (356.3°).

hearing preservation were classified as "potentially structure-preserving." An overview of the electrodes used in the study is shown in **Table 1**.

Eleven (38%) of the patients received the Cochlear™ Nucleus® CI512 (Contour Advance) electrode. This preformed electrode with 22 contacts was designed with the intention of allowing a close position to the modiolus (17). However, several studies showed that, due to its shape, size, and insertion procedure, this electrode array has the potential for a scalar transition and that it does not allow reliable hearing preservation (18, 19). Therefore, it was classified as "not structure-preserving" in our study. Three patients (10%) received

the Cochlear™ Nucleus® CI522 (Slim Straight), which also has 22 platinum electrode contacts (20). It was developed to reduce the frequency of scalar translocation and to improve the odds of hearing preservation (18, 21). Five patients (17%) received the Cochlear™ Nucleus® Profile Implant CI532 (Slim Modiolar Electrode), launched in 2016 and designed as a preformed electrode with 22 platinum contacts and a maximum diameter of 0.4 mm at the electrode tip and 0.5 mm basal, which meant a reduction of volume by 60% compared to previous electrodes. Besides helping to protect the delicate structures of the cochlea (22), the preformed design allows placement close to the modiolus (23). Since it has been proven to enable the preservation of hearing (24), it was classified as "potentially structure-preserving" in this study.

In 2006, MED-EL introduced the straight and flexible FLEX electrode series, all equipped with 12 platinum contacts and currently available in various lengths. In our study, MED-EL® FLEX24 electrode arrays with a length of 24 mm were implanted in two (7%) patients, and the MED-EL® FLEX28 electrodes with a length of 28 mm were implanted in seven (24%) patients. The maximum diameter of both is 0.8 mm at the base, which makes round window insertion possible in most cases (25). FLEX24, in particular, is used for the hearing-preserving surgery of CI candidates with low-frequency residual hearing and classified as "structure-preserving" in this study. Despite its use as an electrode for the standard treatment of deaf or profoundly hearing-impaired patients, FLEX28 also has the potential to preserve structure. Therefore, it was classified here as "potentially structure-preserving."

One patient (4%) received the Advanced Bionics HiFocus™ Mid-Scala electrode carrier. This electrode array, launched in 2013, is 15 mm in length, preformed, and has 16 platinum contacts and a maximum diameter of 0.7 mm at the basal end. The insertion is performed with a stylet similar to the procedure for the Contour Advance electrode from Cochlear™. Therefore, the Mid-Scala electrode carrier was classified as "not structure-preserving" in this study.

The 29 study participants were provided with five electrode carriers of electrode group I, 12 of group II, and 12 of group III (see **Table 1**).

Electrode Insertion Depth

Insertion angle was measured based on postoperative CT images to verify the cochlear implant electrode position (26–28). Electrode insertion angle was determined manually by the application of GeoGebra geometrics software (Version Classic 6) (29) as shown in **Figure 1**. First, the upper semicircular canal (SSC) was identified on CT image. Next, the round window (RW) was marked by drawing a vertical line from the upper edge of the SSC through the semicircular channel (f). This vertical line crosses the electrode in the area of the round window, where the starting point for insertion angle determination is defined. The position of the modiolus (M) was determined, and the deepest apical electrode (Ea) was marked. In cases where the electrode was inserted at a maximum of 30°, the angle between M, RW, and Ea could be calculated directly. If a deeper insertion was present, a second circle was placed in the second turn of the cochlea, again determining the position of the modiolus (M2). The angle between M2, RW, and Ea was calculated, and this result was then summed with 360°.

To evaluate the influence of the insertion depth measured by the insertion angle, the patients were categorized into two groups. The decision to form two insertion angle groups and to select the subdivision at 430° was made after calculating the binomial distribution.

Angle category u included 20 patients, whose electrode was implanted with an insertion angle of <430°. Eight patients formed the angle category o, with an insertion angle greater than and equal to 430 degrees.

Low-Frequency Residual Hearing

Pure tone audiograms of the 29 patients were tested preoperatively and postoperatively (mean = 5.5 M, minimum = 1 M, maximum = 14 M). The average of unaided air conduction thresholds for low frequencies at 125, 250, 500, and 1,000 Hz were calculated. The study participants without residual hearing before surgery ($n = 2$) were not considered for evaluation. Postoperative cases without residual hearing at maximum detectable levels, which were 85 dB HL at 125 Hz, 105 dB HL at 250 Hz, and 110 dB HL at 500 and 1,000 Hz, were also excluded. The rest were grouped by electrode category I to III, and statistical analysis was performed.

Questionnaire

The subjective symptoms of vertigo in patients were assessed before and after implantation using five questionnaires published by Krause et al. (1) to evaluate the complaints of patients with vertigo. Other studies used the Dizziness Handicap Inventory (DHI) developed in 1990, which contains 25 questions that assess the relationship between vertigo symptoms and performance in everyday life (30, 31). The advantage of this standardized test is its reproducibility and comparability with other studies. However, it does not allow conclusions to be drawn about the cause of the vertigo, which is why we modified the test setting. The patients completed the questionnaires 1 day before surgery, 1 week after surgery, at the time of the initial adjustment of the processor, and 3 and 6 months after the initial adjustment. If vertigo was present in the first two questionnaires, detailed follow-up questions were asked, e.g., quality, frequency, duration. The degree of subjective impairment due to vertigo was indicated by the patients on a visual analog scale, with "0" representing "no impairment" and "10" representing "extreme impairment." The last three questionnaires asked about the presence and change of vertigo symptoms. Based on the information obtained by the questionnaires on the occurrence of vertigo, four groups were formed:

Group 0: before and after surgery, no vertigo
Group 1: before surgery, no vertigo; after surgery, vertigo
Group 2: before surgery, vertigo; after surgery, no vertigo
Group 3: before and after surgery, vertigo

The patients were classified into three groups, based on the probable origin of their vestibular symptoms, using the criteria "quality of vertigo" and "accompanying symptoms":

Group A: profound suspicion of vestibular origin (rotational vertigo, swaying vertigo or lifting sensation, *and* accompanying symptoms)

Group B: potential vestibular origin (rotational vertigo, swaying vertigo or lifting sensation *without* accompanying symptoms)

Group C: suspicion of central origin (general feeling of dysbalance).

Vestibular Function Tests

Both preoperatively and at 6 months postoperatively, a comprehensive vertigo testing was conducted, consisting of Romberg test, Unterberger test, subjective visual vertical test (SVV), optokinetic test, video head impulse test (vHIT), and caloric irrigation test. Since only one investigator performed all the measurements within this study, investigator-dependent variation in the experimental procedure could be excluded. Preoperatively, all 29 patients participated in the Romberg test, Unterberger test, and the test of SVV. For the optokinetic test, preoperative data in four patients could not be used due to technical problems, leaving 25 preoperative data sets for evaluation. Due to the same problems, one data set was excluded postoperatively. The vHIT was refused by one patient preoperatively and one study participant postoperatively due to cervical pain, leaving 28 sets of data pre- and post-operatively for evaluation. The caloric irrigation test was performed in all 29 patients preoperatively. Postoperatively, two patients refused the test, and in one case, the irrigation device was unavailable, leaving the data sets of 26 subjects.

Romberg Test

When performing the Romberg test, the patient was in an evenly lit and quiet room and stood upright on a firm surface. The patient stretched his arms forward, with his hands in a supine position. The test was initially carried out with the eyes open; if the patient was confident enough, the test was also carried out with the eyes closed. Swaying and falling tendencies in one direction were rated as conspicuous.

Unterberger Test (Fukuda Test)

The Unterberger test was carried out in an evenly lit and quiet room. The patient stepped on the same spot 50 times with his eyes closed and arms extended forward. At each time, the thighs should be bent at a 90° angle (32). The direction of rotation of the patient was recorded. According to Biesinger and Iro (33), a deviation above 45° was considered conspicuous.

Subjective Visual Vertical

A line was drawn centrally on the bottom inside a bucket. The examiner held the bucket horizontally in front of the patient's face so that the participant could look into it and see the line. The examiner turned the bucket 10 times in a row alternately to the left or right, and the patient should turn it back to the vertical using the line inside the bucket. The examiner then read off a possible deviation from the vertical using a plumb and a protractor, which were attached to the bucket. According to Böhmer (34), the SVV reflects lateral differences in the tonic affinity of the otolith organs (especially the utricle). In the presented study, a deviation of more than 2° was rated outside physiological range.

Optokinetic Test

During the test, the patient was sitting on a fixed chair and wearing glasses with an integrated camera of the Visual Eyes 525 video oculography system (Interacoustics, Middelfart, Denmark). The participant looked at a wall in front where periodic, vertical, and yellow and blue stripe patterns were presented using a video projector. The patient was asked to observe a stripe in the center of the field and let the eyes follow the movement of the stripe until it disappeared. By then, the eyes jumped back to the center of the field, and the gaze was fixed on a new stripe. The speed of the stripes presented affected the slow phase velocity (SPV) of the eyes, which the stripes can normally follow up to a speed of 40°/s. The nystagmus movements were evaluated by the software system OtoAccessTM (Interacoustics, Middelfart, Denmark). The stimulus speeds used for the right and the left sides were 20, 35, and 50°/s, with a recording time of 20 s. The optokinetic nystagmus was assessed according to Haid et al. (35) as irregular if a nystagmus difference between the two eyes of greater than or equal to 20% (of the SPV) was measured to the right and to the left for the same speed. A conspicuous nystagmus difference occurs in patients with central vestibular damage, but not peripheral lesions (35, 36).

Video Head Impulse Test

The vHIT, according to Halmagyi and Curthoys, is used to check the semicircular canals and the vestibulo-ocular reflex triggered by irritation as a reaction to stimuli in the high frequency range (37). In this study, the vHIT was used to check the integrity of the horizontal semicircular canals (hSCC). During the examination, the patient sat 1.5 m from a wall and fixed a point target at eye level while wearing "ICS® Impulse" glasses with an integrated camera (Natus Medical Incorporated, Pleasanton, USA), which recorded the eye movement of the right eye and passed it on to the OTOsuite® UNIVERSE audiometry (Natus Medical Incorporated, Pleasanton, USA). The examiner, standing behind the test person, alternately and as unpredictably as possible performed movements with low amplitude (10–20°) and high acceleration (3,000–4,000°/s) on the patient's head to the left and right in a horizontal movement. The latency with which eye movements occurred, after the head was accelerated, was detected. The correlation between head and eye movements was registered as gain (= quotient eye speed ÷ head speed), with values below 0.8 being considered conspicuous. The gain asymmetry (GA) was calculated using the following formula:

$$\mathbf{GA} = \frac{\mathbf{(gain\ left) - (gain\ right)}}{\mathbf{gain\ left + gain\ right}}\ \mathbf{x100\%}$$

As suggested by Patscheke et al. (38), gain asymmetry of ≥8% was rated as conspicuous.

Caloric Irrigation Test

Before irrigation, ear inspection was performed to ensure the integrity of the tympanic membrane, and a recording of

preexisting horizontal spontaneous nystagmus was obtained. The patient was lying down, and the upper body was raised by 30° (resulting in a vertical position of hSCC). The patient wore video glasses with an integrated camera that recorded the eye movements using the "Visual Eyes 525" video oculography system, which were passed on to the "OtoAccessTM" software. According to Hallpike (39), the caloric response to bithermal stimulation was recorded when flushing with 100 ml of 44 or 30°C warm water for 30 s each. Pauses of at least 5 m were carried out between the rinses (33). Nystagmus reaction was recorded for 80 s, and SPV was determined from a 20-s interval. To measure the caloric response recorded in the implanted ear, the sum of SPV of the cold and warm irrigation was calculated.

For quantitative evaluation, values below 5°/s were counted as loss of the vestibular organ. With a total SPV in the implanted ear below 10°/s, hypoexcitability of this side was determined. Values above 40°/s were considered to be hyperexcitable. The degree of side difference (SD) was evaluated using the JONGKEES formula (40):

$$\mathbf{SD} = \frac{(\mathbf{mSPV\ right\ 30^{\circ}C + mSPV\ right\ 44^{\circ}C}) - (\mathbf{mSPV\ left\ 30^{\circ}C + mSPV\ left\ 44^{\circ}C})}{\mathbf{mSPV\ right\ 30^{\circ}C + mSPV\ right\ 44^{\circ}C + mSPV\ left\ 30^{\circ}C + mSPV\ left\ 44^{\circ}C}}\ \mathbf{x100\%}$$

As suggested by Reiß et al. (41), SD of more than 20% was considered conspicuous.

Data Analysis

The pre- and post-operative results of the test battery were compared and examined for changes.

The postoperative results of caloric irrigation test and vHIT test in the implanted patients were analyzed with regards to the insertion depth of the electrode and the electrode design. Data were tested for normal distribution using the Shapiro–Wilk test. To measure differences in outcomes from pre- to postoperative, paired-samples *t*-test was used when the distribution was normal, and Wilcoxon test was used when the distribution was not normal. To investigate the influence on the development of postoperative vertigo, Fisher's exact test or descriptive statistics was used when the number of cases was less than five patients. To test the influence of nominal test battery scores, we used logistic regression (IBM® SPSS® Statistics, version 27).

RESULTS

Questionnaire

Patients were grouped according to the questionnaire outcome reflecting their vertigo symptoms. As shown in **Table 2**, 13 patients were assigned to group 0 (before and after surgery, no vertigo), 11 to group 1 (before surgery, no vertigo; after surgery, vertigo), three to group 2 (before surgery, vertigo; after surgery, no vertigo), and two to group 3 (before and after surgery, vertigo). Thus, vertigo associated with cochlear implant treatment occurred newly in 11 of 24 cases (45.8%). The patients were classified into groups based on their symptoms, and only in group A was the vertigo most likely to have a vestibular origin. In group B, only one possible cause for a vestibular disorder was identified; in group C, there was none. Five patients had preoperative vertigo (groups 2 and 3). Of these, three were assigned to group A, one to group B, and one to group C. One of these patients (n17) consistently reported vertigo symptoms in all questionnaires, with no change in quality. Patient n3 did not report a recurrence of vertigo until the 6-month questionnaire, with the quality of vertigo remaining the same. Nine patients had a new onset of vertigo within the first week after implantation, and in two patients, the vertigo occurred newly 6 months after the initial fitting (group 1). Of these, five patients were counted as group A, three patients as group B, and three patients as group C. Thus, in eight of 11 cases (72.7%), a vestibular or at least possibly vestibular cause for the postoperative new-onset vertigo could be identified on the basis of the questionnaire data. Respectively, eight out of 24 patients (33%) had new vertigo with a vestibular or possibly vestibular cause.

Vestibular Function Tests

The results obtained from the Romberg test and optokinetic test showed normal results preoperatively and postoperatively in all 29 patients.

Unterberger Test

Already preoperatively, six patients, all of whom had no complaints of vertigo according to the questionnaire evaluation (21%), showed a conspicuous test result. Four of the six patients (67%) deviated to the side to be implanted. Postoperatively, the number of pathologic test results increased to 10 (34%), with eight of these 10 patients (80%) deviating to the implanted side. Thus, this number of patients showing deviation to the implanted side increased from four to eight. This difference was not statistically significant in the Wilcoxon test ($Z = -1.826$; $p = 0.068$). An overview of the conspicuous results of the Unterberger test is shown in **Table 3**. All patients who did not have normal findings preoperatively also had conspicuous findings postoperatively. The four patients who had new-onset conspicuous results in the Unterberger test all showed a deviation to the implanted side. Three of these patients also reported new-onset vertigo in the questionnaire. There was no statistically significant correlation between the results and the incidence of postoperative vertigo in binary logistic regression as shown in **Table 4**.

Subjective Visual Vertical

When measuring SVV, only one study participant (3.4%), who did not perceive vertigo at any time, had an atypical result both pre- and post-operatively. Otherwise, all other results were regular at both test visits. Thus, except for this one case, there was no evidence for utricle or central damage to balance.

Video Head Impulse Test

The vHIT could not be performed postoperatively in one case because the patient had massive neck pain with accompanying vertigo symptoms. Preoperative testing was also missing in one patient who did not have vertigo at any time and had an unremarkable finding on postoperative vHIT. The findings of the implanted side as well as the comparison with the opposite side were evaluated and are shown in **Table 5**.

TABLE 2 | Chronological overview of the occurrence of vertigo (cases without any occurrence of vertigo excluded).

Patient ID	Vertigo group	Etiology	Suspected origin of vertigo	Pre-op	1W	First fit	3M	6M
n8	1	Unknown	B		X	X	X	
n12	1	Unknown	A		X			
n14	1	Congenital	A					X
n15	1	Congenital	A		X			
n18	1	Unknown	B		X	X	X	X
n23	1	Congenital	C		X	X	X	
n27	1	Unknown	C		X			
n28	1	Unknown	B		X	X	X	X
n30	1	Unknown	A		X			
n31	1	Sudden deafness	A		X			
n32	1	Ménière's disease	C					X
n13	2	Unknown	C	X				
n16	2	Ménière's disease	B	X				
n24	2	Congenital	A	X				
n3	3	Apoplexy	C	X				X
n17	3	Unknown	A	X	X	X	X	X

Vertigo group 1 = –/+, 2 = +/+, 3 = +/–, vertigo (+) pre-operative/post-operative, suspected origin of vertigo.
A, profound suspicion of vestibular origin; B, potential vestibular origin; C, suspicion of central origin; Pre-op, 1 day before surgery; 1W, 1 week after surgery; First fit, at the time of initial adjustment; 3M, 3 months after initial adjustment; 6M, 6 months after initial adjustment; X, patient-reported vertigo.

TABLE 3 | Unterberger test, cases with conspicuous results only, pre- and post-operative (for information on vertigo group and origin of vertigo, see **Table 2**).

Vertigo group	Suspected origin of vertigo	Patient ID	Preoperative rotation (degrees)	Postoperative rotation (degrees)
0		n10		45 (–)
0		n19		75 (+)
0		n21	80 (+)	80 (+)
0		n25	70 (+)	70 (+)
0		n26	90 (+)	90 (+)
1	A	n15		90 (+)
1	B	n18	50 (+)	50 (+)
1	B	n28	90 (–)	90 (–)
1	C	n23		80 (+)
1	C	n32	90 (–)	60 (+)

+, rotation toward the implanted side; –, rotation away from the implanted side.

TABLE 4 | Correlation of postoperative test battery scores and development of postoperative vertigo (logistic regression).

	B	SE	Wald	*p*	Odds ratio	95% CI for odds ratio	
						Lower bound	Upper bound
Unterberger deviation toward Implanted side postoperative	−0.009	0.033	0.066	0.797	0.991	0.929	1.058
vHIT gain postoperative Implanted side	27.24	19.789	1.895	0.169	6.76E + 11	0	4.73E + 28
vHIT GA postoperative	0.289	0.206	1.965	0.161	1.335	0.891	2
Caloric SD postoperative Implanted side	−0.027	0.047	0.323	0.57	0.974	0.888	1.068
Caloric SPV postoperative Implanted side	−0.096	0.111	0.749	0.387	0.909	0.731	1.129

Degrees of freedom were 1 for all Wald statistics.

TABLE 5 | vHIT test, conspicuous results only (for information on vertigo group and origin of vertigo, see **Table 2**).

Vertigo group	Suspected origin of vertigo	Patient ID	Gain, preoperative	Gain, postoperative	GA, preoperative [%]	GA, postoperative [%]
0		n1			17 (+)	
0		n4				9 (+)
0		n5			14 (–)	30 (–)
0		n7		0.8	56 (–)	14 (–)
0		n10			12 (+)	22 (+)
0		n11				16 (+)
0		n19			12 (+)	
0		n20			13 (+)	11 (+)
0		n26				15 (+)
1	A	n12			14 (+)	15 (+)
1	A	n14				8 (+)
1	A	n15			10 (–)	18 (–)
1	A	n30	0.6		13 (+)	8 (+)
1	B	n8			12 (+)	
1	B	n28			15 (+)	13 (+)
1	C	n23			17 (–)	
1	C	n27				8 (–)
1	C	n32			12 (–)	
2	A	n24	0.7	0.8		14 (–)
2	C	n13				9 (–)
3	A	n17			20 (+)	12 (–)
3	C	n3				16 (–)

GA, gain asymmetry; +, implanted side; –, opposite implanted side.

Gain Implanted Side

Two pre- and post-operative patients had a conspicuous gain (<0.8). One patient, who had vertigo with a vestibular cause preoperatively and who no longer reported vertigo postoperatively, had conspicuous values at both times. A second patient had pathologic gain only postoperatively, although this participant reported no vertigo in the questionnaire. Another patient, who had vertigo postoperatively with a most likely vestibular origin, showed a conspicuous gain preoperatively only, while the postoperative value was normal. The preoperative mean gain of the implanted side was 1.0 (median: 1.0; SD ± 0.2) and did not change postoperatively (median: 0.9; SD ± 0.17), with an interval from 0.8 to 1.5. There was no significant difference in gain values before and after implantation [$t_{(26)} = 0.383$; $p = 0.705$].

Gain Asymmetry

Preoperatively, 14 cases (50%) with irregular GA (≥8%) with 9/14 (64%) lower gain on the implanted side were observed. Postoperatively, in 17 patients (61%), irregular GA, with 9/17 (53%) lower gain on the implanted side, occurred. Irregular values were measured at both times in patients with and without vertigo. Four patients noticed postoperative vertigo *and* had a conspicuous GA with lower gain on the implanted side. Within this group of patients, a vestibular origin was very likely in three and possible in one patient. However, there were also five patients with conspicuous GA who did not complain about vertigo.

The GA values worsened in seven cases (25%) without being statistically significant in Wilcoxon's test (Z= -0,84; $p = 0.933$). We found no correlation between gain or GA with the self-reported occurrence of postoperative vertigo in binary logistic regression as shown in **Table 4**. Preoperatively, the interval of GA ranged from 0 to 56%, with a mean of 10.5% (median: 8.5%; SD ± 10.48%). Postoperatively, the interval of GA ranged from 1 to 30%, with a mean of 9.9% (median: 8.5%, SD ± 6.92%).

Caloric Irrigation Test

The test was performed preoperatively in all patients and postoperatively in 26 patients. An overview of cases with conspicuous results for both test intervals is given in **Table 6**.

Overall, the SPV of the implanted side worsened in 20/26 (77%) patients. The average caloric response in the implanted side was reduced from 32.78°/s (median: 29.82°/s; SD ± 18.5) preoperatively to 28.74°/s (median: 27.33°/s; SD ± 15.4) postoperatively (see **Figure 2** for further details). There was no statistically significant difference in SPV before and after implantation [$t_{(25)} = 1.290$, $p = 0.209$].

Preoperatively, hypoexcitability of the lateral semicircular canal of the implanted side was found in four patients and hyperexcitability in one. Postoperatively, a complete loss of function was obvious in one case. After implantation, in two patients who showed hypoexcitability and hyperexcitability preoperatively, this was no longer detectable. Based on the questionnaire results, all of these patients showed postoperative

TABLE 6 | Caloric irrigation test result, slow phase velocity, and side difference (SD) conspicuous results only (for information on vertigo group and origin of vertigo, see **Table 2**).

Vertigo group	Suspected origin of vertigo	Patient ID	Interpretation preoperative	Interpretation postoperative	SD preoperative (%)	SD postoperative (%)
0		n1	PH	PH	25 (+)	47 (+)
0		n4	PH	N/A		N/A
0		n7	PH	PH		46 (–)
0		n20	PH	N/A		N/A
0		n21	PH	PH		54 (–)
0		n25	PH	N/A	26 (+)	N/A
0		n29	PH	PH		42 (+)
1	A	n12	PH	PH	30 (–)	
1	A	n14	UN	FA		95 (+)
1	A	n30	UN	PH		
1	A	n15	PH	PH	23 (–)	45 (–)
1	B	n18	PH	UN		47 (+)
1	C	n32	PH	PH		37 (+)
2	A	n24	UN	UN	56 (+)	
2	B	n16	UN	PH	58 (+)	28 (+)
2	C	n13	PH	PH	28 (+)	
3	A	n17	PH	PH		
3	C	n3	HE	PH		

PH, physiological; HE, hyperexcitability; UN, hypoexcitability; FA, failure; N/A, no answer; +, implanted side worse response; –, opposite implanted side worse response.

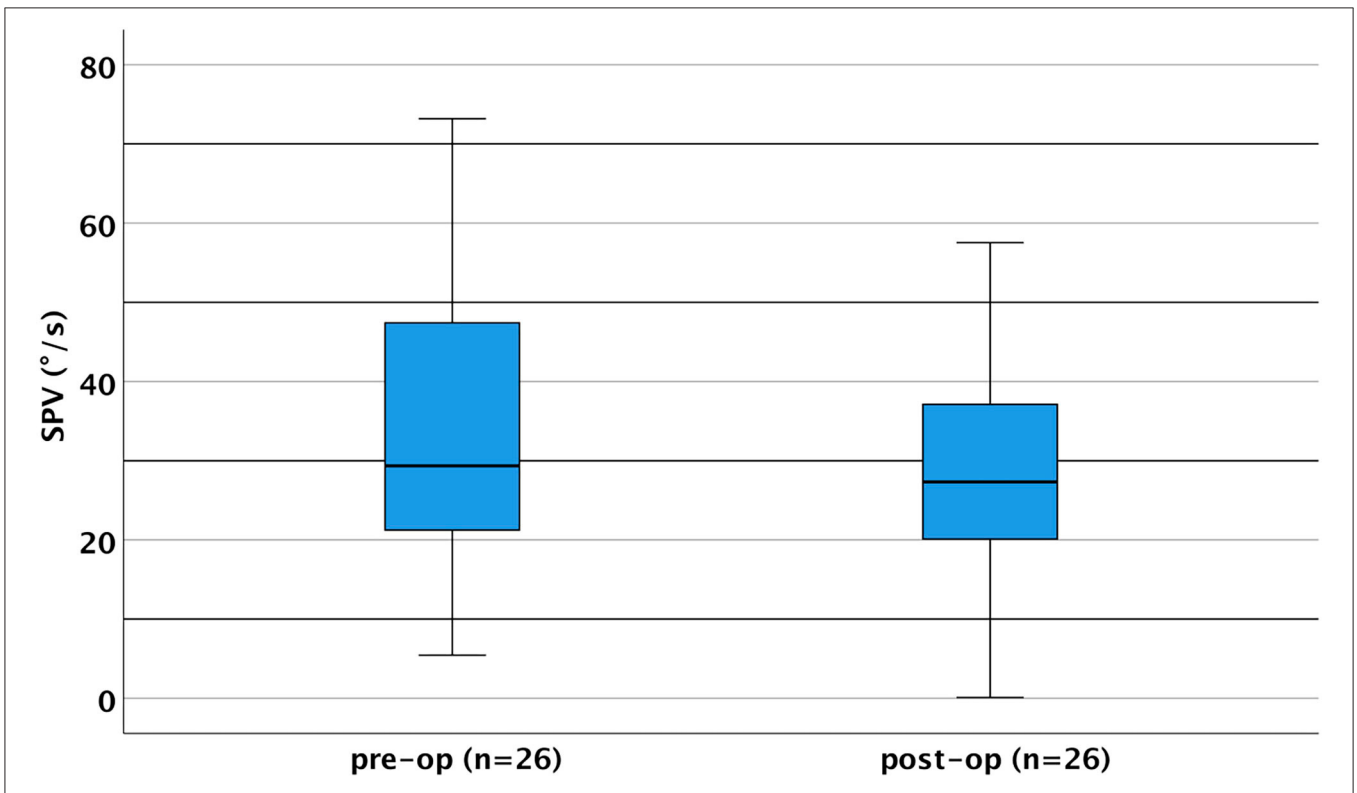

FIGURE 2 | Caloric slow-phase velocity (SPV; sum of cold and warm irrigation) pre- and post-operatively of the implanted side (boxplots). SPV ranged preoperatively from 5.44°/s up to 73.19°/s (mean = 32.78 ± 18.50°/s) and postoperatively from 0.1°/s up to 57.53°/s (mean = 28.74 ± 15.41°/s). SPV was approximately normally distributed for both intervals as assessed by the Shapiro–Wilk test (preoperatively, $p = 0.242$; postoperatively, $p = 0.565$).

signs of vertigo (groups 1 and 3). One group 3 patient who showed a hyperexcitable lateral semicircular canal preoperatively dropped to normal SPV values postoperatively despite ongoing vertigo problems. In one (n14) of the four patients who were considered to be hypoexcitable preoperatively, a SD of 95% was found postoperatively. This individual belonged to group 1, and an evaluation of the questionnaire suggested a vestibular cause. One patient (n18) showed physiological values preoperatively and complained about the onset of vertigo postoperatively, while hypoexcitability was evident, which was also confirmed by SD. A potential vestibular origin was revealed by the questionnaire. In group 1, however, there was one patient (n30) who showed hypoexcitability of the SD side preoperatively, which was not confirmed in the postoperative testing, although the vertigo appeared to be of vestibular origin.

Three of five patients with preoperative vertigo (groups 2 and 3) already showed abnormal results preoperatively, which could indicate a preexisting lesion of the hSCC. The questionnaire confirmed a potential vestibular origin in two of these three cases. One patient (n24) showed hypoexcitability, confirmed by a conspicuous SD that persisted postoperatively, with the SD disappearing. In another case (n16), the preoperative hypoexcitability of the implanted side was also confirmed by a conspicuous SD, which persisted postoperatively. However, the hypoexcitability of the implanted side could no longer be measured postoperatively (as can be seen in **Table 7**).

Side Difference

Conspicuous values of the SD occurred both pre- and postoperatively in all groups. We noticed that the values of our quantitative analysis, based on conspicuous values of excitability, were confirmed by the SD but that conspicuous values of SD also occurred in patients without vertigo. SD related to the implanted side (characterized by decreased caloric response) occurred preoperatively in five patients (17%) and to the non-implanted side in two patients (7%). Postoperatively, SD related to the implanted side was found in six patients (23%) and related to the non-implanted side in three patients (12%). Both the change in SD in the implanted side ($p = 0.281$) and in the non-implanted side ($p = 0.071$) was not statistically significant. There was no difference in SD before and after implantation [$t_{(8)} = -1.155$; $p = 0.281$]. We found no correlation between the SPV values or the SD and the occurrence of self-reported vertigo in binary logistic regression as shown in **Table 4**. Preoperatively, the SD was between 0 and 58%. The mean value was 15% (median 11%, standard deviation ±14%). Postoperatively, the interval of the SD was between 0 and 95%, with a mean of 21% (median 9 ± 24%).

Insertion Angle

Evaluation of the postoperative CT images showed an average insertion angle of 404° for the total collective. The individual values were 389° in the vertigo group 0, 409° in group 1, 463° in group 2, and 379° in vertigo group 3 (see **Figure 3**). Patients with an insertion angle of <430° (IA category u) reported vertigo postoperatively in nine of 20 cases (45%), whereas in the group with insertion of 430° or more (IA category o), four of eight patients reported vertigo (see **Table 8**).

A chi-square test was used to compare the occurrence of postoperative vertigo and insertion angle. As there were two expected cell frequencies below 5, Fisher's exact test was applied instead. The results show no significant relation between the occurrence of postoperative vertigo and insertion angle.

Electrode Design

The electrode carriers were categorized into three groups according to their design–properties, as depicted in **Table 1**. A total of five out of 29 patients (17%) were assigned to electrode category I (structure-preserving), as shown in **Table 9**. After implantation, two out of five (40%) patients newly developed vertigo (group 1). According to the questionnaire, one patient had vertigo with a possible vestibular cause (group B); the other suffered from vertigo due to most likely non-otogenic reasons (group C). Two patients in group 3, who were supplied with electrodes of electrode category I, had vertigo after implantation. However, they already complained about vertigo before operation. Electrode category II (potentially structure-preserving) was assigned to 12 out of 29 (41.4%) patients. Here postoperative vertigo occurred in 5/12 (41.6%) patients, with new onset in all cases (vertigo group 1). All patients belonged to group A or B with assured vestibular or possibly vestibular cause of vertigo. There were 12 (41.4%) patients in electrode category III (not structure-preserving). In four out of these 12 CI users (33.3%), vertigo occurred newly after implantation (vertigo group 1). Based on the questionnaire, we suspected a vestibular cause (group A) in two patients and a non-vestibular cause (group C) in the other two. Due to the small number of cases within the electrode groups, statistical tests were not applied for the comparison (for the results of the descriptive statistics, see **Figure 4**).

Low-Frequency Residual Hearing

After CI provision, eight study participants lost their residual hearing and were excluded. Among these, four cases belonged to electrode category II (2× CI 532, 2× FLEX28), and four cases belonged to electrode category III (1× HiFocus MidScala, 3× CI512), corresponding to a percentage of residual hearing loss of 15% per group. In addition, two cases were excluded from evaluation because of preoperative deafness. Therefore, 19 cases were available for analysis of hearing preservation (**Figure 5**).

In electrode category I, PTAlow ranged preoperatively from 43 dB HL up to 76 dB HL (mean 55 ± 13.05 dB HL) and postoperatively from 59 dB HL up to 86 dB (mean 69 ± 10.47 dB HL), with a mean difference of 14 dB; in electrode category II, it ranged preoperatively from 31 dB HL up to 95 dB HL (mean 70 ± 21.04 dB HL) and postoperatively from 51 dB HL up to 103 dB HL (mean 89 ± 18.34 dB HL), with a mean difference of 19 dB; in electrode category III, it ranged preoperatively from 65 dB HL up to 101 dB HL (mean 86 ± 11.31 dB HL) and postoperatively from 76 dB HL up to 103 dB (mean 96 ± 9.35 dB HL), with a mean difference of 10 dB. The PTAlow difference

TABLE 7 | Result categories of caloric response test (pre- and post-operative) related to vertigo group (for information on vertigo group, see **Table 2**).

	Preoperative vertigo group					Postoperative vertigo group				
	0	2	1	3		0	2	1	3	
Interpretation	**No postoperative vertigo**		**Postoperative vertigo**		**Total**	**No postoperative vertigo**		**Postoperative vertigo**		**Total**
Physiological	13 (100%)	1 (33%)	9 (82%)	1 (50%)	24	10 (77%)	2 (67%)	9 (82%)	2 (100%)	23 (79%)
Hyperexcitable	0	0	0	1 (50%)	1	0	0	0	0	0
Underexcitable	0	2 (67%)	2 (18%)	0	4	0	1 (33%)	1 (9%)	0	2 (7%)
Failure	0	0	0	0	0	0	0	1 (9%)	0	1 (4%)
Not performed	0	0	0	0	0	3 (23%)	0	0	0	3 (10%)
Total	13 (100%)	3 (100%)	11 (100%)	2 (100%)	29 (100%)	13 (100%)	3 (100%)	11 (100%)	2 (100%)	29 (100%)

Postoperative vertigo, occurrence of self-reported vertigo at any interval.

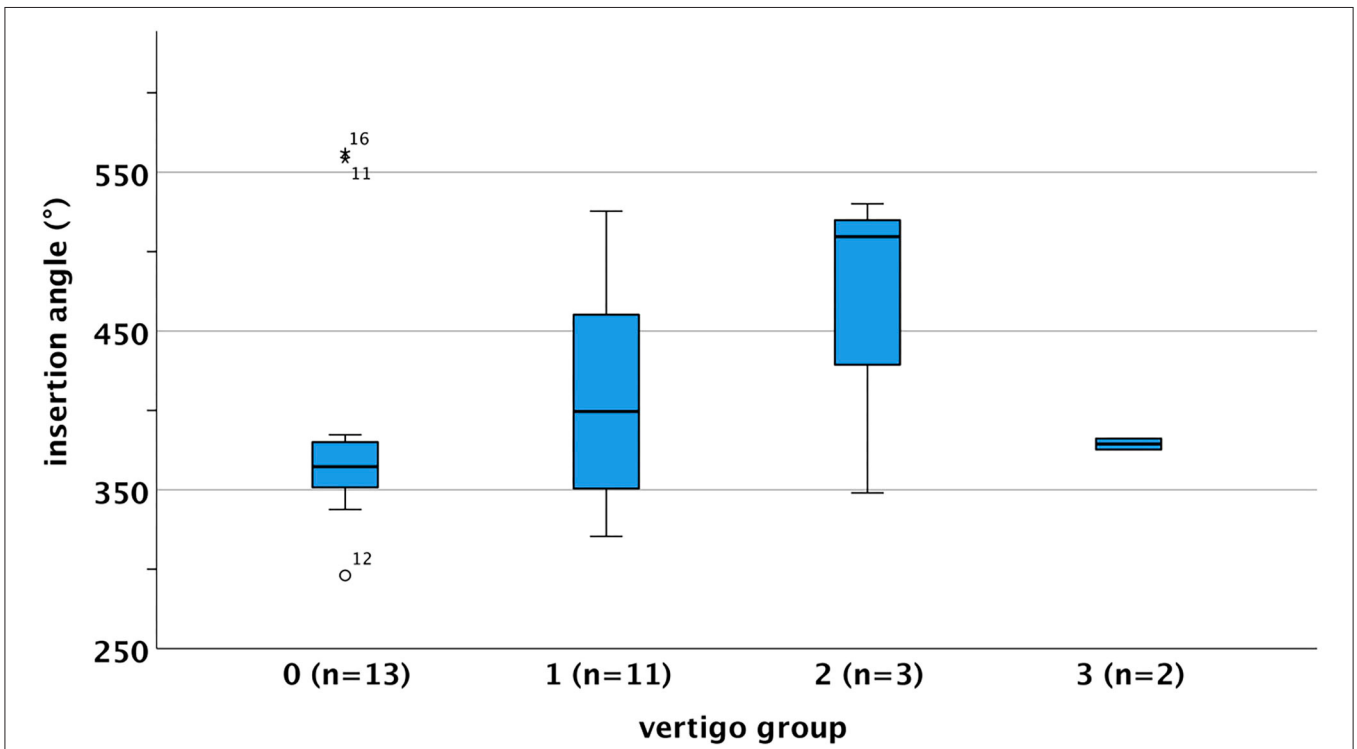

FIGURE 3 | Insertion angle (IA) distributions depending on vertigo group [boxplot, 0 = –/–, 1 = –/+, 2 = +/+, 3 = +/–, vertigo (+) pre-op/postoperative]. The IA ranged in vertigo group 0 from 296.10° up to 562.24° (mean = 389 ± 82.90°), in vertigo group 1 from 320.71° up to 525.5° (mean = 409.21 ± 72.29°), in vertigo group 2 from 348.11° up to 530.18° (mean= 462.58 ± 99.67°), and in vertigo group 3 from 375.39° up to 382.31° (mean = 378.85 ± 4.89°). IA was approximately normally distributed for vertigo group 1 ($p = 0.192$) and vertigo group 2 ($p = 0.199$), but not for vertigo group 0 ($p = 0.001$) as assessed by the Shapiro–Wilk test. As vertigo group 3 consisted of only two cases, no normal distribution could be tested.

was normally distributed, as assessed by the Shapiro–Wilk test ($p = 0.125$).

Over all categories, the PTAlow before and after implantation was statistically different [paired-samples t-test, $t_{(18)} = -5.288$, $p < 0.001$]. Split to the electrode category, the same was observed for electrode category I [$t_{(4)} = -5.199$, $p = 0.007$] and category II [$t_{(7)} = -4.134$, $p = 0.004$], but not for category III [$t_{(5)} = -1.852$, $p = 0.123$].

After calculating the PTAlow difference, testing for normal distribution, testing for variance homogeneity, and removing outliers, we conducted a one-way ANOVA to investigate whether there was a difference in PTAlow difference depending on the electrode categories. The PTAlow difference was statistically significant for the different electrode groups, $F_{(2,23)} = 284$, $p < 0.001$. The Tukey *post-hoc* test showed a significant difference ($p < 0.001$) in PTAlow between electrode groups 2 and 3 [10.4, 95% CI (1.17, 19.61)], while the difference between electrode groups 1 and 2 [$p = 0.435$; 5.7, 95% CI (−5.7, 17.07)] and electrode groups 1 and 3 [$p = 0.573$; 4.7, 05% CI (−6.86, 16.26)] was not significant.

TABLE 8 | Relation of insertion angle category and vertigo group (for information on vertigo group, see **Table 2**).

		Vertigo group				
		0	2	1	3	Proportion of patients with postoperative vertigo within the IA group
IA category	Number of patients	Postoperative no vertigo		Postoperative vertigo		
U	20	10	1	7	2	9/20 (45%)
O	8	2	2	4	0	4/8 (50%)
Not measurable	1	1	0	0	0	0/1 (0%)
Total	29	13	3	11	2	

IA, insertion angle; U, <430°; O, ≥430°.

TABLE 9 | Occurrence of vertigo within electrode categories (for information on vertigo group, see **Table 2**).

		Vertigo group				
		0	2	1	3	Proportion of patients with postoperative vertigo within the electrode group
Electrode category	Number of patients	Postoperative no vertigo		Postoperative vertigo		
I	5	1	0	2	2	4/5 (80%)
II	12	5	2	5	0	5/12 (42%)
III	12	7	1	4	0	4/12 (33%)
Total		13	3	11	2	

I, structure-preserving; II, potentially structure-preserving; III, not structure-preserving.

DISCUSSION

The occurrence of vertigo as a postoperative complication after cochlear implantation has been described in several studies (1, 7, 42). The risk of this has been reported to range in incidence from 12 to 74% (43, 44). In the study presented here, the incidence of new vertigo after CI surgery was 45.8% (11/24 patients). Despite numerous efforts to identify triggers for vertigo and to introduce improvements in CI surgery protocols, vertigo is still considered a common side effect (11).

Romberg Test

Since no patient in our study had a conspicuous result in the Romberg test, it can be concluded that neither preoperatively nor postoperatively was a central lesion present. Kaczmarczyk et al. (45) who used the Romberg test to assess gait stability before and after cochlear implantation, also found no increased stance or gait instability postoperatively.

Unterberger Test

Abnormal rotations were detected in patients of the present cohort with and without vertigo symptoms using the Unterberger test. However, the weak sensitivity and specificity of this test was already described in 1944 by Winkler (46). The authors concluded that a negative result of the test could not exclude vestibular dysfunction, and a positive result could not confirm it. Similarly, a more recent study by Hickey et al. (47) reported no significant Unterberger test result difference between patients with and without vestibular pathology. Our results did show that patients with deviation in the Unterberger test mostly turned to the implanted side postoperatively, and 75% (3/4 patients) of cases complained of vertigo. Nevertheless, as reported in the mentioned previous studies, there were also patients with conspicuous results who were asymptomatic. Thus, we conclude that the test is not sufficiently informative with respect to vestibular damage.

Subjective Visual Vertical

Gnanasegaram et al. (48) demonstrated conspicuous values in the SVV test ∼1 year postoperatively in 45% of patients after cochlear implantation. In the study presented here, these results could not be confirmed, neither in patients with nor without vertigo. The reason for this discrepancy could be the fact that, within the 6-month follow-up period, compensation of otolith function had been achieved, which according to Böhmer (34) can occur within weeks to a few months after damage. On the other hand, this would again contradict the results of Gnanasegaram et al. (48) who showed pathologic results despite a longer observation period, although this could also be caused by increased vestibular damage within the studied patient group.

In their study of 12 patients, le Nobel et al. (49) demonstrated that conspicuous SVV results resulted at all time points before CI surgery, 1 week and 1 month postoperatively, but did not change significantly. According to Sun et al. (50), the SSV test correlates

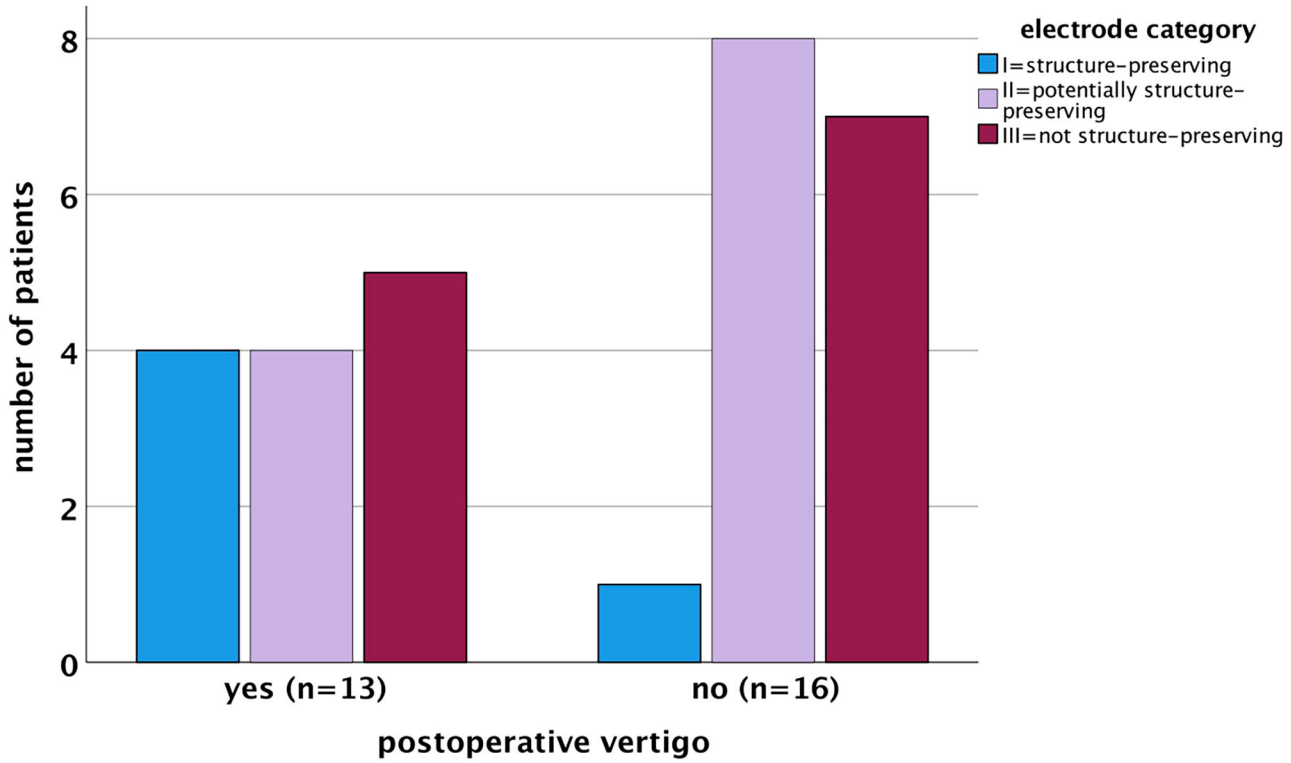

FIGURE 4 | Correlation between the occurrence of postoperative vertigo and electrode categories (bar chart). The electrode categories were not normally distributed in patients with postoperative vertigo ($p = 0.007$) as well as in patients without postoperative vertigo ($p = 0.001$) as assessed by the Shapiro–Wilk test.

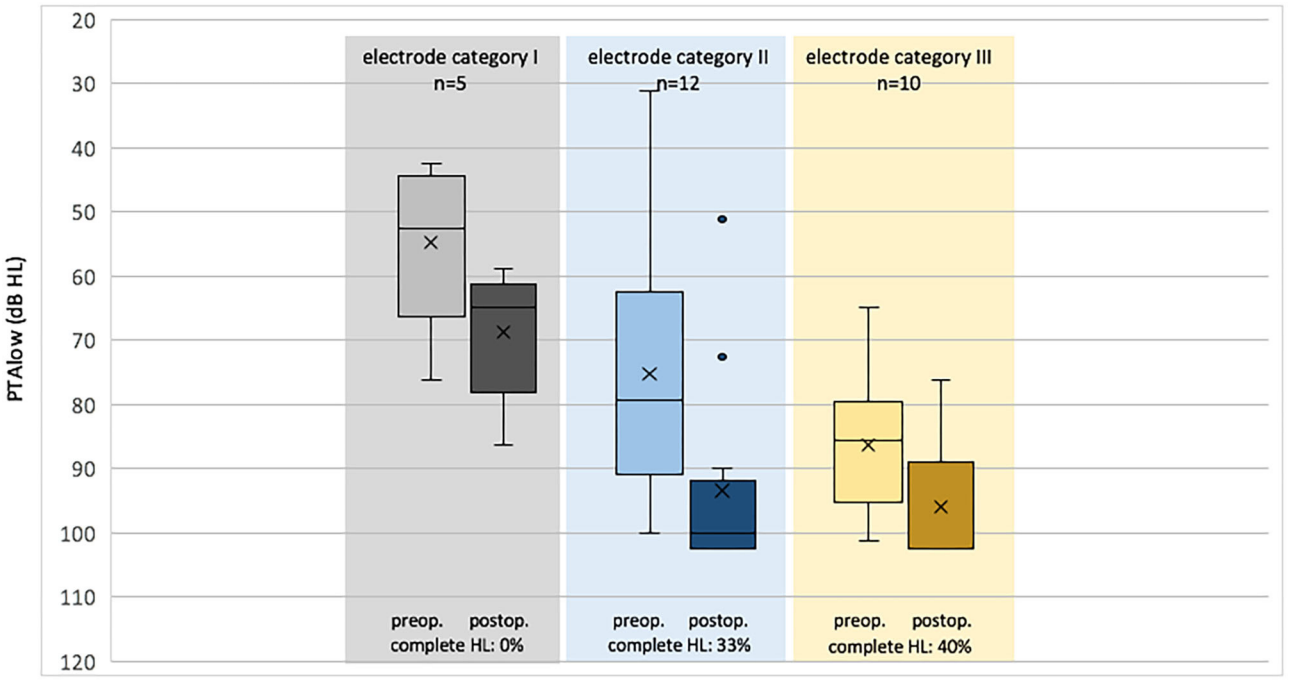

FIGURE 5 | Pre- and post-operative PTAlow (averaged unaided air conduction threshold, 125, 250, 500, and 1,000 Hz, boxplots) grouped by electrode category (I, structure-preserving; II, potentially structure-preserving; III, not structure-preserving).

with the asymmetry ratio of the oVEMP but is easier to perform and also less expensive, which is why it was recommended by the author for measuring the utricle function of patients at the time of vertigo.

Optokinetic Testing

According to Yetiser et al., optokinetic testing can detect evidence of central disorders, particularly cerebellar damage and brainstem damage. Because none of the patients in this study had postoperative abnormalities, it can be concluded that cochlear implantation did not result in central lesions (51). These could be excluded preoperatively as a cause of vertigo among all patients in vertigo classes 2 and 3. No conspicuous values were measured for patient n3 either, who indicated an apoplexy as the etiology of the hearing loss.

Video Head Impulse Test

When considering the vHIT results of this study, it is noticeable that no conspicuous decrease in gain (gain below 0.8) in the implanted side was detected postoperatively in any patient with postoperative vertigo. In contrast, two patients without postoperative vertigo (n7 and n24) had pathologic decrease in gain in the implanted side. Furthermore, it was noticeable that, in patients with preoperative vertigo, both the preoperative mean gain in the implanted side, 1.0 ± 0.2, and in the non-implanted side, 1.1 ± 0.3, were within the normal range. Considering the patients who suffered from vertigo postoperatively, the mean gain of 0.98 ± 0.2 in the implanted side and 0.95 ± 0.15 in the non-implanted side was similar, although a conspicuous result of the implanted side would be expected. In the *t*-test for paired samples, there was no difference in gain values after implantation between both sides [$t_{(27)} = 0.376$, $p = 0.710$].

Similar to previous studies, cases with conspicuous values were identified in the caloric test, while the vHIT gain parameter was in the physiological range, although both tests measure the function of the hSCC (38). Blödow et al. (52) assumed that, in the case of peripheral vestibulopathy, as suspected after implantation, the caloric irrigation test would show conspicuous values more frequently than vHIT. Dagkiran et al. (53) examined 42 CI patients 3 days and 3 months postoperatively and reported that the number of patients with deteriorated vHIT results decreased from 16.6 to 2.3%. Similar observations were described by Jutila et al. who examined patients with acute vestibular loss using vHIT on day 3 and at 3 months after the occurrence of vestibular symptoms. There was a highly significant improvement in gain from deteriorated to normal values as well as a decrease in previously existing asymmetry (54). Ibrahim et al. (55) demonstrated that cochlear implantation had no significant effect on the outcome of vHIT, consistent with our observations.

Furthermore, it became obvious from the results of the present study that the GA parameter was most frequently conspicuous. We suspected that the reason for this could be that the thresholds for deviation used in this study ($>8/\leq 8\%$) were set too low and could also occur physiologically. We examined whether patients with vertigo had a higher GA value but could not find any difference between patients with and without self-reported vertigo. In general, thresholds of deterioration are controversially discussed in the literature and range from 2 to 20% (14, 56–58). In summary, GA was not related to subjectively reported vestibular status. Therefore, evaluation of gain asymmetry in terms of conspicuous or physiological category was not decisive.

In addition, an evaluation of vHIT catch-up saccades was carried out, which are considered typical of peripheral lesions (59). However, we found no association of catch-up saccades with the occurrence of vertigo. Patscheke et al. (38) analyzed the occurrence of vHIT catch-up saccades in 171 patients suffering from vertigo and showed that the sensitivity of the vHIT for detecting a peripheral–vestibular disorder was low and that the two (peripheral) parameters "gain" and "catch-up saccades"—contrary to expectations—were only conspicuous to a small extent (22%) in the same patients.

Caloric Irrigation Test

The caloric irrigation test is a long-established measurement technique that has been used in multiple studies to investigate the function of hSCC after cochlear implantation (9, 42, 60, 61). It has been described frequently that cochlear implantation has a significant impact on the outcome of this functional test (15, 55). However, there are also controversial reports, e.g., Colin et al. (9) reported no significant correlation between caloric irrigation test results and individual vertigo symptoms. This observation was confirmed by Zeng et al., where 18 patients were tested preoperatively and at 1 week and 1 month postoperatively (61).

In the present study, SPV decreased slightly, about 4°, within the total group (pre-operative/post-operative comparison) without statistical significance. Pre-operatively and post-operatively, hypoexcitability, vestibular loss, and/or SD larger than 20% with lower caloric response in the implanted side were found in 31% of the whole collective. This observation is in agreement with the results of Ibrahim et al. (55), who reported 39.5% pathologic cases preoperatively and 28% postoperatively.

Concerning the criteria for classification of pathologic results, SPV values below 10°/s were categorized as hypoexcitability and those SPV below 5°/s as vestibular loss [following the suggestions of Holinski et al. (2)]. Alternatively, SPV values below 3°/s or even 7°/s were discussed as markers for hypoexcitability, with SPV = 0°/s as indicator of vestibular failure (62, 63). Related to the present study, hypoexcitability was present in all patients with self-reported pre- or post-operative vertigo (**Table 6**). Since SPV was above 3°/s in these cases, we consider this limit to be too low. A single individual in this group even showed SPV above 7°/s. We therefore consider a limit of SPV <10°/s to be appropriate to characterize the irregular function of hSCC.

Different limits for physiologic SD (or canal paresis) have likewise been discussed. The generally accepted limit of physiological SD is between 20 and 25% (41, 61, 64, 65).

Remarkably, SPV and SD outcomes had improved in two cases after surgery (n16, n30). On the one hand, this could be due to the limited reliability of the test. On the other hand, an improvement of vestibular function after CI is reported in the literature, which the authors attributed to the chronic stimulation of the labyrinth (9).

Correlation of Vertigo Test Results With Self-Reported Vertigo

In conclusion, the efforts to objectify self-reported vertigo in the present study did not correlate with vestibular test results. The lack of correlation between subjective vertigo and vestibular test outcome in the present study is not unique to CI rehabilitation but has been discussed for almost 30 years (66–68). This lack of correlation is also the central finding of the present study because vestibular disability, as reported by the patients, was not adequately captured by any of the vestibular diagnostic procedures in the current test battery. Interestingly, these results were found not only in patients with postoperative vertigo but also in the small group of patients who reported vertigo preoperatively and did not report vertigo postoperatively (n13, n16, and n24). The analysis of the questionnaire data indicated that one patient (n24) was suffering from vertigo of vestibular origin (group A), one patient (n16) had probably vestibular origin (group B), and in one patient (n13) no indication of vestibular origin was observed (group C). In patient n24, both vHIT and caloric measurements were outside the normal range pre- and post-operatively, supporting the strong suspicion of a vestibular origin of the reported vertigo based on the questionnaire evaluation. A similar result was seen in patient n16, in whom the caloric SPV was out of normal range only preoperatively, but SD was apparent at both test intervals and in whom, according to the questionnaire, a probable vestibular cause of vertigo could be assumed. This indicated that vestibular damage was present in these two patients already before surgery. Assuming that the test results were correct, reasons for the absence of vertigo could be a compensatory process that had occurred in the meantime or the impact of electrical stimulation postoperatively.

Multiple previous studies attempted to define the most reliable protocol for detecting vestibular impairment after CI. Abouzayd et al. (13) recently conducted a systematic review and, after a literature review, summarized the results of eight studies. Their meta-analyses calculated the sensitivity and specificity of the results of caloric irrigation, cVEMP, and vHIT using patient-reported symptoms as a reference. The pooled sensitivity of the caloric test was 21% ($n = 6$ studies), cVEMP 32% ($n = 4$), and vHIT 50% ($n = 2$). Despite certain limitations in interpretation (e.g., variable observation period after intervention, methodological differences), the poor sensitivity suggests that no single vestibular test is particularly sensitive to the relationship between subjective vertigo and vertigo diagnosis. We also hypothesize that a single individual vestibular test in isolation cannot provide sufficient information about the entire vestibular system or that the small group of patients was responsible for the limited validity of the test results.

Low-Frequency Residual Hearing and Electrode Design

Hearing preservation after CI surgery is most likely equivalent to extensive cochlear structure preservation during surgery. The PTAlow results within electrode category group I confirmed the possibility of hearing preservation (**Table 5**); no case of complete loss of residual hearing was observed. In electrode category groups II and III, this was not consistently the case since four cases occurred with total loss of residual hearing in each group. The difference in PTAlow from pre- to postoperative was slightly larger in electrode category II than in electrode category I. This result is not unexpected since, in cases with preserved hearing, the extent of hearing loss caused by implantation is comparable. This fact is consistent with data available in the literature, as mentioned above. In individual category II cases and in electrode category III, this difference is not unexpected because of comparatively worse preoperative thresholds (e.g., PTAlow n21 = 101 dB) in combination with a floor effect limited by the maximum defined hearing loss (103 dB). This bias is responsible for the lack of significance of the PTAlow difference between groups I and III.

Although electrode category showed a correlation with the extent of hearing preservation, no correlation was found between electrode category and vertigo symptoms or the outcome of the various vestibular tests in this study.

Insertion Angle and Electrode Design

Following the suggestion given by Helbig et al., two groups, depending on electrode insertion angle, were formed by subdividing the insertion angle above and below 430° (27). There was no correlation of insertion angle with the occurrence of self-reported vertigo or various parameters of the vertigo test battery. These results are consistent with those of Louza et al., who investigated a cohort of 41 cases (average insertion angle 464°). They reported no statistically significant correlation between insertion angle and the occurrence of vertigo or insertion angle and abnormal caloric irrigation test parameters (10). Nordfalk et al. (69) likewise investigated 39 cases (insertion angle, 405–708°) and reported no correlation between postoperative loss of vestibular function and insertion angle. Consistent with these observations, we did not observe a greater risk of vestibular impairment with deeper electrode insertion.

In order to minimize trauma after CI surgery, work has and will continue to improve the design of the electrode carriers. Due to the fact that category I or II electrodes are specifically or at least in principle suitable for hearing preservation, a reduced incidence of postoperative vertigo was expected for these electrode designs.

Thus, the results of the present study indicate no significant association between electrode category and onset of new vertigo. Similarly, in a prospective observational study by Krause et al. (70) comprising 36 patients implanted with pre-curved electrodes and 11 patients implanted with flexible straight electrodes, no significant difference related to electrode design was found in different parameters of postoperative vestibular diagnostics.

Different from these results, Frodlund et al. (71) reported a significant decrease in caloric response depending on electrode design, where in cases with straight electrodes ($n = 15$) and precurved electrodes ($n = 13$) SPV reduction of 23 and 7.6°/s was observed, respectively, whereas flexible electrodes showed no larger SPV decrease (0.1°/s, $n = 15$). Compared to the results of the present study (straight/precurved/flexible,

−9/−7/+2.6°/s), a similar trend is obvious, however with smaller alterations. This might be related to the different number of cases (straight/precurved/flexible, $n = 3/17/9$) as well as the different test interval. The authors related the delayed onset of vertigo (1 month or later) to the occurrence of mechanical pressure generated by the electrode tip that might cause a lesion of the basilar membrane (71).

The prevalence of self-reported vertigo reported in the questionnaires after CI surgery was 44.8% (13/29 patients), and the incidence was 45.8% (10/24 patients), which is thus in agreement with the results of Krause et al., where an incidence of 45% was reported. In 10/13 cases (77%), new vertigo occurred within the first postoperative week. Thus, these results are similar to those of Krause et al., who reported an incidence of 80% in the same period. While the present study cohort did not report vertigo 3 months after surgery, Krause et al. mentioned one case (5%) with persistent vertigo. At the 6-month test interval, in the present study cohort, vertigo complaints appeared again in 3/13 cases (23%), whereas no vertigo case was reported by Krause et al. (1) at this interval.

Ito (63) categorized the patients with vertigo after cochlear implantation into different groups based on the temporal presence of their symptoms: the early type (vertigo within 2 weeks postoperatively), the prolonged type (persistent symptoms), and the delayed type (vertigo duration longer than 2 weeks). The author described that 58% belonged to the early type, 34% to the prolonged type, and 8% to the delayed type. In the present study, these percentages were 39% for the early type, 38% for the prolonged type, and 23% for the delayed type. In 2009, Hamann (72) described that, within the first 14 days after vestibular damage, there was a significant reduction to complete disappearance of vertigo. This observation had also been made previously by Black et al. (73), who described the likelihood for compensation over time. However, a postoperative increase of balance dysfunction is also possible. Thus, labyrinthitis could be a cause of late onset of cochlear implant-related vertigo (74). The study presented here does not provide evidence for the suspicion of labyrinthitis, as no signs of vestibular dysfunction were present in three cases with delayed-onset vertigo.

Limitations of the Study

One major drawback of this study is the small number of participants ($n = 29$), which, in turn, reduced the size of the four subgroups. Although the aim was a before–after comparison after CI surgery, a control group could be considered an addition. It would be conceivable to include a group of patients who decide not to undergo cochlear implantation in the near future and are monitored for 6 months using the tests and questionnaires described above. Due to the small sample size of electrode group 1 ($n = 5$), the results of the statistical tests calculated by ANOVA and Tukey B are of limited validity. For this reason, the frequency of occurrence of postoperative deafness is probably the more appropriate factor to assess postoperative structural preservation.

CONCLUSION

In the present study, the incidence of self-reported new onset of vertigo after cochlear implant provision was reported to be ∼45%. As shown in a large number of previous studies, vestibular disorders are the most common complications after cochlear implantation. Consistent with this, we also found this complication to be frequent in the patient group studied here. The questionnaire evaluation confirmed new-onset vertigo after CI surgery in 72.7%, with symptoms suggestive of an otogenic etiology of vestibular dysfunction as outlined above. The symptoms indicated an otogenic etiology of vestibular dysfunction in 72.7% of all cases with new vertigo after CI surgery. As objective vestibular test results did not correlate with reported vertigo symptoms, an analysis of the origin of vestibular dysfunction after implantation was difficult. An effect of electrode design, in terms of insertion angle and shape, as an influencing factor for the occurrence of postoperative vertigo could not be confirmed. Further studies should clarify whether the lack of correlation between vestibular test results and reported vertigo is due to a lack of sensitivity of the currently applied methodologies, a central compensatory mechanism, or a multifactorial cause of vertigo.

DATA AVAILABILITY STATEMENT

The raw data supporting the conclusions of this article will be made available by the authors, without undue reservation.

ETHICS STATEMENT

The studies involving human participants were reviewed and approved by Ethikkommission des Fachbereichs Medizin der Goethe-Universität Frankfurt am Main. The patients/participants provided their written informed consent to participate in this study.

AUTHOR CONTRIBUTIONS

CW, UB, and SH made substantial contributions to the conception, ethical approval of the work, and were responsible for the acquisition of patients and analysis as well as interpretation of data. ML and TS helped revising the work critically and added important intellectual content. All authors contributed to the article and approved the submitted version.

REFERENCES

1. Krause E, Louza JPR, Wechtenbruch J, Hempel J-M, Rader T, Gürkov R. Incidence and quality of vertigo symptoms after cochlear implantation. *J Laryngol Otol.* (2009) 123:278–82. doi: 10.1017/S002221510800296X
2. Holinski F, Elhajzein F, Scholz G, Sedlmaier B. Vestibuläre störungen nach cochleaimplantat bei erwachsenen. *HNO.* (2012) 60:880–5. doi: 10.1007/s00106-012-2526-x
3. Krause E, Wechtenbruch J, Rader T, Gürkov R. Influence of cochlear implantation on sacculus function. *Otolaryngol Head Neck Surg.* (2009) 140:108–13. doi: 10.1016/j.otohns.2008.10.008

4. Katsiari E, Balatsouras DG, Sengas J, Riga M, Korres GS, Xenelis J. Influence of cochlear implantation on the vestibular function. *Eur Arch Otorhinolaryngol.* (2013) 270:489–95. doi: 10.1007/s00405-012-1950-6
5. Sampaio ALL, Araújo MFS, Oliveira CACP. New criteria of indication and selection of patients to cochlear implant. *Int J Otolaryngol.* (2011) 2011:573968. doi: 10.1155/2011/573968
6. Sosna M, Tacikowska G, Pietrasik K, Skarzyński H, Lorens A, Skarzyński PH. Effect on vestibular function of cochlear implantation by partial deafness treatment–electro acoustic stimulation (PDT–EAS). *Eur Arch Otorhinolaryngol.* (2019) 276:1951–9. doi: 10.1007/s00405-019-05425-5
7. Hänsel T, Gauger U, Bernhard N, Behzadi N, Romo Ventura ME, et al. Meta-analysis of subjective complaints of vertigo and vestibular tests after cochlear implantation. *Laryngoscope.* (2018) 128:2110–23. doi: 10.1002/lary.27071
8. Louza JPR. *Zum Einfluss der Cochlea Implantation auf das Vestibularorgan.* (2010). Available online at: https://edoc.ub.uni-muenchen.de/12460/ (accessed October 28, 2020).
9. Colin V, Bertholon P, Roy S, Karkas A. Impact of cochlear implantation on peripheral vestibular function in adults. *Eur Ann Otorhinolaryngol Head Neck Dis.* (2018) 135:417–20. doi: 10.1016/j.anorl.2018.10.007
10. Louza J, Mertes L, Braun T, Gürkov R, Krause E. Influence of insertion depth in cochlear implantation on vertigo symptoms and vestibular function. *Am J Otolaryngol.* (2015) 36:254–8. doi: 10.1016/j.amjoto.2014.11.007
11. Todt I, Basta D, Ernst A. Does the surgical approach in cochlear implantation influence the occurrence of postoperative vertigo? *Otolaryngol Head Neck Surg.* (2008) 138:8–12. doi: 10.1016/j.otohns.2007.09.003
12. Dhanasingh A, Jolly C. An overview of cochlear implant electrode array designs. *Hear Res.* (2017) 356:93–103. doi: 10.1016/j.heares.2017.10.005
13. Abouzayd M, Smith PF, Moreau S, Hitier M. What vestibular tests to choose in symptomatic patients after a cochlear implant? A systematic review and meta-analysis. *Eur Arch Otorhinolaryngol.* (2017) 274:53–63. doi: 10.1007/s00405-016-4007-4
14. Chen X, Chen X, Zhang F, Qin Z. Influence of cochlear implantation on vestibular function. *Acta Otolaryngol.* (2016) 136:655–9. doi: 10.3109/00016489.2016.1154186
15. Krause E, Louza JPR, Wechtenbruch J, Gürkov R. Influence of cochlear implantation on peripheral vestibular receptor function. *Otolaryngol Head Neck Surg.* (2010) 142:809–13. doi: 10.1016/j.otohns.2010.01.017
16. Bruce IA, Todt I. Hearing preservation cochlear implant surgery. *Adv Otorhinolaryngol.* (2018) 81:66–73. doi: 10.1159/000485544
17. Aschendorff A, Kubalek R, Turowski B, Zanella F, Hochmuth A, Schumacher M, et al. Quality control after cochlear implant surgery by means of rotational tomography. *Otol Neurotol.* (2005) 26:34–7. doi: 10.1097/00129492-200501000-00007
18. O'Connell BP, Hunter JB, Gifford R, Rivas A, Haynes DS, Noble JH, et al. Electrode location and audiologic performance after cochlear implantation: a comparative study between Nucleus CI422 and CI512 electrode arrays. *Otol Neurotol.* (2016) 37:1032–5. doi: 10.1097/MAO.0000000000001140
19. Shaul C, Dragovic AS, Stringer AK, O'Leary SJ, Briggs RJ. Scalar localisation of peri-modiolar electrodes and speech perception outcomes. *J Laryngol Otol.* (2018) 132:1000–6. doi: 10.1017/S0022215118001871
20. Cochlear Limited. *Nucleus® Implants.* Cochlear. Available online at: ca/en/home/products-and-accessories/nucleus-system/nucleus-implants (accessed April 25, 2019).
21. Wanna GB, Noble JH, Gifford RH, Dietrich MS, Sweeney AD, Zhang D, et al. Impact of intrascalar electrode location, electrode type, and angular insertion depth on residual hearing in cochlear implant patients: preliminary results. *Otol Neurotol.* (2015) 36:1343–8. doi: 10.1097/MAO.0000000000000829
22. Aschendorff A, Briggs R, Brademann G, Helbig S, Hornung J, Lenarz T, et al. Clinical investigation of the nucleus slim modiolar electrode. *AUD.* (2017) 22:169–79. doi: 10.1159/000480345
23. *Cochlear™ Nucleus® Profile Implantat mit Slim-Modiolar-Elektrode (CI532).* (2016). Available online at: http://presse-de.cochlear.com/documents/technische-information-cochlear-nucleus-r-profile-implantat-mit-slim-modiolar-elektrode-ci532-62459 (accessed April 25, 2019).
24. Cochlear Limited. *Cochlear™ Nucleus® CI532 Cochlear Implant Patient Information Important: Warnings, Precautions and Electromagnetic Compatibility.* Lane Cove, NSW (2018).
25. MED-EL Medical Electronics. *MED-EL SYNCHRONY Cochleaimplantat Einzigartige MRT-Sicherheit.* Available online at: https://s3.medel.com/downloadmanager/downloads/synchrony/de-DE/24476.pdf
26. Dirr F, Hempel J, Krause E, Müller J, Berghaus A, Ertl-Wagner B, et al. Value of routine plain x-ray position checks after cochlear implantation. *Otol Neurotol.* (2013) 34:1666–9. doi: 10.1097/MAO.0b013e3182a09cc3
27. Helbig S, Adel Y, Leinung M, Stöver T, Baumann U, Weissgerber T. Hearing preservation outcomes after cochlear implantation depending on the angle of insertion: indication for electric or electric-acoustic stimulation. *Otol Neurotol.* (2018) 39:834–41. doi: 10.1097/MAO.0000000000001862
28. Cohen LT, Xu J, Xu SA, Clark GM. Improved and simplified methods for specifying positions of the electrode bands of a cochlear implant array. *Am J Otol.* (1996) 17:859–65.
29. GeoGebra. *GeoGebra.* Available online at: https://www.geogebra.org/download (accessed July 6, 2018).
30. Jacobson GP, Newman CW. The development of the dizziness handicap inventory. *Arch Otolaryngol Head Neck Surg.* (1990) 116:424–7. doi: 10.1001/archotol.1990.01870040046011
31. Buchman CA, Joy J, Hodges A, Telischi FF, Balkany TJ. Vestibular effects of cochlear implantation. *Laryngoscope.* (2004) 114(10 Pt 2 Suppl. 103):1–22. doi: 10.1097/00005537-200410001-00001
32. Grommes C, Conway D. The stepping test: a step back in history. *J Hist Neurosci.* (2011) 20:29–33. doi: 10.1080/09647041003662255
33. Biesinger E, Iro H, editors. *HNO Praxis heute-Schwindel.* Berlin: Springer (2007).
34. Böhmer A. Zur beurteilung der otolithenfunktion mit der subjektiven visuellen vertikalen. *HNO.* (1997) 45:533–7. doi: 10.1007/s001060050127
35. Haid CT. *Vestibularisprüfung und vestibuläre Erkrankungen: Ein Leitfaden für Praxis und Klinik zur Diagnostik und Therapie von Schwindel und Gleichgewichtsstörungen.* Berlin: Springer-Verlag (2013).
36. Lenarz T, Boenninghaus H-G. *Hals-Nasen-Ohren-Heilkunde.* 14th ed. Heidelberg: Springer (2012).
37. Halmagyi GM, Chen L, MacDougall HG, Weber KP, McGarvie LA, Curthoys IS. The Video Head Impulse Test. *Front Neurol.* (2017) 8:258. doi: 10.3389/fneur.2017.00258
38. Patscheke JH, Plenz P, Ernst S, Klußmann J-P. Video-Head impulse test with little diagnostic impact in vertigo-patients. *Laryngorhinootologie.* (2018) 97:181–8. doi: 10.1055/s-0043-122743
39. Hallpike CS. The caloric tests*. *J Laryngol Otol.* (1956) 70:15–28. doi: 10.1017/S0022215100052610
40. Jongkees LB, Maas JP, Philipszoon AJ. Clinical nystagmography. A detailed study of electro-nystagmography in 341 patients with vertigo. *Pract Otorhinolaryngol.* (1962) 24:65–93. doi: 10.1159/000274383
41. Reiß M, Reiß G, Waldfahrer F, editors. *Gleichgewichtsdiagnostik: Videonystagmographie und neue Untersuchungsmethoden.* Berlin: Springer (2015).
42. Enticott JC, Tari S, Koh SM, Dowell RC, O'Leary SJ. Cochlear implant and vestibular function. *Otol Neurotol.* (2006) 27:824–30. doi: 10.1097/01.mao.0000227903.47483.a6
43. Klenzner T, Neumann M, Aschendorff A, Laszig R. Caloric stimulation of the vestibular organ after cochlear implant surgery. *Laryngorhinootologie.* (2004) 83:659–64. doi: 10.1055/s-2004-825678
44. Steenerson RL, Cronin GW, Gary LB. Vertigo after cochlear implantation. *Otol Neurotol.* (2001) 22:842–3. doi: 10.1097/00129492-200111000-00021
45. Kaczmarczyk K, Błazkiewicz M, Wiszomirska I, Pietrasik K, Zdrodowska A, Wit A, et al. Assessing gait stability before and after cochlear implantation. *Biomed Res Int.* (2019) 2019:2474273. doi: 10.1155/2019/2474273
46. Winkler U. Ein beitrag zur bewertung des tretversuches nach unterberger. *Arch Ohren Nasen Kehlkopfheilkunde.* (1944) 154:331–54. doi: 10.1007/BF01970236
47. Hickey SA, Ford GR, Buckley JG, Fitzgerald O'Connor AF. Unterberger stepping test: a useful indicator of peripheral vestibular dysfunction? *J Laryngol Otol.* (1990) 104:599–602. doi: 10.1017/S0022215100113337
48. Gnanasegaram JJ, Parkes WJ, Cushing SL, McKnight CL, Papsin BC, Gordon KA. Stimulation from Cochlear implant electrodes assists with recovery from asymmetric perceptual tilt: evidence from the subjective visual vertical test. *Front Integr Neurosci.* (2016) 10:32. doi: 10.3389/fnint.2016.00032

49. le Nobel GJ, Hwang E, Wu A, Cushing S, Lin VY. Vestibular function following unilateral cochlear implantation for profound sensorineural hearing loss. *J Otolaryngol Head Neck Surg.* (2016) 45:38. doi: 10.1186/s40463-016-0150-6
50. Sun DQ, Zuniga MG, Davalos-Bichara M, Carey JP, Agrawal Y. Evaluation of a bedside test of utricular function - the bucket test - in older individuals. *Acta Otolaryngol.* (2014) 134:382–9. doi: 10.3109/00016489.2013.867456
51. Yetiser S, Ince D, Yetiser B. Optokinetic analysis in patients with spontaneous horizontal gaze-evoked nystagmus without radiological neuropathology. *Ear Nose Throat J.* (2019) 98:420–4. doi: 10.1177/0145561319840902
52. Blödow A, Helbig R, Wichmann N, Wenzel A, Walther LE, Bloching MB. Video head impulse test or caloric irrigation? Contemporary diagnostic tests for vestibular schwannoma. *HNO.* (2013) 61:781–5. doi: 10.1007/s00106-013-2752-x
53. Dagkiran M, Tuncer U, Surmelioglu O, Tarkan O, Ozdemir S, Cetik F, et al. How does cochlear implantation affect five vestibular end-organ functions and dizziness? *Auris Nasus Larynx.* (2019) 46:178–85. doi: 10.1016/j.anl.2018.07.004
54. Jutila T, Aalto H, Hirvonen TP. Recovery of the horizontal vestibulo-ocular reflex in motorized head impulse test is common after vestibular loss. *Acta Otolaryngol.* (2012) 132:726–31. doi: 10.3109/00016489.2012.656763
55. Ibrahim I, da Silva SD, Segal B, Zeitouni A. Effect of cochlear implant surgery on vestibular function: meta-analysis study. *J Otolaryngol Head Neck Surg.* (2017) 46:44. doi: 10.1186/s40463-017-0224-0
56. Schmid-Priscoveanu A, Böhmer A, Obzina H, Straumann D. Caloric and search-coil head-impulse testing in patients after vestibular neuritis. *J Assoc Res Otolaryngol.* (2001) 2:72–78. doi: 10.1007/s101620010060
57. Park HJ, Migliaccio AA, Della Santina CC, Minor LB, Carey JP. Search-coil head-thrust and caloric tests in Ménière's disease. *Acta Otolaryngol.* (2005) 125:852–7. doi: 10.1080/00016480510033667
58. Celebisoy N. Acute vestibular syndrome: clinical head impulse test versus video head impulse test. *J Neurol.* (2018) 265:44–7. doi: 10.1007/s00415-018-8804-0
59. Bartl K, Lehnen N, Kohlbecher S, Schneider E. Head impulse testing using video-oculography. *Ann N Y Acad Sci.* (2009) 1164:331–3. doi: 10.1111/j.1749-6632.2009.03850.x
60. Bittar RSM, Sato ES, Silva-Ribeiro DJ, Oiticica J, Mezzalira R, Tsuji RK, et al. Caloric test and video head impulse test sensitivity as vestibular impairment predictors before cochlear implant surgery. *Clinics.* (2019) 74:e786. doi: 10.6061/clinics/2019/e786
61. Zeng J, Huang HM, Wang XQ, Zhong KB, Wu PN. Assessment of the horizontal semicircular canal function after cochlear implantation by video head impulse test and caloric test. *Lin Chung Er Bi Yan Hou Tou Jing Wai Ke Za Zhi.* (2018) 32:86–90. doi: 10.13201/j.issn.1001-1781.2018.02.002
62. Bonucci AS, Filho OAC, Mariotto LDF, Amantini RCB, Alvarenga K de F. Vestibular function in cochlear implant users. *Brazil J Otorhinolaryngol.* (2008) 74:273–8. doi: 10.1016/S1808-8694(15)31100-9
63. Ito J. Influence of the multichannel cochlear implant on vestibular function. *Otolaryngol Head Neck Surg.* (1998) 118:9002. doi: 10.1016/S0194-5998(98)70295-5
64. Cerchiai N, Navari E, Miccoli M, Casani AP. Menière's disease and caloric stimulation: some news from an old test. *J Int Adv Otol.* (2019) 15:442–6. doi: 10.5152/iao.2019.7430
65. Choi JE, Kim Y-K, Cho YS, Lee K, Park HW, Yoon SH, et al. Morphological correlation between caloric tests and vestibular hydrops in Ménière's disease using intravenous Gd enhanced inner ear MRI. *PLoS ONE.* (2017) 12:e0188301. doi: 10.1371/journal.pone.0188301
66. Jacobson GP, Newman CW, Hunter L, Balzer GK. Balance function test correlates of the Dizziness Handicap Inventory. *J Am Acad Audiol.* (1991) 2:253–60. doi: 10.1037/t35080-000
67. Mutlu B, Serbetcioglu B. Discussion of the dizziness handicap inventory. *J Vestib Res.* (2013) 23:271–7. doi: 10.3233/VES-130488
68. Pérez N, Martin E, Garcia-Tapia R. Dizziness: relating the severity of vertigo to the degree of handicap by measuring vestibular impairment. *Otolaryngol Head Neck Surg.* (2003) 128:372–81. doi: 10.1067/mhn.2003.102
69. Nordfalk KF, Rasmussen K, Hopp E, Bunne M, Silvola JT, Jablonski GE. Insertion depth in cochlear implantation and outcome in residual hearing and vestibular function. *Ear Hear.* (2016) 37:e129–37. doi: 10.1097/AUD.0000000000000241
70. Krause E, Louza JPR, Hempel J-M, Wechtenbruch J, Rader T, Gürkov R. Effect of cochlear implantation on horizontal semicircular canal function. *Eur Arch Otorhinolaryngol.* (2009) 266:811–7. doi: 10.1007/s00405-008-0815-5
71. Frodlund J, Harder H, Mäki-Torkko E, Ledin T. Vestibular function after cochlear implantation: a comparison of three types of electrodes. *Otol Neurotol.* (2016) 37:1535–40. doi: 10.1097/MAO.0000000000001229
72. Hamann K-F. Vestibuläre kompensation. *HNO.* (2009) 57:487–502. doi: 10.1007/s00106-009-1935-y
73. Black FO, Shupert CL, Peterka RJ, Nashner LM. Effects of unilateral loss of vestibular function on the vestibulo-ocular reflex and postural control. *Ann Otol Rhinol Laryngol.* (1989) 98:884–9. doi: 10.1177/000348948909801109
74. Lipson S, O'Shea R, Gibbons S, Zhou G, Brodsky J. Evolution of Cochlear implant mapping and vestibular function in a pediatric case of Labyrinthitis. *J Otolaryngol Head Neck Surg.* (2020) 49:7. doi: 10.1186/s40463-020-0403-2

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Quality of Life Following Cochlear Implantation in Patients With Menière's Disease

Isabel Sanchez-Cuadrado[1,2], *Miryam Calvino*[1,2,3], *Jose Manuel Morales-Puebla*[1,2,3], *Javier Gavilán*[1,2], *Teresa Mato*[1], *Julio Peñarrocha*[1], *Maria Pilar Prim*[1] *and Luis Lassaletta*[1,2,3]*

[1] Department of Otolaryngology, La Paz University Hospital, Madrid, Spain, [2] IdiPAZ Research Institute, Madrid, Spain, [3] Biomedical Research Networking Centre on Rare Diseases (CIBERER-U761), Institute of Health Carlos III, Madrid, Spain

Background: Menière's disease (MD) is a disorder characterized by auditory and vestibular dysfunction that significantly deteriorates patients' quality of life (QoL). In addition to the management of vestibular symptoms, some patients with bilateral hearing loss meet criteria for cochlear implantation (CI).

Objectives: (1) To assess hearing results and QoL outcomes following CI in patients with MD. (2) To compare these results to a matched control group of patients who had undergone CI. (3) To analyse differences in MD patients who have undergone simultaneous or sequential labyrinthectomy or previous neurectomy.

Methods: A retrospective analysis of a study group of 18 implanted patients with MD and a matched control group of 18 implanted patients without MD, who had CI at a tertiary referral center. Hearing and speech understanding were assessed via pure-tone audiometry (PTA) and disyllabic perception tests in quiet. QoL was assessed *via* the Nijmegen Cochlear Implant Questionnaire (NCIQ), the Glasgow Benefit Inventory (GBI), the Speech, Spatial and Qualities of Hearing Scale (SSQ_{12}), and the Hearing Implant Sound Quality Index ($HISQUI_{19}$). The impact of MD ablative surgeries was analyzed in the study group (MD group).

Results: Mean pre-operative PTA thresholds were significantly lower in the MD group (103 vs. 121 dB). A significant improvement in hearing outcomes was observed following CI in both groups ($p < 0.001$), with a maximum Speech Discrimination Score of 64 and 65% disyllables at 65 dB for the MD and control group, respectively. Subjective outcomes, as measured by the NCIQ, GBI, SSQ_{12}, and $HISQUI_{19}$ did not significantly differ between groups. In the MD group, despite achieving similar hearing results, QoL outcomes were worse in patients who underwent simultaneous CI and labyrinthectomy compared to the rest of the MD group. Post-operative NCIQ results were significantly better in patients who had undergone a previous retrosigmoid neurectomy when compared to those who had undergone only CI surgery in the subdomains "basic sound perception" ($p = 0.038$), "speech" ($p = 0.005$), "activity" ($p = 0.038$), and "social interactions" ($p = 0.038$).

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***Correspondence:**
Luis Lassaletta
llassaletta@salud.madrid.org

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Conclusion: Patients with MD and severe hearing loss obtain hearing results and QoL benefits similar to other CI candidates. Delayed CI after labyrinthectomy or vestibular neurectomy can be performed with similar or better results, respectively, to those of other cochlear implanted patients. Patients who undergo simultaneous CI and labyrinthectomy may achieve similar hearing results but careful pre-operative counseling is needed.

Keywords: Meniere's disease, cochlear implant, quality of life, hearing loss, labyrinthectomy, vestibular neurectomy, quality of sound, matched-control evaluation

INTRODUCTION

Menière's disease (MD) is a disorder of the inner ear that causes auditory and vestibular symptoms. Different scientific societies consider that the diagnosis of definite MD relies on clinical criteria, which include: (i) two or more spontaneous episodes of vertigo (each lasting between 20 min and 12 h), (ii) with audiometrically documented low-to-medium frequency sensorineural hearing loss in one ear, defining the affected ear on at least one occasion before, during, or after one of the episodes of vertigo, (iii) fluctuating aural symptoms (hearing, tinnitus, and/or fullness) in the affected ear, and (iv) not better accounted for by another vestibular diagnosis (1).

Most patients will suffer different degrees of permanent hearing loss, and for 15-38% of patients with unilateral MD the hearing loss will progress to severe sensorineural hearing loss (2). The management of this condition aims to minimize vestibular symptoms while preserving hearing as much as possible. The majority of patients are controlled by lifestyle modifications and conservative medical treatments (Betahistine, diuretics, steroids, etc.). If unsuccessful, intratympanic injections of gentamicin or vestibular neurectomy can be proposed, with both procedures entailing the risk of hearing loss. Surgical labyrinthectomy is the most efficient treatment for vertigo attacks but this surgical procedure forfeits residual hearing (3, 4).

Advanced stages of MD are related to a decrease of subjective well-being and quality of life (QoL) due to vertigo, anxiety, limitation of life, and deafness, as well as communication problems that contribute to patients' isolation (5). The use of cochlear implantation (CI) in MD patients with bilateral severe to profound hearing loss is well-accepted, and the majority of studies show a significant improvement in post-implantation hearing and communication (6, 7). In specific cases, either simultaneous or sequential labyrinthectomy can be performed in addition to CI in order to treat both the hearing loss and the vertigo attacks (8, 9).

However, the impact of CI on the QoL of MD patients is still a controversial issue. Although an improvement of speech perception with the cochlear implant should improve social interactions and thus QoL, the few published papers about CI in MD include very small cohorts and lack specific QoL questionnaires for patients with hearing loss, which leads to uncertain results.

The purpose of this study was to review the audiological and QoL outcomes in MD patients who underwent CI, including general and specific questionnaires. A comparison of the results to a matched control group of postlingually implanted adults with similar characteristics was also performed. In addition, patients requiring ablative surgeries such as a labyrinthectomy (previous or simultaneously) or neurectomy were studied separately.

METHODS

Study Design

A retrospective study was conducted at the Department of Otorhinolaryngology, La Paz University Hospital, Madrid, Spain. The study procedures were approved by the university hospital's ethics committee (PI-3938). The patient database for adult subjects ($\geq$18 years) who had undergone CI between 1995 and 2019 was reviewed. Cochlear implant users who were diagnosed with MD according to the classification of Lopez-Escamez et al. (1) were selected and, from that selection, only patients with the diagnosis of "definitive Menière's disease" were included in the study for review of their medical records.

All patients underwent computed tomography (CT) and magnetic resonance imaging (MRI) to confirm cochlear patency and an intact auditory pathway prior to being considered for CI candidacy.

Assessment consisted of QoL questionnaires, and an audiological evaluation performed at last visit before surgery and at least 1 year after first fitting of the cochlear implant.

Cochlear Implant Users

The MD group consisted of 18 patients who fulfilled the above mentioned inclusion criteria. A control group of 18 postlingually implanted users with hearing loss due to other etiologies (not related to MD) was also selected from university hospital's database of cochlear implantees by the senior otologist (L.L.), who remained blinded to audiometric and QoL data. The control group was matched to the MD group for age at implantation, gender, and type of implant. Members of both groups were unilaterally implanted.

Medical records were reviewed for demographic information, as well as for pre- and post-operative audiometric data. Patient characteristics of both groups are displayed in **Table 1**. In the MD group, all patients presented stage 4 MD (the worst stage and is defined by a PTA $>$ 70 dB) in the implanted ear according to the classification scheme of the American Academy of Otolaryngology—Head and Neck Surgery (10). Eleven of these cases had bilateral MD and the other seven had unilateral MD and profound hearing loss due to other aethiologies on the contralateral ear. No comorbidities such as migraine,

TABLE 1 | Patients' characteristics.

		MD group	Control group	p
N		18	18	–
Age at implantation (years)†		59.7 ± 9.9	59.9 ± 9.9	0.946
Gender‡	Male	9 (50%)	9 (50%)	–
	Female	9 (50%)	9 (50%)	–
Implant‡	Nucleus 22M	1 (5.5%)	1 (5.5%)	–
	Nucleus 512	1 (5.5%)	1 (5.5%)	–
	Combi 40+	1 (5.5%)	1 (5.5%)	–
	Pulsar	3 (17%)	3 (17%)	–
	Sonata	8 (44.5%)	8 (17%)	–
	Concerto	4 (22%)	4 (17%)	–
Ablative surgery for MD‡	Simultaneous CI and labyrinthectomy	2 (11%)		
	Sequential CI and labyrinthectomy	2 (11%)		
	Previous retrosigmoid vestibular neurectomy	3 (16%)		
Hearing aid in the ear to be implanted‡		11 (61%)	15 (83%)	0.589 (Chi2)
Pre-op values in the ear to be implanted†	PTA4 (dB)	102.9 ± 27.2	121.6 ± 15.4	0.031*
	SDS (% disyllables)	22.2 ± 32.6	13.6 ± 20.4	0.606

†*Data are shown as mean ± standard deviation.*

‡*Data are shown as absolute numbers and relative frequencies (%).*

*Pre-op, preoperatively; PTA4, pure tone threshold average of 500, 1,000, 2,000, and 4,000 Hz; SDS, speech discrimination score. When no response was detected, 140 dB value was used. Control patients without MD were implanted within ± 2 years of a correspondingly matched patient with MD. *$p \leq 0.05$.*

autoimmune disorders, or genetic factors were observed in the bilateral MD patients.

In the present study, the majority of patients had no vertiginous episodes at the time of CI due to a remission of vestibular symptoms that is frequent in stage 4 of MD (8) or to previous ablative surgery. Retrosigmoid vestibular neurectomy had been performed in three cases (16%) on the ipsilateral implanted ear long before the CI and two patients (11%) have undergone sequential labyrinthectomy and CI. None of the patients with previous intratympanic gentamicin injection fulfilled the criteria for CI. Only two patients (11%) had frequent vertigo episodes and drop attacks which were resolved with simultaneous CI and labyrinthectomy, and another patient (5%) reported aural fluctuations without vertigo after an initial period of typical MD, that disappeared after CI. In the post-operative period, only patients with synchronic labyrinthectomy presented chronic imbalance and dizziness. MD patients didn't present more vestibular damage than other cochlear implant patients.

Two patients of the MD group required reimplantation: one of the patients for technology upgrade and the other due to electrode extrusion from the cochlea. No cochlea ossification was observed in the revision surgeries; reimplantation were uneventful.

Outcome Measurements

Audiometric and Speech Perception Testing

Audiometric evaluation was performed in an audiometric booth with double-wall and sound isolation. The two-channel Amplaid® audiometer (Amplifon, Milan, Italy) was used for testing. If a patient had better hearing in the non-implanted ear, this ear was masked during the evaluation to reduce the binaural benefit of the non-tested ear.

All subjects underwent the following tests: preoperatively, pure tone thresholds were measured under headphones at 125, 250, 500, 1,000, 2,000, 4,000, and 8,000 Hz, as well as the maximum Speech Discrimination Score (SDS, disyllabic words in silence). Postoperatively, warble tone measurements were evaluated in a free field condition at 250, 500, 1,000, 2,000, 4,000, and 6,000 Hz with the cochlear implant. The position of the patient was 1 m away from the loudspeakers at 0° azimuth, and patient was directly facing the speakers at all times during testing. Post-operative speech perception was assessed *via* a verbal perception test of disyllabic words in same condition of free field in quiet. A recorded standard Spanish-language speech test was used (11). The lists were administered in random order at 65 dB SPL. Subjects were seated 1 m away from the loudspeakers at 0° azimuth. Subjects were assessed at least 12 months after first fitting of their audio processor.

For purposes of the statistical analyses, we considered the mean PTA thresholds at 500, 1,000, 2,000, and 4,000 Hz (PTA4) (12).

Quality of Life

Subjective benefit in terms of QoL was assessed with the Spanish versions of three different self-reported questionnaires: the Nijmegen Cochlear Implant Questionnaire (NCIQ), Glasgow Benefit Inventory (GBI), and the Speech, Spatial and Qualities of Hearing Scale (SSQ_{12}). The $HISQUI_{19}$ was employed to verify the subjective quality of sound. All the tests were completed at least 12 months after first fitting (NCIQ was also filled in before surgery).

The validated Spanish version of the NCIQ was used to quantify health-related QoL in cochlear implant users (13). This questionnaire provides a measure of benefit that can be used to compare the status of the individual before and after surgery. The NCIQ has six subdomains: basic sound perception, advanced sound perception, speech production, self-esteem, activity, and social interactions. The answers to the questionnaire are provided on a five-point Likert scale, with items' scores ranging from 0 (very poor) to 100 (optimal). Scores for the subdomains were computed by adding together the 10-item scores of each subdomain and dividing by the number of completed items.

The GBI is a validated QoL questionnaire developed to assess the outcome of otorhinolaryngology interventions (14, 15). It is comprised of 18 questions and generates a scale from −100 (maximal detriment) to 0 (no change) to +100 (maximal benefit). These 18 questions can be divided into three subscales: a general sub-scale (12 questions), a social support subscale (3 questions), and a physical health subscale (3 questions), and the total score (Overall Benefit) is calculated by adding the scores of all questions. Therefore, the questionnaire assesses the patient's

TABLE 2 | Audiometric data.

	Pre-op		Post-op	
	PTA4 (dB HL)	Disyllables in quiet (%)	PTA4 (dB HL)	Disyllables in quiet (%)
MD group	103 ± 27	22 ± 33	38 ± 7	64 ± 25
Control group	122 ± 15	13 ± 20	37 ± 6	65 ± 18
p-value	0.031*	0.606	0.606	0.901

*Results are shown as mean ± standard deviation. Pre-op, preoperatively; Post-op, postoperatively; PTA4, pure tone threshold average of 500, 1,000, 2,000, and 4,000 Hz; if no response could be elicited at the PTA, 140 dB value was used. *indicates significant difference, $p \leq 0.05$.*

perception at the overall success of surgery, and of the influence of CI on their phychological, social, and physical functioning.

The SSQ_{12} is a 12-item questionnaire that quantifies the severity of hearing disability. Individual items are answered on a 10-point Likert scale: the higher the score, the less disability experienced. The total SSQ_{12} score (max 10, min 0) is the average of item scores (16).

The validated Spanish language version of the $HISQUI_{19}$ was used in this study (17). The $HISQUI_{19}$ is a 19-item questionnaire that measures quality of sound in everyday communication situations (e.g., listening to unfamiliar speakers, understanding speech on the phone, radio or TV, etc.). Each item is answered according to frequency on a seven-point scale, the endpoints of which are "always" (seven points) and "never" (one point). The total $HISQUI_{19}$ score is the sum of the individual item scores. Total scores are assigned a qualitative level of quality of sound: 110–133 is "very good"; 90–109 is "good," 60–89 is "moderate," 30–59 is "poor," and <29 is "very poor."

Data Analysis

Demographic characteristics and outcome measures are shown as absolute (*n*) and relative frequencies (%) and, if appropriate, as mean plus standard deviation (± SD) and range.

The Mann-Whitney *U*-test and unpaired *t*-test (when the data are normally distributed; normal distribution was assessed by the Kolmogorov-Smirnov test and Q-Q plots) were used to examine the difference between both groups' objective and subjective measures, and to explore if any difference was found in terms of type of surgery in the MD group. Use of hearing aid in the ear to be implanted was compared between the MD group and control group with the chi-squared test.

Correlation analysis using Pearson's coefficient or Kendall's tau (normally or non-normally distributed data, respectively) was performed to evaluate the relationship between the patients' scores on the questionnaires, audiometric data, speech perception test results, and age at implantation.

Missing data and the response option "not applicable" were treated as missing values. A level of $p \leq 0.05$ (two-tailed) was considered significant. Statistical analyses were processed in the SPSS software package v24.0 (IBM Corp., Armonk, NY, USA).

RESULTS

Audiometric and Speech Perception Testing

The MD group had significantly better PTA4 before surgery than the control group, although no significant difference was found in terms of pre-operative speech discrimination. For both groups, there was a significant improvement in PTA4 from pre-operative testing to post-operative testing ($p < 0.001$). All patients' post-CI performances improved significantly in comparison to their pre-CI speech perception capabilities (**Table 2**). All patients from both groups were daily users of the CI.

Quality of Life

All patients except one patient in the MD group, who refused to participate in the QoL study, answered the questionnaires.

NCIQ

The NCIQ evaluation showed a significant improvement in all subdomains after surgery for both groups (all $p < 0.05$). No significant intergroup differences between mean scores for any of the specified subdomains were found pre- or postoperatively (**Table 3**). The greatest benefit was observed in basic sound perception: scores improved 50 points in the MD group and 48 points in the control group.

GBI

The mean GBI scores of both groups are shown in **Table 4**. Even though no significant difference was observed between the two groups, the minimum value of the range was negative in all GBI subscales for the MD group. Only two patients reported negative GBI scores. These two patients underwent CI and labyrinthectomy simultaneously.

SSQ_{12}

The total SSQ_{12} score was 4.0 ± 1.5 in the MD group and 5.0 ± 2.0 in the control group. No significant difference was noted between the two groups, although the control group rated the degree of self-perceived hearing disability slightly higher than the MD group.

$HISQUI_{19}$

Regarding the quality of sound, the $HISQUI_{19}$ questionnaire showed no significant difference between the MD group (79 ± 26) and the control group (70 ± 24). Both groups rated the quality of sound as "moderate."

Relations Between Variables

The impact of variables such as age, sex, previous use of a hearing aid in the implanted ear, type of implant, and post-operative audiometric outcomes on the QoL were analyzed. Patients in the MD group who had previous hearing aid use performed better than those with no previous use of a hearing aid in the pre-operative subdomain "advanced sound perception" of the NCIQ ($p = 0.027$). Patients in the control group with previous hearing aid use performed significantly better than non-users on the $HISQUI_{19}$ ($p = 0.027$). The hearing aid users referred to their subjective quality of sound with the CI as "moderate"

TABLE 3 | NCIQ scores.

	Basic sound perception		Advanced sound perception		Speech production		Self-esteem		Activity		Social interaction	
	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post
MD group	24 ± 25	74 ± 18	62 ± 23	77 ± 17	23 ± 28	61 ± 22	43 ± 16	65 ± 13	36 ± 26	67 ± 29	35 ± 23	59 ± 18
Control group	27 ± 19	75 ± 24	59 ± 20	78 ± 20	31 ± 21	56 ± 24	47 ± 19	68 ± 23	43 ± 26	76 ± 25	37 ± 21	67 ± 21
p-value	0.463	0.613	0.757	0.613	0.163	0.546	0.660	0.546	0.369	0.287	0.732	0.134

Results are shown as means ± standard deviation of pre- and post-operative assessments.

TABLE 4 | GBI scores by group.

GBI	MD group	Control group	*p*-value
Overall benefit	27 (−31 to 67)	29 (3 to 69)	0.807
General health	38 (−50 to 88)	40 (0 to 83)	0.732
Social benefit	12 (−17 to 50)	13 (0 to 67)	0.987
Physical health	0 (−17 to 50)	5 (0 to 50)	0.303

Results are shown as mean (range).

(mean = 85 points) compared to the "poor" subjective quality of sound reported by the non-users (mean = 50 points). No other significant associations were found.

In the MD group, no significant difference was found between patients who underwent sequential or simultaneous labyrinthectomy with CI and those who underwent only CI in terms of auditory or QoL results. Nevertheless, despite no significant difference, when observing the results of the two simultaneous labyrinthectomy patients, a negative impact in the GBI, a post-operative decrease in some subdomains of the NCIQ and a poor benefit with the cochlear implant in the $HISQUI_{19}$ was observed. The three patients who had undergone a previous neurectomy performed significantly better than patients who underwent only CI in the subdomains "basic sound perception" ($p = 0.038$), "speech" ($p = 0.005$), "activity" ($p = 0.038$), and "social interactions" ($p = 0.038$) of the NCIQ. No other significant differences were observed within the MD group.

DISCUSSION

General Results

CI is gaining acceptance in the population who has MD when hearing improvement cannot be achieved with hearing aids. This retrospective study demonstrates that patients with MD can undergo CI surgery with similar expectations to those of other adults with postlingual severe to profound hearing loss, because significant improvement can be observed in both audiological and QoL measures in the great majority of cases.

Difference in Pre-operative Hearing and in Hearing Aid Use Between MD and Control Groups

Hearing fluctuation is common in patients with MD, who frequently report reduced dynamic range and speech perception, which leads to difficulties in hearing aid fitting (18). In this study, the use of hearing aids in the ear to be implanted was less common in the group of patients with MD, and only 61% used a hearing aid before CI vs. 83% of the control group. Interestingly, these hearing aid users of the control group reported a significantly better quality of sound with their cochlear implant when compared to non-hearing aid users of the control group.

In this study, patients with MD had better pre-operative hearing (PTA4 = 103 dB HL) than patients with severe to profound hearing loss due to other pathologies (PTA4 = 122 dB HL), the difference being significant. This disparity has been reported in previous studies (19) and suggests that patients with MD, as a group, may undergo CI with relatively higher levels of residual hearing compared to that of the "general" population of cochlear implantees, since the residual hearing of patients with MD is not useful for communication even with a careful hearing aid fitting. Nevertheless, all patients who underwent CI in this study had bilateral severe to profound hearing loss (defined as PTA > 70 dB HL) with no benefit with hearing aids after a trial period, in accordance to the NICE guidance (20) and the American Academy of Otolaryngology—Head and Neck Surgery (10).

Post-operative Hearing With the Cochlear Implant Is Similar in the MD and Control Groups

The hearing outcome of CI in patients with MD has been a matter of debate. McRackan et al. (21) evaluated 21 patients with MD and postulated that these patients achieve worse word recognition scores after CI than their standard sample of 178 adult implant recipients without MD, probably due to a nitric oxide-induced neuronal injury produced by endolymphatic hydrops. On the other hand, Chen et al. (22) suggested that extensive neuronal degeneration in the spiral ganglion is unusual in patients with MD, even in those undergoing a labyrinthectomy. Our post-operative speech discrimination results in quiet in patients with MD were similar to those of the control group, which supports the latter theory. In a similar way, Prenzler et al. (6) compared 27 implanted patients who have MD to a matched control group of cochlear implant users and concluded that speech understanding in the MD group was at least equal to that of "general population" CI recipients. Kocharyan et al. (23) also found no auditory differences between 24 patients with MD and an aged-matched control group of adults with cochlear implants.

TABLE 5 | QoL publications on patients with MD who undergo CI.

References	Number of MD patients	Control group	Bilateral/unilateral MD	Ablative surgery on implanted ear	QoL test(s)	Results	Observations
Kurz et al. (24)	8	No	4 Bilateral 4 Unilateral	No	MDOQ	QoL improvement ($p = 0.035$)	
Fife et al. (25)	10	No	Not specified	No	HHI MDFLS	Post-op HHI = 55.8 ± 25.3. Similar pre-op and post-op QoL according to MDFLS ($p = 0.52$).	No pre-op HHI.
Vermeire et al. (26)	7	No	Not specified	No	NCIQ	No pre-op evaluation. Poorer post-op NCIQ results than other studies.	
Perkins et al. (27)	3	No	Unilateral SSD	Labyrinthectomy	SSQ APHAB	Improvement in subjective QoL in all three patients.	No statistical analysis.
Mick et al. (28)	20	Yes $N = 20$	17 Bilateral 3 Unilateral	Not specified	SF36 ($N = 12$)	Improvement in functioning domain ($p = 0.046$) and trend to improvement in social functioning domain ($p = 0.08$).	Did not compare QoL to control group (only eight matched pairs completed QoL tests).
Canzi et al. (29)	4	No	4 Unilateral	Translabyrinthine neurectomy	MDPOSI	All parameters improved post-op.	No statistical analysis.
Present study	18	Yes $N = 18$	11 Bilateral 7 Unilateral	3 Previous vestibular neurectomy 2 Simultaneous labyrinthectomy 2 Sequential labyrinthectomy	NCIQ GBI SSQ_{12} $HISQUI_{19}$	Post-op improvement with similar results to control group.	

MD, Menière disease; QoL, quality of life; Pre-op. pre-operative; Post-op, post-operative; SSD, single side deafness; MDOQ: Menière disease outcome questionnaire; HHI, hearing handicap inventory; MDFLS, Menière disease-functional level scale; NCIQ, Nijmegen Cochlear Implant Questionnaire; SSQ, Speech, Spatial and Qualities of Hearing Scale; APHAB, abbreviated profile of hearing aid benefit; SF36, 36-item Short Form; MDPOSI, Menière disease patient oriented severity index; GBI, Glasgow Benefit Inventory; HISQUI, Hearing Implant Sound Quality Index.

Post-operative QoL and Quality of Sound

Regarding QoL and quality of sound, the majority of patients from both groups reported a positive benefit following CI. This improvement was seen in the GBI with an overall benefit of +27 (MD group) and +29 (control group) after surgery. Similarly, there was a significant improvement in all the subdomains of the NCIQ (especially in "basic sound perception," "speech production," and "activity") after CI and a moderate self-perception of auditory disability in the SSQ_{12}. When the subjective quality of sound was studied, patients with MD and those in the control group reported a mean score of 79 and 70, respectively, which indicates a moderate benefit for both groups.

To the best of the authors' knowledge, this study represents the most extensive QoL research in MD patients who underwent CI (**Table 5**).

In most published studies, there is great variability in the QoL tests used and, more importantly, no specific hearing QoL tools were used. Vermeire et al. (26) assessed the QoL of seven unilateral CI patients with MD using the post-operative NCIQ. The authors reported mean values for the following subdomains: "basic sound perception" 46, "advanced sound perception" 34, "speech production" 64, "self-esteem" 51, "activity" 47, and "social interaction" of 46 points. All subdomain scores are lower than those found in the present study as well as in previous studies that used the NCIQ (13, 30).

The patients with MD in the present study showed similar health-related QoL than the control group with results similar to those reported in the literature (13, 30). However, in agreement with Vermeire et al., no correlation between speech perception and QoL was found (26). According to previous studies, the subdomain "advanced sound perception" seemed to be the most susceptible to the effect of CI, because it was correlated more often with the objective measures (13). As commonly stated in QoL studies, we think that other parameters such as the patient's capacity to perceive benefit could influence the correlation between the objective measures and some of the subdomains.

Labyrinthectomy and CI

Surgical labyrinthectomy may be offered for patients with persistent MD who fail more conservative treatments. It can provide a definitive solution for vertigo attacks but

this destructive technique involves the removal of the ipsilateral vestibular receptors and the cochlear function. The decompensation of the system can generate a sensation of dizziness and imbalance that it should be compensated by central, visual and proprioceptive mechanisms. But the final lost of residual hearing add an extra disability not always expected by patients and cochlear implantation becomes the only alternative.

Controversy also exists about performing simultaneous or sequential CI. On one hand, performing both surgeries at the same time reduces the duration of deafness, while avoiding the hypothetical risk of cochlea obliteration (9). On the other hand, although residual hearing in these patients is usually not useful, some prefer to delay CI until they are used to living with no residual hearing following the labyrinthectomy (31).

QoL parameters can be affect by audiological parameters and their own experience of vestibular function that it is difficult to quantify and it can be multifactorial.

The two patients who had simultaneous labyrinthectomy and CI in this study reported poor results in their quality of life and quality of sound. The patients were a 57-year-old man with unilateral MD and severe hearing loss following a radical cavity long time before, and a 70-year-old woman with bilateral MD. Both presented severe sensorineural hearing loss with contralateral anacusis. Following extensive and careful counseling, both decided to undergo simultaneous labyrinthectomy and CI due to frequent vertigo and drop attacks, as well as fluctuating hearing loss and aural symptoms on the ear to be implanted. Neither of the two patients reported any further attacks of vertigo after surgery, but they did report problems with their balance and dizziness attributed to poor compensation. After a two-year follow-up neither of the two patients had any more complaints about vestibular symptoms. Interestingly, the post-operative PTA4 and percentage of discrimination of disyllables in quiet of these particular patients were 33 dB and 75%, and 36 dB and 67%, respectively. They had better auditory results than both the whole MD group and the control group. In our opinion, this discrepancy between very good auditory results and the poor self-reported QoL scores may be explained by both the impact of bilateral vestibular hypofunction and the loss of residual hearing. In agreement with Hansen et al. (32), we believe that patients with pre-operative residual hearing and simultaneous labyrinthectomy and CI "will have not experienced the full consequences of deafness and may not fully appreciate the benefit of the cochlear implant for rehabilitation of the new deficit."

On the other hand, two other patients had undergone labyrinthectomy 3 and 8 years before ipsilateral CI. As mentioned earlier, the possibility of cochlear obliteration must be considered following inner ear procedures. Both patients, a 68-year-old man with unilateral MD and a 65-year-old woman with bilateral MD, had good auditory and QoL results, similar to other cochlear implantees. Normal cochlear fluid signal was observed in the pre-operative MRI, and no difficulties were observed during electrode insertion. However, the patient with unilateral MD presented electrode extrusion 1 year after CI, but no difficulties were noted for reintroduction of the electrode array.

Limited evidence exists to date on cochlear obliteration after labyrinthectomy. Charlett and Biggs (31) reported that a third of patients who had undergone translabyrinthine removal of acoustic neuroma presented a partial or total obliteration of the cochlea in the MRI after 36 months of follow-up (range 4–185 months). The authors concluded that the time elapsed since the labyrinthectomy did not seem to be a predictor for obliteration. Nevertheless, Sargent et al. (33) conducted a study of 18 patients who had undergone transmastoid labyrinthectomy without internal auditory canal dissection. Results suggested that patency of the cochlea after surgery does not result in a loss of cochlear fluid signal in MRI, probably because there is no vascular compromise as in tumor removal. In agreement with these studies, Mukherjee et al. (8) found no MRI alterations or intraoperative difficulties in three patients undergoing CI and sequential labyrinthectomy, despite 2, 9, and 11 years of delay in surgery. In agreement with these results, Osborn et al. (34) reported that a woman who underwent CI, had good audiological outcomes and improved QoL 21 years after labyrinthectomy for MD treatment.

Vestibular Neurectomy and CI

Three patients in the study presented here had undergone a previous retrosigmoid vestibular neurectomy on the ipsilateral implanted ear 15, 19, and 25 years earlier. All of them initially preserved their hearing thresholds, but a slow progressive decline in hearing thresholds led to severe to profound hearing loss. No MRI alterations were observed, and no complications were found during CI. These three patients had similar auditory results to the rest of the MD group, but they performed better in the subdomains "basic sound perception" ($p = 0.038$), "speech" ($p = 0.005$), "activity" ($p = 0.038$), and "social interactions" ($p = 0.038$) in the NCIQ.

To the best of our knowledge, there are no published studies that report on CI after vestibular neurectomy for MD. Nowadays, retrosigmoid vestibular neurectomy is less frequently performed as an alternative for refractory vertigo, even though the success rate is very high (89–96%) (35, 36). Hearing preservation (within 10 dB of the pre-operative level) can be achieved in the majority of patients (36, 37).

Even when the associated QoL results should be taken with caution due to the small sample size, our study suggests that CI can be a good solution for patients with MD who undergo vestibular neurectomy when hearing cannot be preserved during surgery, or if there is a post-operative decrease in hearing.

Limitations

As most publications in this field, we report a retrospective study with a relatively small number of patients, which could limit the statistical significance of the results. Nevertheless, as shown in **Table 5**, to our knowledge, this is the only QoL study that includes QoL questionnaires that specifically focuses on cochlear implants and a matched control group.

Throughout the long follow-up of patients with MD, vestibular function was measured with different vestibular tests (including video head impulse test (vHIT), caloric and rotatory testing). However, due to the heterogeneity of tests conducted

among patients, as well as the known lack of correlation of many of the results with the clinical findings, we have not included this information in this paper. In patients with MD, a personalized approach is recommended, and treatment decisions are mainly based on the clinical findings, especially the frequency of vertigo, drop attacks, and hearing impairment (4).

CONCLUSION

This group of 18 patients with severe hearing loss and MD demonstrated excellent improvement in hearing and a significant QoL benefit after CI comparable to cochlear implant users with other conditions who were matched for demographic factors.

Delayed CI after transmastoid labyrinthectomy or retrosigmoid vestibular neurectomy can be performed and similar or better results can be expected as to those seen in other implanted patients. Delayed CI remains a viable treatment option when a normal cochlear fluid signal can be seen on T2-weighted MRI.

Patients undergoing simultaneous CI and labyrinthectomy may achieve similar hearing results as the population of cochlear implantees who did not require labyrinthectomy, but careful counseling is needed in this subset of patients.

DATA AVAILABILITY STATEMENT

The original contributions presented in the study are included in the article/supplementary material, further inquiries can be directed to the corresponding author/s.

ETHICS STATEMENT

The studies involving human participants were reviewed and approved by CEICC La Paz University Hospital. The patients/participants provided their written informed consent to participate in this study.

AUTHOR CONTRIBUTIONS

IS-C, MC, JM-P, JG, TM, JP, MP, and LL provided substantial contributions to the conception or design of the work or the interpretation of data for the work, worked on the draft or revised it critically for important intellectual content, and agreed on accountability for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. The final version was approved for publishing by all authors.

REFERENCES

1. Lopez-Escamez JA, Carey J, Chung WH, Goebel JA, Magnusson M, Mandalà M, et al. Diagnostic criteria for Menière's disease. *J Vestib Res.* (2015) 25:1-7. doi: 10.3233/VES-150549
2. Hoa M, Friedman RA, Fisher LM, Derebery MJ. Prognostic implications of and audiometric evidence for hearing fluctuation in Meniere's disease. *Laryngoscope.* (2015) 125:S1-12. doi: 10.1002/lary.25579
3. Magnan J, Özgirgin ON, Trabalzini F, Lacour M, Escamez AL, Magnusson M, et al. European position statement on diagnosis, and treatment of Meniere's disease. *J Int Adv Otol.* (2018) 14:317-21. doi: 10.5152/iao.2018.140818
4. Nevoux J, Barbara M, Dornhoffer J, Gibson W, Kitahara T, Darrouzet V. International consensus (ICON) on treatment of Ménière's disease. *Eur Ann Otorhinolaryngol Head Neck Dis.* (2018) 135:S29-32. doi: 10.1016/j.anorl.2017.12.006
5. Levo H, Stephens D, Poe D, Kentala E, Pyykkö I. Use of ICF in assessing the effects of Meniere's disorder on life. *Ann Otol Rhinol Laryngol.* (2010) 119:583-9. doi: 10.1177/000348941011900903
6. Prenzler NK, Bültmann E, Giourgas A, Steffens M, Salcher RB, Stolle S, et al. Cochlear implantation in patients with definite Meniere's disease. *Eur Arch Otorhinolaryngol.* (2017) 274:751-6. doi: 10.1007/s00405-016-4356-z
7. Masood MM, Farquhar DR, Brown KD, Pillsbury HC, King ER, O'Connell BP. Hearing preservation and speech outcomes after cochlear implantation in Meniere's disease. *Laryngoscope.* (2020) 130:2874-8. doi: 10.1002/lary.28470
8. Mukherjee P, Eykamp K, Brown D, Curthoys I, Flanagan S, Biggs N, et al. Cochlear implantation in Ménière's disease with and without labyrinthectomy. *Otol Neurotol.* (2017) 38:192-8. doi: 10.1097/MAO.0000000000001278
9. Doobe G, Ernst A, Ramalingam R, Mittmann P, Todt I. Simultaneous labyrinthectomy and cochlear implantation for patients with single-sided Ménière's disease and profound sensorineural hearing loss. *Biomed Res Int.* (2015) 2015:457318. doi: 10.1155/2015/457318
10. Committee on Hearing and Equilibrium guidelines for the diagnosis and evaluation of therapy in Menière's disease. American Academy of Otolaryngology-Head and Neck Foundation, Inc. *Otolaryngol Head Neck Surg.* (1995) 113:181-5. doi: 10.1016/S0194-5998(95)70102-8
11. Cárdenas MR, Marrero V. *Cuaderno de Logoaudiometría, cuadernos de la Universidad de Educación a Distancia.* Simancas, editor. Madrid (1994). p. 184.
12. Zwartenkot, J. Auditory Implants in Otology. Active Middle Ear Implants and Direct Acoustic Cochlear Stimulation: Indications and Outcome. Enschede: Ipskamp Printing (2017). p. 203.
13. Sanchez-Cuadrado I, Gavilan J, Perez-Mora R, Muñoz E, Lassaletta L. Reliability and validity of the Nijmegen Cochlear Implant Questionnaire in Spanish. *Eur Arch Otorhinolaryngol.* (2015) 272:1621-5. doi: 10.1007/s00405-014-2983-9
14. Robinson K, Gatehouse S, Browning GG. Measuring patient benefit from otorhinolaryngological surgery and therapy. *Ann Otol Rhinol Laryngol.* (1996) 105:415-22. doi: 10.1177/000348949610500601
15. Sanchez-Cuadrado I, Lassaletta L, Perez-Mora R, Muñoz E, Gavilan J. Reliability and validity of the Spanish Glasgow Benefit Inventory after cochlear implant surgery in adults. *Eur Arch Otorhinolaryngol.* (2015) 272:333-6. doi: 10.1007/s00405-013-2844-y
16. Noble W, Jensen NS, Naylor G, Bhullar N, Akeroyd MA. A short form of the speech, spatial and qualities of hearing scale suitable for clinical use: the SSQ12. *Int J Audiol.* (2013) 52:409-12. doi: 10.3109/14992027.2013.781278
17. Calvino M, Gavilán J, Sánchez-Cuadrado I, Pérez-Mora RM, Muñoz E, Díez-Sebastián J, et al. Using the HISQUI29 to assess the sound quality levels of Spanish adults with unilateral cochlear implants and no contralateral hearing. *Eur Arch Otorhinolaryngol.* (2016) 273:2343-53. doi: 10.1007/s00405-015-3789-0
18. Valente M, Mispagel K, Valente LM, Hullar T. Problems and solutions for fitting amplification to patients with Ménière's disease. *J Am Acad Audiol.* (2006) 17:6-15. doi: 10.3766/jaaa.17.1.2
19. Manrique-Huarte R, Calavia D, Alvarez-Gomez L, Huarte A, Perez-Fernández N, Manrique M. Vestibulo-cochlear function after cochlear implantation in patients with Meniere's disease. *J Int Adv Otol.* (2018) 14:18-21. doi: 10.5152/iao.2018.4536
20. NICE Technology Appraisal Guidance 166. *Cochlear Implants for Children and Adults With Severe to Profound Deafness.* (2009). Available online at: https://www.nice.org.uk/guidance/TA166 (accessed September 25, 2020).

21. McRackan TR, Gifford RH, Kahue CN, Dwyer R, Labadie RF, Wanna GB, et al. Cochlear implantation in Ménière's disease patients. *Otol Neurotol.* (2014) 35:421-5. doi: 10.1097/MAO.0000000000000247
22. Chen DA, Linthicum FH Jr, Rizer FM. Cochlear histopathology in the labyrinthectomized ear: implications for cochlear implantation. *Laryngoscope.* (1988) 98:1170-2. doi: 10.1288/00005537-198811000-00004
23. Kocharyan A, Mark ME, Ascha MS, Murray GS, Manzoor NF, Megerian C, et al. Cochlear implantation in patients with Menière's disease: does disease activity affect the outcome? *Otol Neurotol.* (2020) 41:1296-304. doi: 10.1097/MAO.0000000000002750
24. Kurz A, Auinger A, Arnoldner C. Long-term vertigo control after cochlear implantation in patients with end-stage Menière's disease: a retrospective questionnaire-based cross-sectional study. *Wien Klin Wochenschr.* (2020) 132:521-5. doi: 10.1007/s00508-019-01605-9
25. Fife TA, Lewis MP, May JS, Oliver ER. Cochlear implantation in Ménière's disease. *JAMA Otolaryngol Head Neck Surg.* (2014) 140:535-9. doi: 10.1001/jamaoto.2014.550
26. Vermeire K, Van Yper L, De Vel E, Dhooge I. Is cochlear implantation an effective treatment for Menière's disease? *B-ENT.* (2014) 10:93-8.
27. Perkins E, Rooth M, Dillon M, Brown K. Simultaneous labyrinthectomy and cochlear implantation in unilateral Meniere's disease. *Laryngoscope Investig Otolaryngol.* (2018) 3:225-30. doi: 10.1002/lio2.163
28. Mick P, Amoodi H, Arnoldner C, Shipp D, Friesen L, Lin V, et al. Cochlear implantation in patients with advanced Ménière's disease. *Otol Neurotol.* (2014) 35:1172-8. doi: 10.1097/MAO.0000000000000202
29. Canzi P, Manfrin M, Perotti M, Aprile F, Quaglieri S, Rebecchi E, et al. Translabyrinthine vestibular neurectomy and simultaneous cochlear implant for Ménière's disease. *Acta Neurochir (Wien).* (2017) 159:123-30. doi: 10.1007/s00701-016-2996-9
30. Cohen SM, Labadie RF, Dietrich MS, Haynes DS. Quality of life in hearing-impaired adults: the role of cochlear implants and hearing aids. *Otolaryngol Head Neck Surg.* (2004) 131:413-22. doi: 10.1016/j.otohns.2004.03.026
31. Charlett SD, Biggs N. The prevalence of cochlear obliteration after labyrinthectomy using magnetic resonance imaging and the implications for cochlear implantation. *Otol Neurotol.* (2015) 36:1328-30. doi: 10.1097/MAO.0000000000000803
32. Hansen MR, Gantz BJ, Dunn C. Outcomes after cochlear implantation for patients with single-sided deafness, including those with recalcitrant Ménière's disease. *Otol Neurotol.* (2013) 34:1681-7. doi: 10.1097/MAO.0000000000000102
33. Sargent EW, Liao E, Gonda RL Jr. Cochlear patency after transmastoid labyrinthectomy for Ménière's syndrome. *Otol Neurotol.* (2016) 37:937-9. doi: 10.1097/MAO.0000000000001105
34. Osborn HA, Yeung R, Lin VY. Delayed cochlear implantation after surgical labyrinthectomy. *J Laryngol Otol.* (2012) 126:63-5. doi: 10.1017/S0022215111002374
35. Magnan J, Bremond G, Chays A, Gignac D, Florence A. Vestibular neurotomy by retrosigmoid approach: technique, indications, and results. *Am J Otol.* (1991) 12:101-4.
36. Pareschi R, Destito D, Falco Raucci A, Righini S, Colombo S. Posterior fossa vestibular neurotomy as primary surgical treatment of Menière's disease: a re-evaluation. *J Laryngol Otol.* (2002) 116:593-6. doi: 10.1258/00222150260171560
37. Lemnos L, Aubry K, Moreau JJ, Caire F, Salle H. Postoperative compensation after neurotomy in Meniere's disease: retrospective study of 15 cases. *Neurochirurgie.* (2019) 65:20-6. doi: 10.1016/j.neuchi.2018.11.002

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Saccades Matter: Reduced Need for Caloric Testing of Cochlear Implant Candidates by Joint Analysis of v-HIT Gain and Corrective Saccades

Constanza Fuentealba Bassaletti[1], *Babette F. van Esch*[1], *Jeroen J. Briaire*[1], *Peter Paul G. van Benthem*[1], *Erik F. Hensen*[1] *and Johan H. M. Frijns*[1,2]*

[1] Department of Otorhinolaryngology and Head and Neck Surgery, Leiden University Medical Center, Leiden, Netherlands, [2] Leiden Institute for Brain and Cognition, Leiden, Netherlands

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***Correspondence:**
Johan H. M. Frijns
j.h.m.frijns@lumc.nl

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Objectives: Video head impulse test (v-HIT) is a quick, non-invasive and relatively cheap test to evaluate vestibular function compared to the caloric test. The latter is, however, needed to decide on the optimal side to perform cochlear implantation to avoid the risk on inducing a bilateral vestibular areflexia. This study evaluates the effectiveness of using the v-HIT to select cochlear implant (CI) candidates who require subsequent caloric testing before implantation, in that way reducing costs and patient burden at the same time.

Study Design: Retrospective study using clinical data from 83 adult CI-candidates, between 2015 and 2020 at the Leiden University Medical Center.

Materials and Methods: We used the v-HIT mean gain, MinGain_LR, the gain asymmetry (GA) and a newly defined parameter, MGS (Minimal Gain & Saccades) as different models to detect the group of patients that would need the caloric test to decide on the ear of implantation. The continuous model MGS was defined as the MinGain_LR, except for the cases with normal gain (both sides $\geq$0.8) where no corrective saccades were present. In the latter case MGS was defined to be 1.0 (the ideal gain value).

Results: The receiver operating characteristics curve showed a very good diagnostic accuracy with and area under the curve (AUC) of 0.81 for the model MGS. The v-HIT mean gain, the minimal gain and GA had a lower diagnostic capacity with an AUC of 0.70, 0.72, and 0.73, respectively. Using MGS, caloric testing could be avoided in 38 cases (a reduction of 46%), with a test sensitivity of 0.9 (i.e., missing 3 of 28 cases).

Conclusions: The newly developed model MGS balances the sensitivity and specificity of the v-HIT better than the more commonly evaluated parameters such as mean gain, MinGain_LR and GA. Therefore, taking the presence of corrective saccades into account in the evaluation of the v-HIT gain can considerably reduce the proportion of CI-candidates requiring additional caloric testing.

Keywords: sensorineural hearing loss, cochlear implant, cochlear implantation, candidacy criteria, vestibular outcome, caloric test, v-HIT, vestibular areflexia

INTRODUCTION

The cochlear implant (CI) presents an option of treatment for people with sensorineural hearing loss (SNHL) who benefit insufficiently from hearing aids. In many countries, including the Netherlands, only one CI per patient is reimbursed in the adult population. Unfortunately, there is currently no consensus on cochlear implantation criteria with respect to selecting the side of the primary implantation in bilateral SNHL (1–3).

In bilateral SNHL, the question whether the "worse" or the "better" hearing ear should be implanted is still under debate (3, 4). Some centers advise to implant the better hearing ear to obtain the best outcome from the implanted ear. This is based on the observed outcome when implantation was performed in ears with a shorter duration of deafness (4). Other centers, including ours, hesitate to give up hearing in the better hearing ear because of the risk of compromising a patient's communication abilities in case of a poor outcome of CI (5). The additional advantage of implanting the worst hearing ear is that there is more room for improvement with CI (6, 7).

Although it is questioned whether the vestibular state should play a significant role in the decision on the side of the implantation, West et al. showed that vestibulopathy was present in 25% of the pre-operative CI-candidates (8). This underscores the relevance of the vestibular evaluation as a part of the criteria for the selection of CI-candidates in order to prevent inducing bilateral vestibular areflexia. Therefore, it is often decided to select the better hearing ear for cochlear implantation if this ear has a vestibular areflexia and the only residual vestibular function is present in the contralateral ear.

Caloric testing is the gold standard to distinguish between vestibular areflexia and hyporeflexia (9), using a non-physiological stimulus but allowing for an ear-by-ear assessment, which is relevant in the context of the choice of CI side. However, it is relatively time consuming and places a considerable burden on the patients. In contrast, the video head impulse test (v-HIT), a non-invasive test to evaluate vestibular function, uses a physiological stimulus (i.e., head movements) and is relatively quick, cheap and less bothersome to patients compared to the caloric test. Classically, the vestibular-ocular reflex (VOR) gain is the main parameter to consider in order to classify vestibular dysfunction (9–12), and some researchers have suggested that the parameter of VOR asymmetry can be correlated with the canal paresis score (9). However, several studies have advocated the use of corrective saccades for this purpose, considering this phenomenon an indicator of a vestibular lesion (13–15). Therefore, one can argue that it is important to consider and analyze the previously mentioned v-HIT parameters to correctly classify a semicircular canal (SCC) dysfunction. This study evaluates the effectiveness of using the v-HIT to reduce costs and patient burden by selecting CI-candidates who do not require caloric testing before implantation.

MATERIALS AND METHODS

This is a retrospective cohort study comprising a complete review of CI data at Leiden University Medical Center (LUMC). We have examined the records of all 354 adult CI-recipients (age at implantation >18 yrs), implanted between 2015 and 2020. Only patients with a complete pre-operative caloric test and v-HIT results were included. Exclusion criteria were bilateral implantation, incomplete or unreliable caloric test and v-HIT results. The vestibular evaluation with the v-HIT was introduced at the LUMC in 2015 and has been increasingly used. Up till recently, however, it was not the standard of care for all CI-candidates. This is one of the reasons for the final inclusion of 83 patients.

Subjects

The current study includes 83 patients (31 female, 37%), between 18 and 89 years of age at the time of the implantation (mean 60 yrs, SD (standard deviation) 13 yrs). The duration of deafness varied between 1 and 70 years (mean 20;02 yrs, SD 18;07 yrs). Bilateral SNHL was the diagnosis for 82 patients, and one patient had bilateral severe mixed hearing loss. Sixty-five patients had post-lingual deafness on the right ear, and sixty-six on the left ear. There were five patients with missing data on this matter. Data on the etiology of the hearing loss are summarized in **Table 1**. The CI was implanted in 42 candidates on the right side, and in 41 candidates on the left side. During the intake, all patients were asked whether they experienced vestibular symptoms. Forty-three patients had vestibular complaints, viz. imbalance (26.5%), dizziness (15.7%), vertigo (14.5%), imbalance in the dark (10.8%), oscillopsia (7.2%), vomiting (2.4%), falls (2.4%), light-headedness (2.4%). The other 40 patients did not exhibit vestibular symptoms.

Caloric Test

The bithermal caloric testing, using cool and warm water at 30 and 44°C, respectively, was performed to provoke vestibular responses in both ears. The patient was in supine position with its head inclined at 30 degrees to the horizontal to bring the horizontal semicircular canal into the vertical plane. The eye movements were recorded with VNG system (Vestlab 7.0®, Otometrics, Germany). The caloric responses were measured in terms of the maximum slow-phase velocity (SPV) of the nystagmus in degrees per second. The canal paresis (CP) or unilateral weakness (UW) and directional preponderance (DP) were quantified according to the Jongkees formula in percentages (16). Caloric test results were considered abnormal if the unilateral weakness was ≥22%, the directional preponderance was ≥25% or the SPV was below 15°/s for each ear (9, 17). Vestibular areflexia was defined as a complete absence of caloric responses. The bilateral vestibulopathy was determined by a SPV below 6°/s in all four traces (warm right, warm left, cold right, and cold left). The outcomes were carefully reviewed and analyzed by three specialists within LUMC. A group of 28 patients was identified in which the caloric test results played a decisive role in selecting the optimal side for cochlear implantation.

Video Head Impulse Test

The video head impulse test (v-HIT) of horizontal canal function was measured using the commercial video oculography system

TABLE 1 | Etiology of hearing loss per ear.

Etiology	Ear	Frequency (%)
Idiopathic acquired	Left	65 (78.3)
	Right	61 (73.5)
Idiopathic congenital	Left	9 (10.8)
	Right	9 (10.8)
Ménière's disease	Left	0
	Right	5 (6)
Otosclerosis	Left	3 (3.6)
	Right	2 (2.4)
Rubella	Left	1 (1.2)
	Right	1 (1.2)
Birth asphyxia	Left	1 (1.2)
	Right	1 (1.2)
Usher syndrome	Left	1 (1.2)
	Right	1 (1.2)
Meningitis	Left	1 (1.2)
	Right	1 (1.2)
Premature birth	Left	1 (1.2)
	Right	1 (1.2)
DFN8	Left	1 (1.2)
	Right	1 (1.2)
Total	Left	83 (100)
	Right	83 (100)

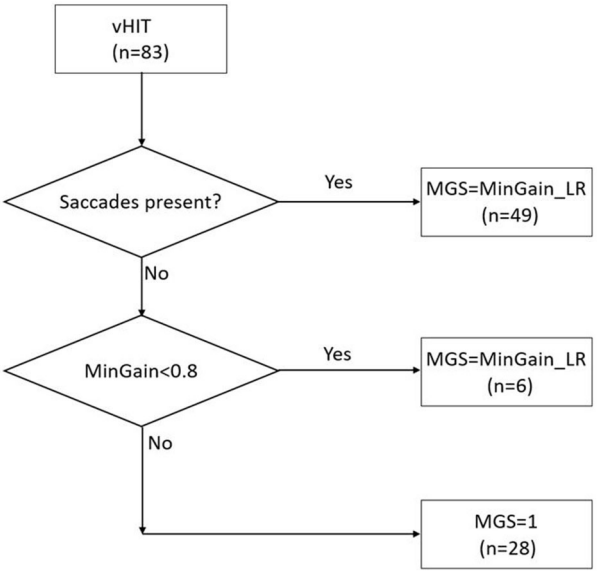

FIGURE 1 | The MGS (minimal gain & saccades) value is calculated based on the combination of the presence of saccades in the v-HIT and MinGain_LR, the lower of the two values of the v-HIT gain to the left and right. The numbers between brackets indicate the number of patients in the various categories in the present study sample.

(ICS Impulse System, GN Otometrics, Denmark). During the test, the patients wore goggles with a built-in video camera that recorded real time eye movements. Before starting the test, a calibration was performed to ensure accurate recordings. Patients were tested while sitting upright in a lighted room with an eye level target at a minimum of 1 meter in front of them. They were asked to stare at the fixed target and minimize blinking, while the evaluator performed sharp and fast head rotations, delivered randomly to left and right. Horizontal v-HIT results were deemed acceptable when the peak head velocity reached 150–200°/s. The corrective saccades were traced as a delayed eye movement during (covert saccades) or after (overt saccades) the head movement. The constant presence of covert or overt catch-up saccades was considered as indicator of VOR abnormality. It turned out that 23 out of the 28 patients requiring a caloric test were in the group with corrective saccades. The VOR gain was calculated by the software as the ratio of peak slow phase eye velocity to peak head velocity (18, 19). In line with the literature, we defined a cut-off value of 0.8 for the v-HIT gain indicating an abnormal horizontal VOR (9, 20, 21).

In order to be able to analyze the data with receiver operating characteristics (ROC) curves (see section **Statistical Analysis**), the v-HIT outcomes were used as a continuous variable. We used the v-HIT mean gain, minimal gain of both ears and the gain asymmetry (GA) as different models to select the group of patients that would require the caloric test to decide the side of implantation. In addition, we wanted to make use of the abovementioned observation that the vast majority of CI-candidates requiring caloric testing exhibit corrective saccades, and to combine it with the intuitive parameter of at least unilateral low gain, i.e., minimal gain of left and right ear (MinGain_LR). The presence of saccades was checked visually by two authors (CFB and BFE) independently, disagreement was resolved with a consensus discussion. In fact, we had three groups of patients: (a) 49 cases with corrective saccades (irrespective of the gain), (b) 28 cases with normal gain ($\geq$0.8) and no saccades, and (c) six cases with abnormal gain ($<$0.8) without saccades. Therefore, we introduced the continuous model MGS (Minimal Gain & Saccades). MGS is defined as MinGain_LR, the lower of the two values of the v-HIT gain to the left and right, except for the cases with normal gain (both sides $\geq$0.8) where no corrective saccades were present (group b). In the latter case, MGS was defined to be 1.0 (the ideal gain value). This is further illustrated in **Figure 1**.

Statistical Analysis

We performed descriptive statistics for categorical variables, including sex, age, hearing loss etiology by means of the IBM SPSS Statistics v.25. Means and SDs were calculated for age and duration of deafness.

First, we evaluated to what extent the side with vestibulopathy or areflexia found with the caloric test result corresponded with an abnormal horizontal angular VOR as found with the v-HIT. Differences between groups were assessed by means of cross-tabulation and analyzed using the Chi-square test. A p-value $<$0.05 was considered significant. Positive predictive value (PPV), negative predictive value (NPV), sensitivity and specificity

and their 95% confidence interval (CoIn) were calculated with the online software of MedCalc (available at www.medcalc.org).

More importantly, ROC curves were constructed to analyze the sensitivity, specificity and area under the curve (AUC) values for the various v-HIT parameters. An ROC curve is a graphical plot that is commonly used to analyze a test's ability to discriminate between a subject with and without a disease (22). In this study such ROC curves were used to evaluate to which extent the various v-HIT parameters (also called models) can be used to determine whether a CI-candidate needs additional caloric testing to decide on the side of implantation. The sensitivity in this curve (vertical axis) indicates the proportion of candidates requiring calorics that is detected by the test ("true positive rate"). The horizontal axis denotes the "false positive rate," also known as "1-specificity" shows the fraction of cases that would undergo caloric testing despite the fact that they don't need it. The v-HIT mean gain, MinGain_LR, the GA and the MGS were used as continuous variables in this analysis, for which the optimal cut-off points can be determined. The analysis also included the construction of the curve showing the trade-off between increasing the sensitivity and the number of CI-candidates who need additional caloric testing.

RESULTS

Caloric test showed abnormal results in 28 out of 83 patients (34%). The mean UW was 26% (SD 25%) and the mean DP was 21% (SD 23%). Complete bilateral areflexia was found in 4 (14%) of the patients and asymmetrical hypofunction in 24 patients (86%). Twelve patients had hypofunction in both the left and the right side. All but one patient (who had a left gain of 0.76 and right gain of 0.75) with bilateral low gain in the v-HIT also had bilateral areflexia in the caloric test.

The v-HIT gain was abnormal in 20 (24%) out of 83 patients. The v-HIT results showed a mean gain of 0.87 (SD 0.16; Range 0.11–1.15) to the left and 0.94 (SD 0.22; Range 0.05–1.36) to the right. In total 20 patients had a VOR gain below 0.8, of which six did not exhibit corrective saccades. Of the remaining patients with a VOR gain below 0.8, eight had just overt saccades and six had both overt and covert saccades. Eight patients had a normal VOR gain and presence of corrective saccades.

Data of caloric testing and v-HIT results per patient is represented in **Supplementary Digital Content 1**.

Table 2 directly compares the v-HIT outcomes with the caloric test results in a classical way. As explained in the Methods section, caloric test results were considered abnormal if the unilateral weakness was ≥22%, the directional preponderance was ≥25% or the SPV was below 15°/s for at least one ear, while a v-HIT was considered to show vestibular dysfunction if the mean VOR gain was <0.8. It turned out that the v-HIT, used in this way to predict an abnormal caloric test, had a positive predictive value (PPV) of 65% (95% CoIn: 46–81%), a negative predictive value (NPV) of 76% (95% CoIn: 69–82%), a sensitivity of 46 % (95% CoIn: 28–66%) and a specificity of 87% (95% CoIn: 76–95%).

TABLE 2 | Results of the caloric testing and the v-HIT with an horizontal VOR gain cut-off value of <0.8.

v-HIT	Caloric test*		Total
	Abnormal	Normal	
Gain < 0.8	13	7	**20**
Gain ≥ 0.8	15	48	**63**
Total	**28**	**55**	**83**

Sensitivity was 46% (95% CoIn: 28–66%), specificity 87 % (95% CoIn: 76–95%), positive predictive value (PPV) 65% (95% CoIn: 46–81%), negative predictive value (NPV) 76% (95% CoIn: 69–82%).

**For abnormal caloric test, cut-off values were a UW ≥22%, DP ≥25% and/or a SPV <15°/s for each ear.*

Figure 2 shows the ROC curves, which quantify the trade-off between true positives and false positives when deciding whether a CI-candidate will need additional caloric testing on the basis of v-HIT outcomes. The cut-off values of v-HIT mean gain, MinGain_LR, the GA and the MGS were continuously varied as described in the Methods section.

The ROC curve for the v-HIT mean gain had an AUC of 0.70 (95% CoIn 0.57–0.82), which means that for this commonly used variable the model has a poor-to-moderate diagnostic capacity. For MinGain_LR, the AUC was 0.72 (95% CoIn 0.60–0.84), which represents a good diagnostic capacity. If we select the common cut-off point of 0.8, the sensitivity is 49% and the specificity is 87%. When the sensitivity is increased to 80% (cut-off point at 0.93), the specificity decreases to 47%. In case of selecting a sensitivity of 90% (cut-off point at 0.99), the specificity is lowered to 27%. The percentage of GA between the left and right ear had an AUC of 0.73 (95% CoIn 0.61–0.85), also representing a good diagnostic capacity. A sensitivity of 80% was associated with a specificity of 48%, and reached for the cut-off point GA = 7.7. Ninety percent sensitivity was reached for the cut-off point of 4.5 for GA, with a specificity of just 25%. The newly designed parameter MGS, had an AUC of 0.81 (95% CoIn 0.71–0.91), representing a very good diagnostic accuracy for identifying subjects needing caloric testing. When we selected a cut-off point of 0.8 for MGS, this resulted in a 87% specificity and we found a sensitivity of 49%. For a sensitivity of 80%, the cut-off point for MGS is 0.94, with a specificity of 76%. If we want to improve the sensitivity up to 90% (i.e., missing just 10% of cases requiring caloric testing) the cut-off value of MGS is 1, and the specificity decreases to 62%.

Figure 3 shows the trade-off between the desired sensitivity and the percentage reduction of patients undergoing caloric tests (horizontal axis) if MGS, the best test parameter, is used. The vertical axis denotes the "false negative rate" (1-sensitivity), i.e., the fraction of CI-candidates requiring caloric testing, but not undergoing it. The asterisks indicate the points on the curve, representing the abovementioned cut-off points of MGS (0.8, 0.94, and 1.0). From this analysis it became clear that the latter cut-off value, associated with a sensitivity of 90% resulted in a reduction of the number of patients needing to undergo caloric testing by 46%.

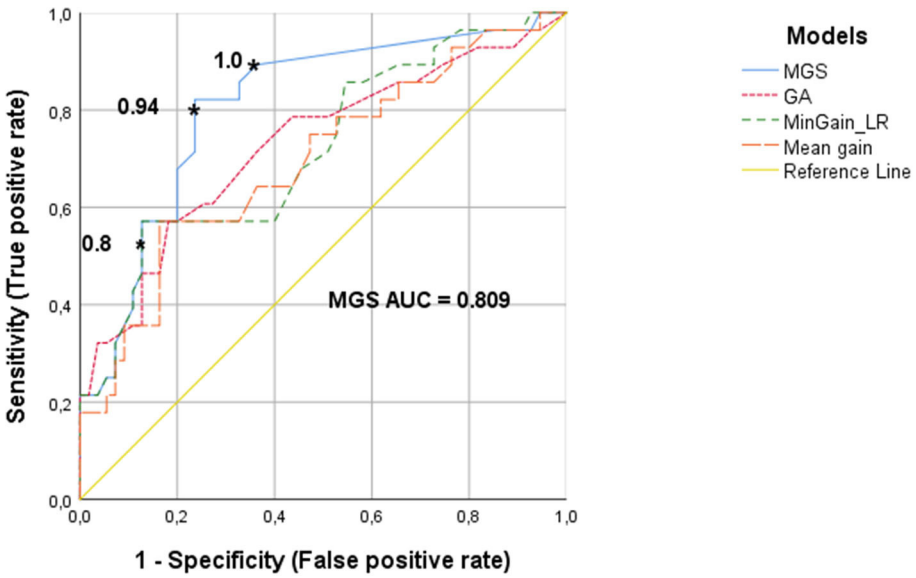

FIGURE 2 | ROC curves of the v-HIT for determining the need for an additional caloric test, using the parameters MGS (minimal gain & saccades), GA (gain asymmetry), MinGain_LR and mean gain. The asterisks show the cut-off values for the MGS parameter. The cut-off point of 0.8 resulted in 87% specificity and 49% sensitivity. The value 0.94 has a specificity of 76 and 80% sensitivity. The cut-off value of 1 has a specificity of 62% with a sensitivity of 90%.

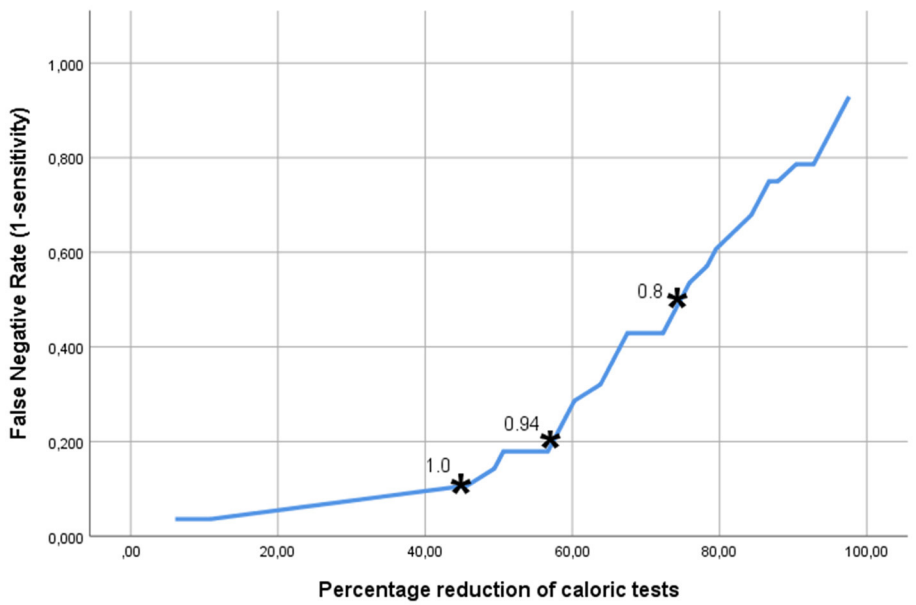

FIGURE 3 | The trade-off between the accepted fraction of CI-candidates requiring caloric testing, but not undergoing it, and the reduction in the number of the caloric tests, which can be achieved if the MGS (minimal gain & saccades) is used as discriminating parameter. The asterisks indicate the points on the curve representing the MGS cut-off points 0.8, 0.9, and 1.0. The latter cut-off value, associated with a sensitivity of 90% resulted in a reduction of the number of patients in need of caloric testing by 46%.

DISCUSSION

Key Findings

In this retrospective study, our aim was to evaluate the effectiveness of the v-HIT to select CI-candidates who require caloric testing before the implantation in order to use this information as part of the selection criteria, thereby avoiding the induction of bilateral vestibular areflexia. The v-HIT conveys different parameters that reflect the VOR function. Usually,

the gain is used to identify the lesion side and magnitude of dysfunction (10–12). In our study we analyzed the mean gain, MinGain_LR, the GA and the MGS (a novel combination of gain and/or presence of corrective saccades) to identify the cases with abnormal caloric function. The AUC of 0.81 found for the MGS parameter, indicates a very good accuracy of this model. Further analysis (**Figure 3**) indicated that one can dispense of almost half of the caloric tests with false negative rate of 10% (i.e., missing 10% of the CI-candidates that need caloric testing) if the vestibular assessment is started with a v-HIT evaluation based on the MGS. The ROC curves analysis for the v-HIT mean gain, MinGain_LR and GA showed a lower AUC. Therefore, the MGS model was identified as the one that better balances the true positive and the false positive rate for predicting the necessity of a further caloric test in CI-candidates.

It is possible to observe and analyze different parameters of the v-HIT, however the average gain of the VOR is one of the variables that is classically chosen to decide the vestibular hypofunction side (10–12). In our data set we could confirm other authors' findings (17, 21, 23) with respect to sensitivity and specificity of the v-HIT gain compared to the caloric test as the golden standard: When using the cut-off value of v-HIT gain <0.8 to classify vestibular hypofunction, we found a PPV of 65%, a NPV of 76%, a sensitivity of 46% and a specificity of 87%, which is in line with the literature.

Comparison With Other Studies

To our knowledge this is the first study that included the presence of corrective saccades in the analysis to determine if further caloric testing is necessary in CI-candidates. Such corrective saccades will occur when the VOR is insufficient to keep the gaze on the target, i.e., move the eyes at the same velocity of the head movement. Thus, the brainstem will compensate by generating corrective saccades to adjust the eyes back to the earth-fixed target (24, 25). Their presence could indicate an abnormality of the VOR or that vestibular compensation is taking place, as demonstrated in previous studies, which underscore the relevance of considering the corrective saccade as a variable that denotes SCC dysfunction, besides the gain value (13–15, 26, 27).

Janky et al. characterized saccades in a control group and then compared these data to subjects with vestibular loss (14). Their analysis showed that a combined gain value <0.78 with a corrective saccade frequency $>81.89\%$ resulted in a 90% specificity and 78.8% sensitivity, with an overall correct classification rate of 84.6%, compared with the v-HIT gain value alone. They suggested that the presence of repeatable saccades could indicate a VOR deficit, regardless the gain value, indicating v-HIT abnormality. In our study, the MGS model was obtained with a formula that included the presence of corrective saccades, even if the gain was normal (>0.8), see **Figure 1**. With 87% our specificity was similar to Janky et al., but the sensitivity was 49% with a cut-off value of 0.8 in the ROC curve. This difference can be explained by the methodology used. In their study, Janky et al. analyzed the first corrective saccade based on his frequency, peak velocity and latency, where in our sample with CI-candidates we classified the corrective saccades as present or absent. Also, it is relevant to mention that Janky et al. studied the value of corrective saccades in a group of patients to diagnose vestibular loss, which is different from our aim that was to use the v-HIT parameters to specifically identify CI-candidates who need additional caloric testing.

Other studies reported the presence of corrective saccades and normal VOR gain values in subjects after CI surgery (13, 28). The authors postulated that the corrective saccades may represent a partial dysfunction of the VOR and that the gain by itself might not reflect all the physiologic changes after a CI surgery, which affects the vestibular function.

In the field of otoneurology, several studies have been comparing the caloric test and the v-HIT performance to show their predictive values as a diagnostic tool. Moreover, many researchers and clinicians have wondered whether it is necessary to use both tests. However, we must remember that the v-HIT evaluates the VOR at a high frequency of stimulation, >5 Hz, during a physiological head movement, while the caloric test evaluates the vestibular system at a low frequency, 0.003 Hz, during a non-physiological ear irrigation. As a result, both tests provide complementary information (9).

We noticed a high specificity and moderate sensitivity of the v-HIT gain using the caloric testing as a reference. Similar outcomes were presented in previous studies when comparing both vestibular tests (17, 21, 23, 29, 30). However, the study of Aalling et al. (29) showed a higher PPV of 90% compared with our PPV of 65%. This could be explained by the fact that their study evaluated all 6 semicircular canals, whereas we evaluated only the 2 horizontal semicircular canals, making their assessment more accurate. The other studies did not mention PPV or NPV (17, 21, 23, 30). Beynon et al. (17) made a correlation between the severity of the caloric hyporeflexia and a higher true positive rate; of those patients with complete canal areflexia, 87% (21 out of 24) had a positive v-HIT result. That is also shown in our study, but to a lower scale (75%; 3 out of 4 patients).

Other studies (31, 32) reported different sensitivity and specificity values. This could be explained because they used a different cut-off point to classify the caloric hypofunction, viz., an absolute value of UW 25% (31). In Bartolomeo et al. (32) study, the higher sensitivity of 100% in the v-HIT was found when the caloric hypofunction was $\geq 62.5\%$. Their mean caloric vestibular deficit in a vestibular neuritis population was $78.7 \pm 21.24\%$, which is considerably higher than our population of CI-candidates ($26 \pm 25\%$). This fact might explain the substantial difference in sensitivity. In our study, the presence of a value of $\geq 22\%$ UW, $\geq 25\%$ DP or a $<15°/s$ SPV, classifies the result of a caloric test as abnormal. In that respect, our classification is more refined than the aforementioned studies in identifying vestibular dysfunctions.

A previous study on v-HIT normalization with 50 healthy subjects found that 100% of the subjects had a GA below 8% (20). However, this is not the value being used in the clinical practice. Clinicians usually consider GA to be normal between 0 and 13% (9). Although the use of the GA is not universally used to classify a patient with vestibular dysfunction, we have decided to include this parameter due to his comparability with the canal paresis score from the caloric test (9).

Strengths of the Study

Based on our results, corrective saccades (as taken into account with the MGS parameter) have added value for interpreting the VOR in CI-candidates. The saccades can show subtleties in the VOR function, providing objective evidence of changes in SCC function that sometimes the v-HIT gain alone will not explain completely. It turned out that using just the gain value as a main parameter could guide us into an overestimation of the vestibular function of the subject. Moreover, the present study showed that by using the MGS to include the presence of corrective saccades in the analysis, the v-HIT -contrary to expectations based upon classical parameters- is effective to select CI-candidates who will require caloric testing before surgery, reducing patients burden and costs.

Limitations of the Study

It is important to be mindful of the limitations of this study in order to interpret study results. This a retrospective cohort study based on the information retrieved from the files of CI-candidates, and not patients who specifically complained about vestibular symptoms like in most studies. Although CI-candidates were exactly the population we had in mind for the research question, one has to consider the presence of selection bias when trying to generalize the outcomes, e.g., to a specific population with vestibular dysfunction. In this context it is relevant to mention that 33.7% of the CI-candidates had a vestibular hypofunction as measured by means of the caloric test.

As explained in the introduction, the vestibular evaluation with the v-HIT was not a standard of care for the population of CI-candidates in our center until recently. As a result, only 23% (83 out of 354) of the CI-candidates in the period 2015–2020 had a complete vestibular assessment, including caloric testing and v-HIT, allowing them to be included in this study.

Another limitation to take into account is that the MGS does not reflect a per ear analysis. However, the test characteristics for v-HIT gain per ear turned out to be even poorer when identifying the patients who need calorics. Therefore, these scores cannot be used in clinical practice to directly diagnose the best side of implantation since the side with the most prominent vestibular loss is not identified. Thus, we could not predict the side of the hypofunction as a caloric test could do, but the data allowed to decide whether an additional caloric test is warranted in a particular CI-candidate.

Clinical Applications

Although the classic analysis considers the v-HIT gain value as the main VOR status parameter, we strongly advise to also consider the corrective saccades as an additional parameter when classifying a vestibular dysfunction. Using the v-HIT (with MGS as the main parameter) at the beginning of the vestibular evaluation of CI-candidates, and more importantly before the caloric test, could help us to eliminate almost 50% of the caloric assessments, by finding the cases that do not need caloric testing to identify the side with the vestibular hypofunction. As a result, starting with the v-HIT could optimize both the evaluation time per patient (31) and the invasiveness of the diagnostic trajectory. However, it is necessary to have a group of experienced professionals who are able to correctly identify the presence of corrective saccades, despite the presence of artifacts in the v-HIT trace.

CONCLUSION

The v-HIT can help to more efficiently decide which side to implant with minimal risk of inducing bilateral vestibular areflexia. Adding the presence of corrective saccades to the evaluation of the v-HIT gain improves the diagnostic power of the v-HIT to determine which CI-candidates need additional caloric testing to detect nuanced differences in case of a significant vestibular loss, which the v-HIT is unable to predict by itself. The newly developed model MGS balances the sensitivity and specificity of the v-HIT better than the more commonly evaluated parameters such as mean gain, MinGain_LR and GA.

DATA AVAILABILITY STATEMENT

The raw data supporting the conclusions of this article will be made available by the authors, without undue reservation.

ETHICS STATEMENT

The studies involving human participants were reviewed and approved by LUMC LDD G21.007. Written informed consent for participation was not required for this study in accordance with the national legislation and the institutional requirements.

AUTHOR CONTRIBUTIONS

JF was responsible for the research idea. JF, JB, BE, CF, and EH were responsible for the study design. CF, BE, and JB for data extraction and statistical analysis. CF, BE, JB, JF, EH, and PB for draft writing and critical revision. All authors contributed to the article and approved the submitted version.

SUPPLEMENTARY MATERIAL

The Supplementary Material for this article can be found online at: https://www.frontiersin.org/articles/10.3389/fneur.2021.676812/full#supplementary-material

REFERENCES

1. Firszt JB, Holden LK, Reeder RM, Cowdrey L, King S. Cochlear implantation in adults with asymmetric hearing loss. *Ear Hear.* (2012) 33:521–33. doi: 10.1097/AUD.0b013e31824b9dfc
2. Varadarajan VV, Sydlowski SA, Li MM, Anne S, Adunka OF. Evolving criteria for adult and pediatric cochlear implantation. *Ear Nose Throat J.* (2021) 100:31–7. doi: 10.1177/0145561320947258
3. Group UKCIS. Criteria of candidacy for unilateral cochlear implantation in postlingually deafened adults I: theory and measures of effectiveness.

Ear Hear. (2004) 25:310–35. doi: 10.1097/01.AUD.0000134549.48718.53
4. Chen JMSD, Al-Abidi A, Ng A, Nedzelski J. Does choosing the worse ear for cochlear implantation affect outcome? *Otol Neurotol.* (2001) 22:335–9. doi: 10.1097/00129492-200105000-00011
5. Buchman CA, Gifford RH, Haynes DS, Lenarz T, O'Donoghue G, Adunka O, et al. Unilateral cochlear implants for severe, profound, or moderate sloping to profound bilateral sensorineural hearing loss: a systematic review and consensus statements. *JAMA Otolaryngol Head Neck Surg.* (2020) 146:942–53. doi: 10.1001/jamaoto.2020.0998
6. Snel-Bongers J, Netten AP, Boermans PBM, Rotteveel LJC, Briaire JJ, Frijns JHM. Evidence-based inclusion criteria for cochlear implantation in patients with postlingual deafness. *Ear Hear.* (2018) 39:1008–14. doi: 10.1097/AUD.0000000000000568
7. Lustig LR, Yeagle J, Niparko JK, Minor LB. Cochlear implantation in patients with bilateral Meniere's syndrome. *Otol Neurotol.* (2003) 24:397–403. doi: 10.1097/00129492-200305000-00009
8. West N, Klokker M, Caye-Thomasen P. Vestibular screening before cochlear implantation: clinical implications and challenges in 409 cochlear implant recipients. *Otol Neurotol.* (2020) 42:e137–44. doi: 10.1097/MAO.0000000000002898
9. Jacobson GPS, *N. T. Balance Function Assessment and Management*. 2nd ed. San Diego, CA (2016). p. 905.
10. Yip CW, Glaser M, Frenzel C, Bayer O, Strupp M. Comparison of the bedside head-impulse test with the video head-impulse test in a clinical practice setting: a prospective study of 500 outpatients. *Front Neurol.* (2016) 7:58. doi: 10.3389/fneur.2016.00058
11. Manzari L, Burgess AM, MacDougall HG, Bradshaw AP, Curthoys IS. Rapid fluctuations in dynamic semicircular canal function in early Meniere's disease. *Eur Arch Otorhinolaryngol.* (2011) 268:637–9. doi: 10.1007/s00405-010-1442-5
12. Macdougall HG, McGarvie LA, Halmagyi GM, Curthoys IS, Weber KP. The video Head Impulse Test (vHIT) detects vertical semicircular canal dysfunction. *PLoS ONE.* (2013) 8:e61488. doi: 10.1371/journal.pone.0061488
13. Batuecas-Caletrio A, Klumpp M, Santacruz-Ruiz S, Benito Gonzalez F, Gonzalez Sanchez E, Arriaga M. Vestibular function in cochlear implantation: correlating objectiveness and subjectiveness. *Laryngoscope.* (2015) 125:2371–5. doi: 10.1002/lary.25299
14. Janky KL, Patterson J, Shepard N, Thomas M, Barin K, Creutz T, et al. Video Head Impulse Test (vHIT): the role of corrective saccades in identifying patients with vestibular loss. *Otol Neurotol.* (2018) 39:467–73. doi: 10.1097/MAO.0000000000001751
15. Bharadwaj S, Petrak MR, Bahner CM, Sharp LE, Mosey-Claycomb SF, Matsuoka AJ. Diagnostic value of refixation saccades in the Video Head Impulse Test (vHIT) in unilateral definite Meniere's disease. *Acta Otolaryngol.* (2020) 140:537–43. doi: 10.1080/00016489.2020.1744720
16. British Society of Audiology. *Recommended Procedure for the Caloric test British Society*. Berkshire: British Society of Audiology (2015).
17. Beynon GJ, Jani P, Baguley DM. A clinical evaluation of head impulse testing. *Clin Otolaryngol.* (1998) 23:117–22. doi: 10.1046/j.1365-2273.1998.00112.x
18. McGarvie LA, Curthoys IS, MacDougall HG, Halmagyi GM. What does the dissociation between the results of video head impulse versus caloric testing reveal about the vestibular dysfunction in Meniere's disease? *Acta Otolaryngol.* (2015) 135:859–65. doi: 10.3109/00016489.2015.1015606
19. Hamilton SS, Zhou G, Brodsky JR. Video head impulse testing (VHIT) in the pediatric population. *Int J Pediatr Otorhinolaryngol.* (2015) 79:1283–7. doi: 10.1016/j.ijporl.2015.05.033
20. Yang CJ, Lee JY, Kang BC, Lee S, Yoo MH, Park HJ. Quantitative analysis of gains and catch-up saccades on video head impulse testing by age in normal subjects. *Clin Otolaryngol.* (2015) 41:532–8. doi: 10.1111/coa.12558
21. Moreira Bittar RS, Sersuo Sato E, Silva-Ribeiro DJ, Oiticica J, Mezzalira R, Tsuji RK, et al. Caloric test and video head impulse test sensitivity as vestibular impairment predictors before cochlear implant surgery. *Clinics (São Paulo).* (2019) 74:e786. doi: 10.6061/clinics/2019/e786
22. Lasko TA, Bhagwat JG, Zou KH, Ohno-Machado L. The use of receiver operating characteristic curves in biomedical informatics. *J Biomed Inform.* (2005) 38:404–15. doi: 10.1016/j.jbi.2005.02.008
23. van Esch BF, Nobel-Hoff A, van Benthem PPP, van der Zaag H, Bruintjes T. Determining vestibular hypofunction: start with the video-head impulse test. *Eur Arch Otorhinolaryngol.* (2016) 273:3733–9. doi: 10.1007/s00405-016-4055-9
24. Halmagyi GM, Curthoys IS. A clinical sign of canal paresis. *Arch Neurol.* (1988) 45:737–9. doi: 10.1001/archneur.1988.00520310043015
25. Weber KP, Aw ST, Todd MJ, McGarvie LA, Halmagyi GM. Head impulse test in unilateral vestibular loss. *Neurology.* (2008) 70:454–63. doi: 10.1212/01.wnl.0000299117.48935.2e
26. Yang CJ, Cha EH, Park JW, Kang BC, Yoo MH, Kang WS, et al. Diagnostic value of gains and corrective saccades in video head impulse test in vestibular neuritis. *Otolaryngol Head Neck Surg.* (2018) 159:347–53. doi: 10.1177/0194599818768218
27. West N, Klokker M, Caye-Thomasen P. Video head impulse test saccades and loss of cervical vestibular evoked myogenic potentials are late vestibular footprints of cochlear implantation. *J Vestib Res.* (2021) 31:61–7. doi: 10.3233/VES-190760
28. Korsager LE, Faber CE, Schmidt JH, Wanscher JH. Refixation saccades with normal gain values: a diagnostic problem in the video head impulse test: a case report. *Front Neurol.* (2017) 8:81. doi: 10.3389/fneur.2017.00081
29. Aalling M, Skals RK, Abrahamsen ER, Hougaard DD. Comparison of test results from two separate video head impulse test systems in a cohort of patients diagnosed with a unilateral vestibular schwannoma. *Eur Arch Otorhinolaryngol.* (2020) 277:3185–93. doi: 10.1007/s00405-020-06116-2
30. Bell SL, Barker F, Heselton H, MacKenzie E, Dewhurst D, Sanderson A. A study of the relationship between the video head impulse test and air calorics. *Eur Arch Otorhinolaryngol.* (2015) 272:1287–94. doi: 10.1007/s00405-014-3397-4
31. Rambold HA. Economic management of vertigo/dizziness disease in a county hospital: video-head-impulse test vs. *caloric irrigation*. *Eur Arch Otorhinolaryngol.* (2015) 272:2621–8. doi: 10.1007/s00405-014-3205-1
32. Bartolomeo M, Biboulet R, Pierre G, Mondain M, Uziel A, Venail F. Value of the video head impulse test in assessing vestibular deficits following vestibular neuritis. *Eur Arch Otorhinolaryngol.* (2014) 271:681–8. doi: 10.1007/s00405-013-2451-y

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Long-Term Vestibular Outcomes in Cochlear Implant Recipients

Kasper Møller Boje Rasmussen[1,2]*, *Niels West*[1,2], *Luchen Tian*[1] and *Per Cayé-Thomasen*[1,2]

[1] Department of Otorhinolaryngology Head and Neck Surgery and Audiology, Rigshospitalet, University Hospital of Copenhagen, Copenhagen, Denmark, [2] Faculty of Health and Medical Sciences, University of Copenhagen, Copenhagen, Denmark

Background: Vestibular dysfunction is likely the most common complication to cochlear implantation (CI) and may, in rare cases, result in persistent severe vertigo. Literature on long-term vestibular outcomes is scarce.

Objective: This paper aims to evaluate vestibular dysfunction before and after cochlear implantation, the long-term vestibular outcomes, and follows up on previous findings of 35 consecutive adult cochlear implantations evaluated by a battery of vestibular tests.

Methods: A prospective observational longitudinal cohort study was conducted on 35 CI recipients implanted between 2018 and 2019; last follow-up was conducted in 2021. At the CI work-up (T0) and two postoperative follow-ups (T1 and T2), 4 and 14 months following implantation, respectively, all patients had their vestibular function evaluated. Evaluation with a vestibular test battery, involving video head impulse test (vHIT), cervical vestibular evoked myogenic potentials (cVEMP), caloric irrigation test, and dizziness handicap inventory (DHI), were performed at all evaluations.

Results: vHIT testing showed that 3 of 35 ears had abnormal vHIT gain preoperatively, which increased insignificantly to 4 of 35 at the last follow-up ($p = 0.651$). The mean gain in implanted ears decreased insignificantly from 0.93 to 0.89 ($p = 0.164$) from T0 to T2. Preoperatively, 3 CI ears had correction saccades, which increased to 11 at T2 ($p = 0.017$). Mean unilateral weakness increased from 19 to 40% from T0 to T2 ($p < 0.005$), and the total number of patients with either hypofunctioning or areflexic semicircular canals increased significantly from 7 to 17 ($p < 0.005$). Twenty-nine percent of CI ears showed cVEMP responses at T0, which decreased to 14% ($p = 0.148$) at T2. DHI total mean scores increased slightly from 10.9 to 12.8 from T0 to T1 and remained at 13.0 at T2 ($p = 0.368$). DHI scores worsened in 6 of 27 patients and improved in 4 of 27 subjects from T0 to T2.

Conclusion: This study reports significant deterioration in vestibular function 14 months after cochlear implantation, in a wide range of vestibular tests. vHIT, caloric irrigation, and cVEMP all measured an overall worsening of vestibular function at short-term postoperative follow-up. No significant deterioration or improvement was measured at the last postoperative follow-up; thus, vestibular outcomes reached a plateau. Despite vestibular dysfunction, most of the patients report less or unchanged vestibular symptoms.

Keywords: cochlear implant, vestibular testing, dysfunction, vertigo, video head impulse test, cervical vestibular-evoked myogenic potentials, caloric irrigation test, dizziness handicap inventory

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***Correspondence:**
Kasper Møller Boje Rasmussen
kasper.moeller.boje.rasmussen@regionh.dk

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INTRODUCTION

Cochlear implantation (CI) is regarded as a safe and minimally invasive procedure due to its low prevalence of severe complications (<2%) (1). However, because of the proximity to the vestibular organs, there is a risk of mechanical damage to the labyrinth, saccule, or the horizontal semicircular canal presumably caused by cochleostomy and insertion of the implant electrode (2). Vestibular dysfunction is likely the most common complication to CI. Vertigo or disequilibrium accounts for 25–30% of complications and is usually transient and presents as mild to moderate postoperative dizziness or imbalance (1, 3–5). Some CI recipients experience prolonged and severe vertigo affecting daily and social activities and report lower quality of life (6, 7). These severe cases of postimplantation vertigo may in part be explained by preoperative vestibular dysfunction as a result of underlying inner ear pathology, leading to bilateral vestibular areflexia after implantation (8). It is of utmost importance to identify these patients before implantation, as patients with severe dizziness handicap may be at risk of social isolation, anxiety, and depression and falls and injuries.

Vestibular evaluation may be performed before CI potentially to reduce the risk of permanent vestibular dysfunction (9). No standard protocol for vestibular testing exists; however, the following tests are the most widely applied tests, but usually not represented all together (10): The video Head Impulse Test (vHIT) measures the vestibulo-ocular reflex (VOR) originating from the three semi-circular canals (horizontal, lateral, and posterior) (11), caloric irrigation tests the horizontal semi-circular canal and the inferior branch of the vestibular nerve, and cervical vestibular evoked myogenic potentials (cVEMP) tests the saccule and the inferior branch of the vestibular nerve (2); and the dizziness handicap inventory (DHI), a commonly used assessment tool for evaluation of quality of life in vestibular disorders (12). Previous studies apply various test strategies often resulting in contradictive findings (13–15).

Cochlear implantation can lead to vestibular impairment (16–20), and most frequently, the cVEMP and VOR are affected (13, 15, 21). Although vHIT combined with corrective saccades is a sensitive measure for detecting the impaired ear prior to implantation (16, 22), it has also been suggested that this test may be the least affected measure following implantation (10, 23). Excluding one of these tests may lead to an underestimation of vestibular affection after cochlear implantation (1, 10). Poor correlations between DHI scores and objectively measured outcomes are found in most studies, and in some studies, subjective improvement in self-perceived vertigo is indicated, despite objective vestibular deterioration (3, 13, 17, 24–26). Most of these studies urge for further research in long-term outcomes (27, 28).

We aim to evaluate long-term vestibular dysfunction after cochlear implantation, using a broad test battery including four vestibular test measures used in the clinical setting at our tertiary CI censer. Currently, all patients are subjected to vestibular examination, to guide our clinicians in the choice of treatment. We will report raw data on a prospective patient cohort and examine differences in vestibular test results at the short- and long-term postoperative follow-ups. The study therefore aims to provide important evidence on vestibular dysfunction after cochlear implantation and may show possible correlations between the subjective and objective outcome measures.

MATERIALS AND METHODS

Study Design

The study design was prospective and observational and included participants who met the following inclusion criteria: adult (>18 years) first time CI recipients having bilateral moderate to profound sensorineural hearing loss (SNHL) eligible for CI. Individuals who were unfit for participation due to blindness, language barriers, patient reluctancy, or poor cooperation were excluded. Recruitment took place between February 2018 and April 2019, and the last follow-ups were carried out in February 2021.

The round window surgical procedure was applied throughout the study and performed by a team of senior CI surgeons. Each participant was assessed thrice: before implantation (in this study, referred to as T0), participants underwent vHIT, caloric irrigation, and cVEMP and completed the DHI. This test battery was repeated at two postoperative follow-ups at ∼4 and 14 months after implantation, respectively (referred to as T1 and T2). All tests at all time points were performed by the same vestibular pathologist. The tests were performed with the CI turned on. No routine physiotherapy was performed postimplantation. However, patients experiencing marked dizziness were offered vestibular rehabilitation.

Video Head Impulse Test

Impulsive testing of the lateral semicircular canals was measured using the Eyebeams vHIT system (Interacoustics, Middelfart, Denmark) with lightweight vHIT goggles, to test bilateral vestibulo-ocular reflexes (VOR) (29). Prior to testing, calibration of the equipment was performed according to standard recommendations. Patients were instructed to sit in an upright position and fixate on a visual target in front of them. The vestibular pathologist, standing behind the patient, generated the head impulses by moving the patient's head abruptly and unpredictably in the horizontal plane ∼10–20° to each side with a range of peak head velocity between 150 and 300°/s. Any impulses outside this range were rejected by the software. Peak head velocities pre- and postimplantation were comparable. Head impulses were repeated 5–10 times each side until a satisfying result was recorded. The implant did not affect the placement of the vHIT strap or delivery method. Gain is calculated by the ratio of head velocity to eye velocity. vHIT gain results were considered abnormal if the gain was equal to or below 0.7. Gain asymmetry ratio (AR) was calculated by

$$GA = \left[\frac{G_{CL} - G_{CI}}{G_{CL} + G_{CI}}\right] \times 100 \quad (1)$$

where G_{CL} denotes contralateral ear mean gain, and G_{CI} denotes cochlear implant ear mean gain (30). Gain AR >8.5% is considered abnormal.

Bilateral vHIT gains were measured at 40, 60, and 80 ms; however, only 60 ms was analyzed. Catch-up saccades were recorded and were considered abnormal in the presence of consistent overt or covert correction saccades, which depended on the amplitude of the saccade as a qualitative measure. Saccades with corresponding normal vHIT gain values were also considered abnormal.

Caloric Irrigation

Low frequency testing of the lateral semicircular canals by caloric irrigation test was performed at standard caloric temperatures (30 and 44°C) by water stimulation (Aqua Stim, Interacoustics) and measured using videonystagmography (VNG). To improve patient communication, warm irrigations were performed before cold irrigations, and the worst hearing ear was tested first. Duration of the irrigations was 30 s, followed by a 60-s pause allowing eye monitoring. A 5-min pause between each irrigation was standard. Patients were denied visual input and performed alerting tasks to reduce central suppression during caloric testing. Slow phase velocity (SPV) was considered, and values below 25°/s were considered abnormal. Any outliers were excluded by the software. Unilateral weakness, a measure of afferent vestibular function loss, defined as partial (>25%, e.g., canal paresis) or complete (100%, e.g., unilateral areflexia), was calculated by the software using Jongkees formula.

Cervical Vestibular Evoked Myogenic Potential

Otolithic function was measured using the vestibulospinal reflex elicited in response to cVEMP. Prior to cVEMP testing, the test equipment (Eclipse, Interacoustics) controls for EMG activation. In-ear air-conducted sound stimuli (100 dBnHL tone bursts at 500 Hz) (31) were used, and the electrode monitoring the elicited myogenic response was placed on the sternocleidomastoid muscle. cVEMP responses with both P1 and N1 present were considered [dichotomous outcomes (+/–)]. We did not report on the cVEMP asymmetry ratio because of the high variability of results reported in the literature (23).

Dizziness Handicap Inventory

Preoperatively (T0) and at each of the two follow-ups (T1 and T2), patients completed the 25-item DHI, answering questions regarding perceived severity of vertigo and effects on quality of life (12). Patients rated each item with "yes," "sometimes," or "no," corresponding to 4, 2, and 0 points, respectively. The total DHI scores range from 0 (no self-reported symptoms) to 100 (severe self-reported symptoms). A score of 0–15 points corresponds to no handicap, 16–34 points corresponds to mild handicap, 35–52 points corresponds to moderate handicap, and 53–100 corresponds to severe handicap (20). Validity evidence of the DHI shows that an 11-point difference is considered significantly different between repeated measures (12).

Statistical Analysis

Statistical processing was carried out in SPSS (32), and graphs were processed with GraphPad Prism (33). Descriptive data were evaluated by number, mean, 95% confidence intervals, and percentage. Distribution normality was tested using boxplots and QQ plots. vHIT gain and SPV were normally distributed; vHIT gain AR, UW, and DHI scores were non-normally distributed. Saccades and cVEMP results are dichotomous data. Parametric data are analyzed using repeated measures linear mixed models with an unstructured covariance structure. Friedman test was applied on non-parametric data and Cochrane's Q test on dichotomous data, both designed to analyze repeated measures. Analyses were carried out to determine whether there was any statistically significant difference between preimplantation (T0) and postimplantation (T1 and T2). Spearman (r) correlation analysis was conducted when the significance of the relationships was tested. The significance level was a two-tailed $p < 0.05$.

TABLE 1 | Demographic characteristics of the 35 study patients.

Age	26–85 years (mean, 59)
Gender	16 female (46%), 19 male (54%)
Implanted side	17 left, 16 right, 2 bilateral
Type of implant	1 (3%) Advanced Bionics HiRes Ultra 3D SlimJ
	1 (3%) Advanced Bionics HiRes90K Midscale
	1 (3%) Advanced Bionics ULTRA 3D Midscale
	1 (3%) MEDel Flex 28 Synchrony
	21 (60%) Nucleus Cochlear CI522
	6 (17%) Nucleus Cochlear CI622
	4 (11%) Oticon Medical Zti EVO
Days after implantation	
T1	122 days, 69–222 (mean, range)
T2	406 days, 265–532 (mean, range)

RESULTS

Forty-three patients were initially included. Three patients later withdrew because of reluctancy due to coronavirus disease 2019 (COVID-19). Another five patients were excluded: one patient was explanted due to late-onset device infection, one moved abroad, one had deceased, and two had comorbidity that excluded them from the study. All participants received unilateral CI; two of these were consequentially implanted on the contralateral side. Data from both unilateral and bilateral CI recipients were included. **Table 1** shows demographic characteristics, **Table 2** reports raw data for the 35 patients, and **Table 3** summarizes the data.

Patients 3 and 16 (raw data represented in **Figure 1** and highlighted in **Table 1**) demonstrated clearly deteriorating vestibular function from T0 to T2. At baseline, they presented normal vHIT gains, normal vHIT gain asymmetry ratio, no saccades, and unilateral weakness lower than 25%. Patient 16 showed a positive cVEMP response at T0; however, patient 3 did not. At T2, both patients had a vHIT gain drop below 0.70 and vHIT gain asymmetry ratio above 8.5%. Both had developed corrective saccades, none of them had positive cVEMP responses at T2, and both had unilateral canal paresis (UW = 100%). Interestingly, patient 16 did not report any symptoms of vertigo in the DHI at T0 and T1, and patient 3 scored 28 at T0, which

TABLE 2 | Complete raw data set on all 35 patients.

ID	Hearing loss aetiology	vHIT gain						vHIT gain asymmetry ratio (%)			Saccades		cVEMP		SPV total			UW			DHI		
		CI ear			Non-CI ear						CI ear	Non-CI ear	CI ear	Non-CI ear									
		T0	T1	T2	T0	T1	T2	T0	T1	T2	T0/T1/T2	T0/T1/T2	T0/T1/T2	T0/T1/T2	T0	T1	T2	T0	T1	T2	T0	T1	T2
1	Ménière's disease	0.65	0.73	0.73	0.87	0.88	0.88	14.5	9.3	9.3	ov/0/ov	0/ov/0	NA/–/–	NA/–/–	NA	NA	46.6	NA	6	6	12	32	32
2	Otitis media	1.10	1.01	1.06	1.00	1.06	1.08	4.8	2.4	0.9	0/0/0	0/0/0	–/–/–	–/–/–	244.10	9.3	92.6	7	46	58	36	26	30
3	Otosclerosis	0.84	0.39	0.36	1.00	0.67	0.67	8.7	26.4	30.1	0/0/ov + cov	0/ov + cov/ov + cov	–/–/–	–/–/–	23.30	39.2	17.6	14	55	100	28	20	NA
4	Congenital (unknown aetiology)	0.86	1.00	0.86	0.94	0.95	0.95	4.4	2.6	5.0	0/0/0	0/0/0	+/+/+	+/+/+	121.10	108.2	109.6	22	21	24	0	0	0
5	Unknown	0.79	0.79	0.85	1.04	0.74	0.73	13.7	3.3	7.6	0/0/0	0/0/0	–/–/–	–/–/–	161.2	121.3	129.5	4	20	10	0	0	0
6	Unknown	1.13	0.81	0.76	0.94	1.05	0.89	9.2	12.9	7.9	0/0/ov	ov/ov/ov	–/–/–	–/–/–	82.0	27.4	29.5	6	60	76	0	38	52
7	Late-onset progressive hereditary	1.23	0.97	1.41	1.14	1.12	1.29	3.8	7.2	4.4	0/0/0	0/0/0	–/+/+	–/+/+	134.3	108.2	121.5	19	7	12	0	6	14
8	Superficial siderosis	0.55	0.45	0.43	0.57	0.65	0.41	1.8	18.2	2.4	ov/ov/ov	ov/ov/0	–/–/–	–/–/–	23.4	18.6	11.2	43	23	34	60	64	72
9	Late-onset progressive hereditary	0.93	0.77	0.73	0.87	0.96	0.88	3.3	11.0	9.3	0/0/0	0/0/0	–/–/–	–/–/–	84.8	61.8	78.0	40	30	23	0	0	0
10	Hereditary congenital	0.73	0.82	0.97	0.80	1.11	1.07	4.6	15.0	4.9	0/ov/0	0/0/0	–/–/–	–/–/–	95.7	69.2	69.9	19	100	83	0	0	0
11	Unknown	1.31	0.89	1.09	1.02	0.91	1.08	12.4	1.1	0.5	0/0/0	0/0/0	–/–/–	–/–/–	NA	65.3	50.0	NA	86	22	0	0	0
12	Unknown	1.05	1.02	1.10	1.14	1.07	1.02	4.1	2.4	3.8	0/0/0	0/0/0	–/–/–	–/–/–	118.5	92.5	98.4	14	29	22	0	6	0
13	Usher syndrome	0.95	0.81	0.93	0.89	0.88	0.94	3.3	4.1	0.5	0/0/0	0/0/0	–/–/–	–/–/–	116.0	147.8	143.9	30	47	6	0	0	0
14	Late-onset progressive hereditary	0.88	0.69	0.88	0.96	0.75	0.88	4.3	4.2	0.0	ov/ov/ov	ov/ov/ov	+/+/–	+/+/–	22.5	23.0	18.8	25	2	42	10	20	10
15	Late-onset progressive hereditary	1.10	1.03	1.14	0.97	0.89	0.97	6.3	7.3	8.1	0/ov/0	ov/ov/ov	–/–/–	–/–/–	92.8	71.1	60.0	65	74	57	80	56	34
16	Unknown	0.73	0.25	0.21	0.81	0.88	0.72	5.2	55.8	54.8	0/ov/ov	0/0/ov	+/–/–	+/+/–	40.5	13.1	19.8	20	100	100	0	0	NA

(Continued)

TABLE 2 | Continued

ID	Hearing loss aetiology	vHIT gain						vHIT gain asymmetry ratio (%)			Saccades		cVEMP		SPV total			UW			DHI		
		CI ear			Non-CI ear						CI ear	Non-CI ear	CI ear	Non-CI ear									
17	Late-onset progressive hereditary	0.99	1.01	1.04	0.96	0.98	1.08	1.5	1.5	1.9	0/0/cov	0/0/cov	–/–//NA	–/+/NA	84.7	52.4	35.8	9	24	5	0	0	0
20	Unknown	1.00	1.04	0.84	0.93	1.15	0.87	3.6	5.0	1.8	0/0/cov	0/0/cov	+/–/NA	+/–/NA	116.0	91.9	85.9	8	32	69	0	0	NA
22	Unknown	1.09	1.06	1.09	1.12	1.06	1.09	1.4	0.0	0.0	0/0/0	0/0/0	–/–/NA	–/+/NA	70.6	45.0	43.5	27	16	11	0	4	NA
23	Unknown	0.92	0.84	0.88	0.85	0.90	0.81	4.0	3.4	4.1	0/0/ov	0/0/ov	–/–/+	–/+/+	87.3	71.2	64.5	51	75	76	30	52	NA
25	Congenital (unknown aetiology)	0.80	0.76	0.90	0.76	0.86	0.68	2.6	6.2	13.9	0/0/0	0/0/ov	–/–/–	–/–/–	50.7	24.2	29.6	18	20	28	0	6	12
27	Pendred syndrome	0.96	1.10	1.04	1.04	1.18	1.04	4.0	3.5	0.0	0/0/cov	0/0/cov	+/+/+	+/+/+	48.8	62.0	51.0	1	23	25	0	0	0
28	Hereditary congenital	0.74	0.76	0.93	0.67	0.76	0.81	5.0	0.0	6.9	0/0/cov	0/0/ov	–/–/–	–/–/–	NA	NA	NA	NA	NA	NA	0	0	0
29	Unknown	0.99	1.03	1.21	1.06	1.07	1.48	3.4	1.9	10.0	0/0/0	0/0/0	–/–/+	–/–/+	NA	60.0	78.7	NA	29	10	0	56	46
30	Late-onset progressive hereditary	1.04	0.95	0.71	1.09	0.92	1.08	2.3	1.6	20.7	0/ov/0	0/0/0	–/–/–	–/–/–	143.5	96.6	102.5	6	28	28	0	0	0
31	Unknown	1.19	0.85	0.93	1.10	1.05	0.96	3.9	10.5	1.6	0/0/0	0/0/0	+/–/–	+/–/+	28.6	26.3	21.1	15	16	14	0	0	0
32	Unknown	0.89	1.05	0.87	1.06	1.06	0.84	8.7	0.5	1.8	0/0/0	0/0/0	+/–/NA	+/+/NA	57.5	74.2	67.1	5	22	13	0	0	0
33	Otosclerosis	0.80	0.95	0.82	0.75	1.07	0.73	3.2	5.9	5.8	0/0/0	0/0/ov	+/–/–	+/+/+	60.2	53.2	50.9	18	14	16	0	0	0
34	Pneumococcal meningitis	0.50	0.90	0.78	0.73	1.00	0.88	18.7	5.3	6.0	0/0/0	0/0/ov	–/–/–	–/–/–	57.9	32.2	19.9	19	12	27	38	28	44
36	Late-onset progressive hereditary	1.29	1.22	1.16	1.41	1.40	1.26	4.4	6.9	4.1	0/0/0	0/0/0	+/–/–	+/+/–	113.4	58.3	74.6	28	71	89	12	5	0
39	Unknown	1.06	0.91	0.75	0.92	0.97	0.78	7.1	3.2	2.0	0/0/0	0/0/0	–/–/–	–/–/–	137.9	70.1	50.4	16	36	0	46	0	0
40	Unknown	0.82	0.93	0.90	0.91	1.02	0.94	5.2	4.6	2.2	0/0/0	0/0/0	–/–/–	–/–/–	56.5	40.7	35.4	4	7	73	0	2	6
41	Usher syndrome	1.03	1.10	0.65	1.10	1.07	0.78	3.3	1.4	9.1	0/0/0	0/0/0	–/–/NA	–/–/NA	128.8	88.2	52.9	7	29	27	0	0	NA
42	Late-onset progressive hereditary	0.84	0.91	0.91	0.87	0.98	0.97	1.8	3.7	3.2	0/0/0	0/0/0	+/+/–	+/+/+	81.0	52.7	54.2	21	4	14	0	0	NA
43	Hereditary congenital	0.91	0.63	1.19	0.90	0.77	1.25	0.6	10.0	2.5	0/0/0	0/ov/0	–/–/–	–/–/+	34.5	17.3	15.1	3	100	64	0	28	NA

CI, cochlear implant; cov, covert; ov, overt; cVEMP, cervical vestibular evoked myogenic potential; DHI, dizziness handicap inventory; NA, not available; T0, baseline before implantation; T1, first postoperative follow-up; T2, second postoperative follow-up; SPV, slow phase velocity; UW, unilateral weakness; VHIT, video head impulse test; +, present response; –, absent response.

TABLE 3 | Summary data of vestibular test battery results at baseline before implantation (T0), first postoperative follow-up (T1), and second postoperative follow-up (T2).

	T0	T1	T2
Video head impulse test			
Implanted ear, mean gain (95% CI)	0.93 (0.87–1.00)	0.87 (0.80–0.94)	0.89 (0.81–0.97)
Non-implanted ear, mean gain (95% CI)	0.95 (0.89–1.00)	0.97 (0.91–1.02)	0.94 (0.87–1.01)
vHIT gain asymmetry ratio (%), mean (95% CI)	5.4 (4.0–6.8)	7.4 (3.9–10.8)	7.1 (3.5–10.6)
Abnormal vHIT gain on implanted ear, n (%)	3 (9)	5 (14)	4 (11)
Abnormal vHIT gain on non-implanted ear, n (%)	2 (6)	2 (6)	3 (9)
Abnormal vHIT gain asymmetry ratio, n (%)	7 (20)	9 (26)	8 (23)
Correction saccades present on implanted ears, n (%)	3 (9)	6 (17)	11 (31)
Correction saccades present on non-implanted ears, n (%)	4 (11)	7 (20)	12 (34)
Caloric irrigation test			
Slow phase velocity (SPV, °/s), mean (95% CI)	87.7 (69.8–105.6)	60.2 (47.5–73.0)	59.8 (46.4–73.2)
Unilateral weakness (%), mean (95% CI)	19 (13–24)	37 (26–47)	40 (28–51)
Hypofunction, n (%)	7 (20)	15 (43)	15 (43)
Areflexia, n (%)	0	3 (9)	2 (6)
Cervical vestibular evoked myogenic potentials			
cVEMP present on implanted ears, n (%)	10 (29)	6 (17)	5 (14)
cVEMP present on non-implanted ears, n (%)	10 (29)	12 (34)	9 (26)
Dizziness handicap inventory			
Total score, mean (95% CI)	10.9 (2.4–19.4)	12.8 (4.9–20.7)	13.0 (4.9–21.1)
No handicap (0–15), n (%)	28 (80)	24 (69)	20 (74)
Mild handicap (16–34), n (%)	2 (6)	6 (17)	3 (11)
Moderate handicap (35–52), n (%)	3 (9)	2 (6)	3 (11)
Severe handicap (53−100), n (%)	2 (6)	3 (9)	1 (4)

dropped to 20 at T1 (mild handicap). None of the patients answered DHI at T2. On the contrary, some patients (e.g., ID 27, 29, and 34) show clear improvement in vHIT. However, both patients 29 and 34 report moderate handicaps in DHI.

vHIT Results

On implanted ears, a total of three (9%), five (14%), and four (11%) patients had abnormal vHIT gain values at T0, T1, and T2, respectively (**Table 3** and **Figure 1**). There was no significant difference between T0, T1, and T2 ($p = 0.164$). On implanted ears, three patients (ID 3, 16, and 41) changed from preoperatively normal gain values to abnormal T2 gain values on their implanted ears. As summarized in **Table 3**, three patients (ID 1, 8, and 34) presented abnormal vHIT gain values on the implanted ear. At T2, four patients (ID 3, 8, 16, and 41) had abnormal vHIT gain values, so three patients had deteriorated at T2. Patients 3, 8, and 16 stands out in **Figure 2** by having the lowest vHIT gain values. One patient (ID 8) had abnormal gain values in all tests in both ears. Eight patients had abnormal vHIT gain AR at T2 compared to the seven at T0—again patients 8 and 16 stood out. Mean vHIT gain asymmetry ratio did not change significantly ($p = 0.917$), but patients 3, 16, and 30 had a marked increase at T2 (**Table 2** and **Figure 2**). Correction saccades occurred as reported in **Table 3** and **Figure 3**. A significant increase in present correction saccades on both CI ears and contralateral ears was observed ($p = 0.017$ for both analyses).

Caloric Irrigation Results

On implanted ears, the mean total SPV was 87.7°/s at T0, 60.2°/s at T1, and 59.8°/s at T2 (**Table 3** and **Figure 4**). A significant decrease in SPV was observed from preimplantation to short-term follow-up (T1) ($p < 0.005$) and stayed low at T2 ($p = 0.915$).

At T0, the mean unilateral weakness was 19%. UW increased significantly to 37% at T1 and 40% at T2 ($p < 0.005$). Eleven patients (ID 2, 3, 6, 10, 16, 20, 27, 30, 36, 40, and 43) all had noticeable increases in UW. Seven patients (20%) had caloric hypofunction preimplantation, and none were areflexic. This number increased significantly to 18 patients at T1 and 17 patients at T2 ($p < 0.005$), and of those, 3 (9%) and 2 (6%) patients had areflexia, respectively. Caloric test data were incomplete for four patients.

cVEMP Results

At T0, 10 patients (29%) presented cVEMP responses on the implanted ears, and 10 (29%) patients presented cVEMP responses on non-implanted ears (**Figure 5**). At T2, five cVEMP responses were lost on the implanted ears, and one was lost at the non-implanted ears. No significant difference was observed on both ear when comparing all three time points ($p = 0.148$). Patients with present cVEMP responses at T2 had a mean vHIT gain of 1.05 ($n = 5$) compared with 0.86 ($n = 30$) in the group with absent cVEMP. The mean unilateral weakness was 29.5% ($n = 5$) in the group with present cVEMPs compared with 38.5% ($n = 30$) in the group with absent cVEMPs. cVEMP data were incomplete for six patients.

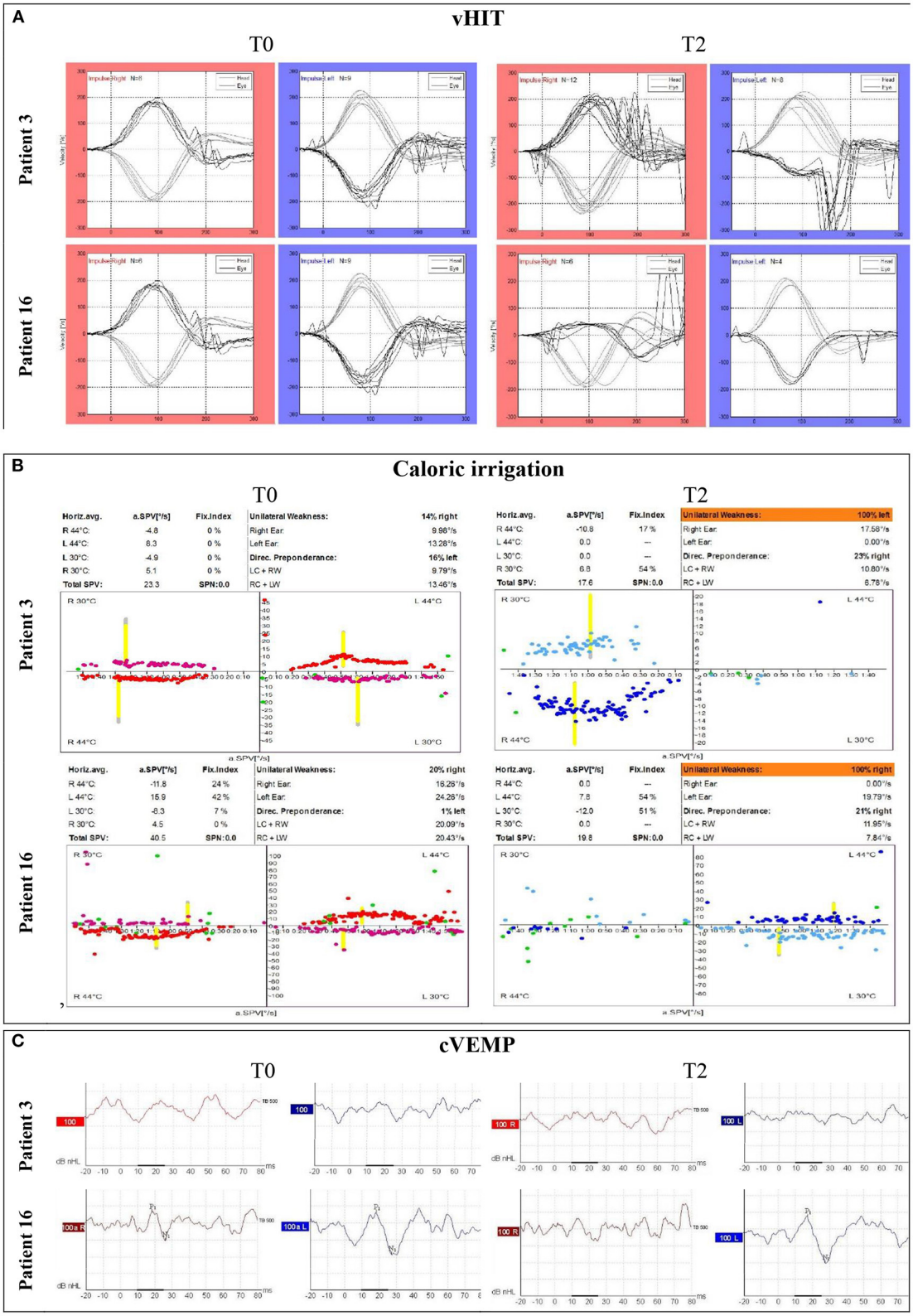

FIGURE 1 | Preoperative and postoperative raw data for patients 3 and 16 at T0 and T2, respectively. **(A)** vHIT tracings, **(B)** raw caloric irrigation test data including total SPV and UW, and **(C)** cVEMP tracings.

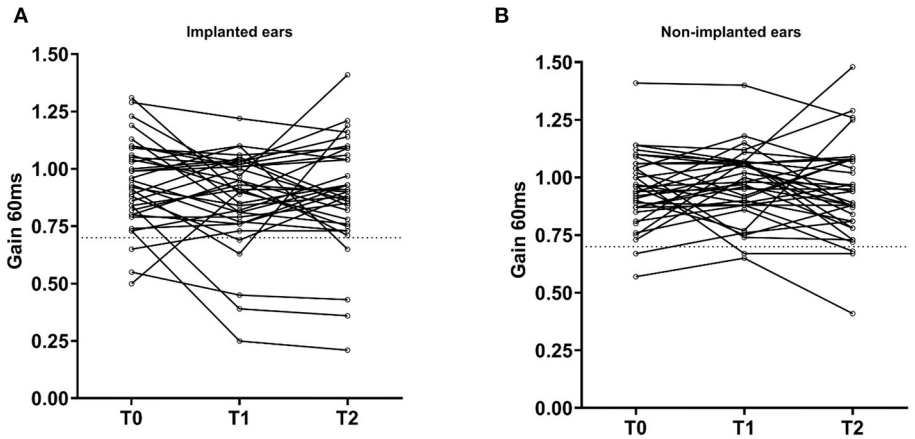

FIGURE 2 | Individual changes in vHIT gains ($n = 35$) on **(A)** implanted and **(B)** non-implanted ears, respectively. Patients 3, 8, and 16 stand out with the lowest vHIT gain values. ms, milliseconds; T0, baseline before implantation; T1, first postoperative follow-up; T2, second postoperative follow-up; vHIT, video head impulse test. Observations below the dotted line are considered abnormal (vHIT = 0.7).

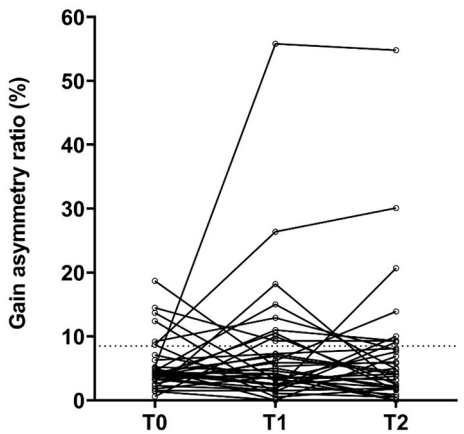

FIGURE 3 | Individual changes in vHIT gain asymmetry ratio (AR, %) ($n = 35$). T0, baseline before implantation; T1, first postoperative follow-up; T2, second postoperative follow-up. Observations above the dotted line are considered abnormal (gain AR = 8.5%).

DHI Results

DHI mean scores at T0, T1, and T2 were 10.9, 12.8, and 13.0, respectively (**Table 3** and **Figure 6**). No significant differences in DHI totals were found pre- and postimplantation DHI scores ($p = 0.368$). At T2, 16 patients (36%) reported no symptoms (DHI = 0), but 2 patients (6%) improved and 7 patients (20%) worsened compared to their T0 value. Eight patients had incomplete DHI data at T2. At T2, no association were found between the DHI scores and caloric irrigation ($r_s = 0.369$; $p = 0.084$) and vHIT gain ($r_s = -0.313$; $p = 0.259$) on implanted ears. Most frequently, patients reported DHI total scores corresponding to no handicap. Two patients (ID 8 and 15) had severe handicaps at T0. As the only patient in the cohort, Patient 8 was still seriously affected by dizziness at T2.

DISCUSSION

We herein present follow-up data to a previously conducted study from our institution (3) investigating postoperative vestibular function in a patient cohort after cochlear implantation. In the present study, we investigated long-term vestibular outcomes of 35 cochlear implant recipients using a recognized set of vestibular tests and correlated the results from two consecutive postoperative follow-ups. This study adds evidence to the research field regarding vestibular dysfunction after cochlear implantation. We applied a comprehensive vestibular test battery on a medium-sized patient cohort and found that patients' vestibular function deteriorated 3–6 months after implantation and tended to stabilize ∼14 months postimplantation. The present study observes no associations between objective vestibular testing and self-reported symptoms, and only a small group of patients report moderate to severe dizziness symptoms. In this study, we found no significant decrease in vHIT gain but a significant increase in number of corrective saccades. Unilateral weakness increased significantly, but no correlation between vHIT and caloric irrigation was observed. cVEMP responses were reduced although not significantly.

In summary, 9% showed preoperatively abnormal vHIT gains, 20% had hypofunctioning caloric responses, and 61% did not elicit cVEMP responses. Postoperatively at first follow-up, an overall deterioration in vestibular function was observed, as 14% of patients had abnormal vHIT gains, 52% had either caloric hypofunction including areflexia, and 83% had absent cVEMP responses. The results from the last postoperative follow-up showed a stabilization of vestibular

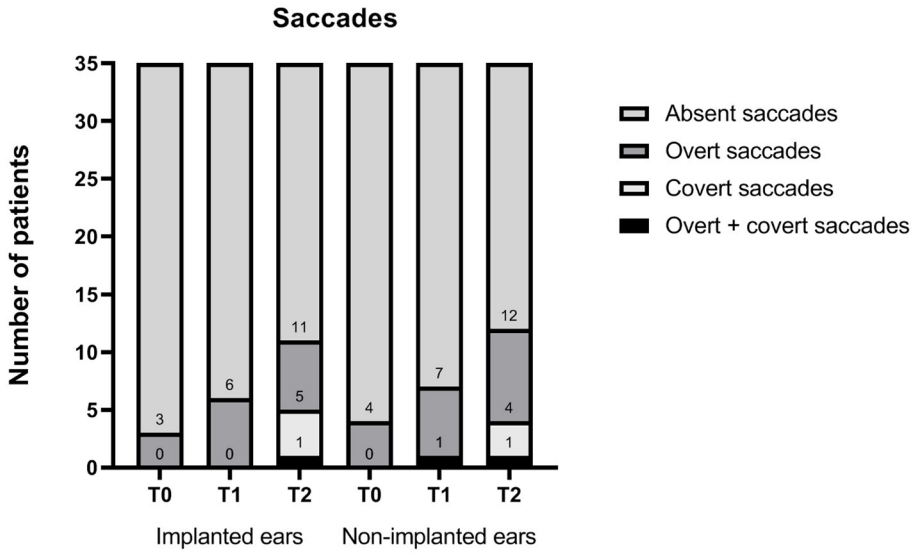

FIGURE 4 | Pre- and postoperative saccades for implanted and non-implanted ears ($n = 35$). T0, baseline before implantation; T1, first postoperative follow-up; T2, second postoperative follow-up. Numbers indicate accumulated sums.

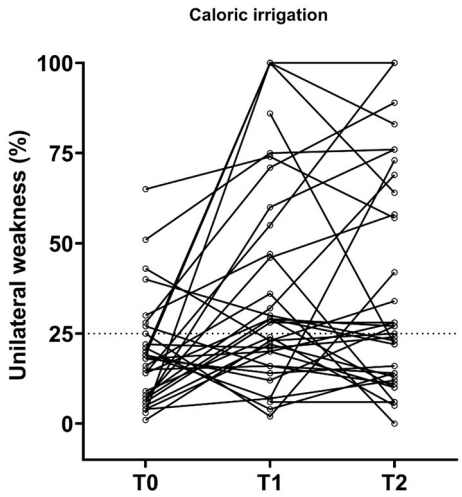

FIGURE 5 | Individual changes in caloric function before implantation and at the postoperative follow-ups. T0, baseline before implantation; T1, first postoperative follow-up; T2, second postoperative follow-up. Observations above the dotted line represent vestibular hypofunction (UW = 25%); UW = 100% means areflexia.

dysfunction: 11% had abnormal vHIT gain, 49% had either hypofunctioning or areflexic caloric responses, and 86% had absent cVEMP responses. Despite detectable vestibular dysfunction, fewer patients from T0 to T2 exhibit moderate or severe handicaps. Thus, the DHI score remains virtually unchanged, suggesting that the symptom burden has plateaued. Even though vestibular function is preserved objectively, the patients may experience symptoms and vice versa. Therefore, the results show that the objective and subjective vestibular outcomes are inconsistent, which also has been stated by West et al. (3) and supported by other conducted studies in the field (23). In a systematic review including 27 studies, Ibrahim et al. showed great variability in vestibular test results but concluded that CI surgery can significantly affect caloric irrigation and cVEMP responses but not vHIT and DHI. The authors argued that the effect is clinically insignificant because DHI total scores was not affected by cochlear implantation (10). Other studies also reported diverse and often contradictory results (17, 19, 20). The current study shows that when we focus on individual patients, we may see both worsening and improving vestibular function. The causes of vestibular dysfunction after cochlear implantation have been attributed to various factors including direct surgical trauma, endolymphatic hydrops, and inflammatory reaction (34). These theories are supported by histopathological studies, which have revealed vestibular organ damage in post-mortem specimens (35, 36). Additionally, the vestibular deficits pre- and postimplantation may differ depending on the hearing impairment aetiology. For instance, patient 8 with superficial siderosis presented bilateral vestibular dysfunction, and the present test battery may be incapable of determining any meaningful difference pre- and postimplantation. On the other hand, it has been argued that vestibular function improves with recovering auditory function. Due to better auditory function, patients become increasingly socially and physically active, improving their postural function and well-being. According to Colin et al., this improvement in quality of life may improve the subjective feeling of balance (17). This could reinforce the idea proposed by Abouzayd et al. that we need to apply a case-by-case strategy based on the patient's symptoms and hearing impairment aetiology (23).

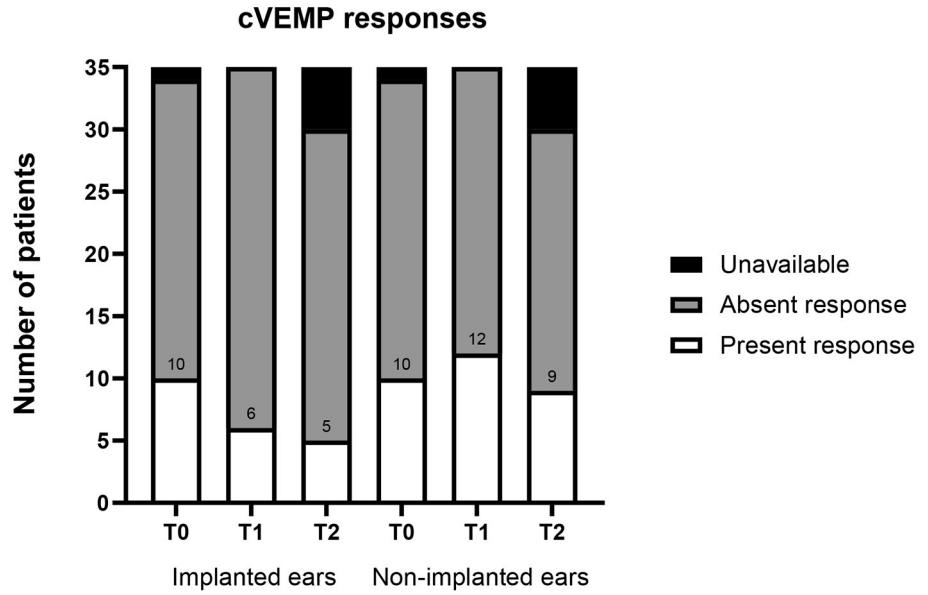

FIGURE 6 | Pre- and postoperative cVEMP responses for implanted and non-implanted ears ($n = 35$). T0, baseline before implantation; T1, first postoperative follow-up; T2, second postoperative follow-up; cVEMP, cervical evoked myogenic potentials. Numbers indicate number of present responses.

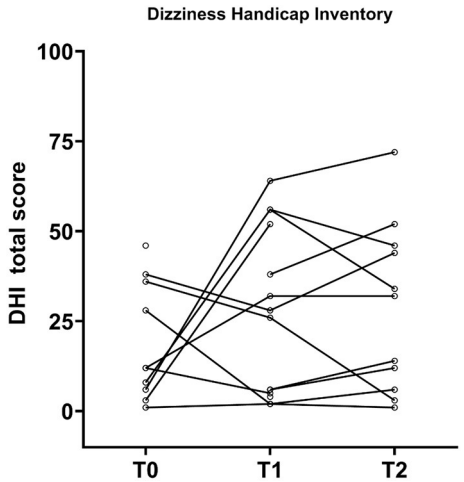

FIGURE 7 | Patient-reported vestibular outcomes measured by the dizziness handicap inventory (DHI) before and after implantation ($n = 35$). No significant change in total score were reported between pre- and postimplantation. Eighteen patients with both pre- and postoperative DHI 0 are not visualized on the plot. T0, baseline before implantation; T1, first postoperative follow-up; T2, second postoperative follow-up.

Systematic long-term vestibular assessment after cochlear implantation has been performed in two previous studies (27, 37), reporting caloric outcomes and vHIT/cVEMP outcomes, respectively. Another study performed the caloric test, posturography, and rotatory chair test 365 days postimplantation but failed to provide quantitative results from the follow-up, making comparisons difficult (38). Buchman et al. reported that 29% of their cohort had a substantial reduction in the slow velocity VOR, as measured by the caloric test (27). In the recent paper from our institution, 45 individuals were retrospectively evaluated long term after cochlear implantation. It was found that the high velocity VOR function as measured by vHIT gain was preserved, but a tendency to demonstrate vHIT saccades on implanted ears was observed. Furthermore, cVEMP potentials were significantly reduced (21).

We found a discrepancy in self-perceived symptoms of vertigo and objective test findings, and one explanation may be that each test is unsuccessful in determining vestibular deficiency. Second, central compensation may alleviate symptoms of vertigo, while objective tests still detect vestibular dysfunction (25). Third, the findings may indicate that only subparts of the vestibular organs are evaluated, so the test battery is incapable of analyzing the full complexity of the vestibular apparatus. To our knowledge, no recent studies have examined all five vestibular organs. In this study, we focused on the lateral semicircular canal, tested with vHIT and caloric irrigation test, and sacculus, tested with cVEMP responses, and found some degree of vestibular deterioration. Although we consider this comprehensive test battery a strength to the study, not all vestibular end organs are studied. The vestibular test battery could also encompass impulsive testing (vHIT) of the RALP (right anterior and left posterior semicircular canals) and LARP (left anterior and right posterior semicircular canals), referred to as vertical vHIT. In addition, ocular VEMP (oVEMP) data were not part of the evaluation. Imai et al. previously demonstrated that oVEMP is a useful measure of utricular function (15). Thus, the omission of vertical vHIT and oVEMP may contribute to the outcome mismatch observed between subjective and objective vestibular evaluations. As we did not examine the remaining parts of the vestibular apparatus

(i.e., anterior and posterior semicircular canals and utriculus), an existing and possibly enhanced association between objective vestibular test results may not have been appointed.

We did not observe a correlation between self-reported symptoms and objectively measured vestibular dysfunction, and it may be argued that psychological factors, such as anxiety and depression, contribute to the disagreement. Our study did not investigate development of anxiety and depression, and this may be a focus for future studies. Another study limitation includes patient loss to follow-up. There is no indication that patients dropped out due to severe vertigo; the reason was most likely due to the COVID-19 pandemic. Furthermore, the absolute follow-up may represent a limitation, as 14 months may be insufficient to determine the final vestibular function. Future studies should address whether vestibular function normalizes with longer postimplant follow-up time or if vestibular function has already reached a nadir 14 months following implantation. Age and aetiology of SNHL may affect vestibular function. Therefore, future studies are also needed to investigate whether age and aetiology of SNHL play a role in the end vestibular function or if the deterioration from 4 to 14 months merely is a result from an age-related dysfunction.

CONCLUSION

We present a prospective observational study of long-term subjective and objective vestibular outcomes in 35 cochlear implant recipients. Our study demonstrates that cochlear implantation can worsen vestibular function and that long-term effects tend to plateau rather than deteriorate vestibular function. vHIT, caloric irrigation, and cVEMP all measured an overall worsening of vestibular function at long-term postoperative follow-up. Despite vestibular dysfunction, a large proportion of patients report less or unchanged vestibular symptoms. Pre- and post-implantation vestibular evaluations can give short- and long-term prognostic information, and guide implantation side selection, treatment, and vestibular rehabilitation.

DATA AVAILABILITY STATEMENT

The raw data supporting the conclusions of this article will be made available by the authors, without undue reservation.

ETHICS STATEMENT

The studies involving human participants were reviewed and approved by The Danish National Committee on Health Research Ethics (H-17034918) and The Danish Data Protection Agency (RH-2017-308). The patients provided their written informed consent to participate in this study.

AUTHOR CONTRIBUTIONS

KR: drafting of the manuscript. NW and PC-T: study design. All authors revision of the manuscript, final approval, and final agreement.

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REFERENCES

1. Hansen S, Anthonsen K, Stangerup S-E, Jensen JH, Thomsen J, Cayé-Thomasen P. Unexpected findings and surgical complications in 505 consecutive cochlear implantations: a proposal for reporting consensus. *Acta Oto-Laryngol.* (2010) 130:540–9. doi: 10.3109/00016480903358261
2. Veroul E, Sabban D, Blexmann L, Frachet B, Poncet-Wallet C, Mamelle E. Predictive factors of vertigo following cochlear implantation in adults. *Eur Arch Oto-Rhino-Laryngol.* (2020). doi: 10.1007/s00405-020-06449-y. [Epub ahead of print].
3. West N, Tian L, Petersen LKV, Bille M, Klokker M, Cayé-Thomasen P. Objective vestibular test battery and patient reported outcomes in cochlear implant recipients. *Otol Neurotol.* (2020) 42:e416–24. doi: 10.1097/MAO.0000000000002959
4. Jeppesen J, Faber CE. Surgical complications following cochlear implantation in adults based on a proposed reporting consensus. *Acta Oto-Laryngol.* (2013) 133:1012–21. doi: 10.3109/00016489.2013.797604
5. Terry B, Kelt RE, Jeyakumar A. Delayed complications after cochlear implantation. *JAMA Otolaryngol Head Neck Surg.* (2015) 141:1012. doi: 10.1001/jamaoto.2015.2154
6. Kusuma S, Liou S, Haynes DS. Disequilibrium after cochlear implantation caused by a perilymph fistula. *Laryngoscope.* (2005) 115:25–6. doi: 10.1097/01.mlg.0000150680.68355.cc
7. Perez N, Garmendia I, García-Granero M, Martin E, García-Tapia R. Factor analysis and correlation between dizziness handicap inventory and dizziness characteristics and impact on quality of life scales. *Acta Oto-Laryngol.* (2001) 121:145–54. doi: 10.1080/000164801750388333
8. Huygen PLM, Hinderink JB, Van Den Broek P, Van Den Borne S, Brokx JPL, Mens LHM, et al. the risk of vestibular function loss after intracochlear implantation. *Acta Oto-Laryngol.* (1995) 115:270–2. doi: 10.3109/00016489509125245
9. Backous DD, Quigley SM. Vestibular assessment and ear selection for cochlear implantation: the role of bedside testing. *Adv Oto-Rhino-Laryngol.* (2000) 57:168–72. doi: 10.1159/000059230
10. Ibrahim I, Da Silva SD, Segal B, Zeitouni A. Effect of cochlear implant surgery on vestibular function: meta-analysis study. *J Otolaryngol Head Neck Surg.* (2017) 46:44. doi: 10.1186/s40463-017-0224-0
11. McGarvie LA, MacDougall HG, Halmagyi GM, Burgess AM, Weber KP, Curthoys IS. The Video Head Impulse Test (vHIT) of semicircular canal function - age-dependent normative values of VOR gain in healthy subjects. *Front Neurol.* (2015) 6:154. doi: 10.3389/fneur.2015.00154
12. Jacobson GP, Newman CW. The development of the Dizziness handicap inventory. *Arch Otolaryngol Head Neck Surg.* (1990) 116:424–7. doi: 10.1001/archotol.1990.01870040046011
13. Barbara M, Talamonti R, Benincasa T, Anna, Tarentini S, Filippi C, et al. Early assessment of vestibular function after unilateral cochlear implant surgery. *Audiol Neurotol.* (2020) 25(Suppl. 1-2):50–9. doi: 10.1159/000502252

14. Dagkiran M, Tuncer U, Surmelioglu O, Tarkan O, Ozdemir S, Cetik F, et al. How does cochlear implantation affect five vestibular end-organ functions and dizziness? *Auris Nasus Larynx.* (2019) 46:178–85. doi: 10.1016/j.anl.2018.07.004
15. Imai T, Okumura T, Ohta Y, Oshima K, Sato T, Kamakura T, et al. Effects of cochlear implants on otolith function as evaluated by vestibulo-ocular reflex and vestibular evoked myogenic potentials. *Auris Nasus Larynx.* (2019) 46:836–43. doi: 10.1016/j.anl.2019.03.011
16. Bittar RSM, Sato ES, Silva-Ribeiro DJ, Oiticica J, Mezzalira R, Tsuji RK, et al. Caloric test and video head impulse test sensitivity as vestibular impairment predictors before cochlear implant surgery. *Clinics.* (2019) 74:e786. doi: 10.6061/clinics/2019/e786
17. Colin V, Bertholon P, Roy S, Karkas A. Impact of cochlear implantation on peripheral vestibular function in adults. *Eur Ann Otorhinolaryngol Head Neck Dis.* (2018) 135:417–20. doi: 10.1016/j.anorl.2018.10.007
18. Parmar A, Savage J, Wilkinson A, Hajioff D, Nunez DA, Robinson P. The role of vestibular caloric tests in cochlear implantation. *Otolaryngol Head Neck Surg.* (2012) 147:127–31. doi: 10.1177/0194599812442059
19. Kuang H, Haversat HH, Michaelides EM. Impairment of caloric function after cochlear implantation. *J Speech Lang Hear Res.* (2015) 58:1387–95. doi: 10.1044/2015_JSLHR-H-15-0010
20. Piker EG, Riska K, Garrison D, Kaylie DM. Vestibular function after cochlear implantation: A test battery and case-by-case approach. *Laryngoscope Investig Otolaryngol.* (2020) 5:560–71. doi: 10.1002/lio2.413
21. West N, Klokker M, Cayé-Thomasen P. Video head impulse test saccades and loss of cervical vestibular evoked myogenic potentials are late vestibular footprints of cochlear implantation. *J Vestib Res.* (2020) 31:61–7. doi: 10.3233/VES-190760
22. Janky KL, Patterson J. The relationship between rotary chair and video head impulse testing in children and young adults with cochlear implants. *Am J Audiol.* (2020) 29:898–906. doi: 10.1044/2020_AJA-20-00079
23. Abouzayd M, Smith PF, Moreau S, Hitier M. What vestibular tests to choose in symptomatic patients after a cochlear implant? a systematic review and meta-analysis. *Eur Arch Otorhinolaryngol.* (2017) 274:53–63. doi: 10.1007/s00405-016-4007-4
24. Todt I, Basta D, Ernst A. Does the surgical approach in cochlear implantation influence the occurrence of postoperative vertigo? *Otolaryngology-Head Neck Surg.* (2008) 138:8–12. doi: 10.1016/j.otohns.2007.09.003
25. Melvin T-AN, Della Santina CC, Carey JP, Migliaccio AA. The effects of cochlear implantation on vestibular function. *Otol Neurotol.* (2009) 30:87–94. doi: 10.1097/MAO.0b013e31818d1cba
26. Robard L, Hitier M, Lebas C, Moreau S. Vestibular function and cochlear implant. *Eur Arch Oto-Rhino-Laryngol.* (2015) 272:523–30. doi: 10.1007/s00405-014-3040-4
27. Buchman CA, Joy J, Hodges A, Telischi FF, Balkany TJ. Vestibular effects of cochlear implantation. *Laryngoscope.* (2004) 114:1–22. doi: 10.1097/00005537-200410001-00001
28. Batuecas-Caletrio A, Klumpp M, Santacruz-Ruiz S, Gonzalez FB, Sánchez EG, Arriaga M. Vestibular function in cochlear implantation: Correlating objectiveness and subjectiveness. *Laryngoscope.* (2015) 125:2371–5. doi: 10.1002/lary.25299
29. Halmagyi GM, Chen L, Macdougall HG, Weber KP, Mcgarvie LA, Curthoys IS. The video head impulse test. *Front Neurol.* (2017) 8:258. doi: 10.3389/fneur.2017.00258
30. Schmid-Priscoveanu A, Bühmer A, Obzina H, Straumann D. Caloric and search-coil head-impulse testing in patients after vestibular neuritis. *J Assoc Res Otolaryngol.* (2001) 2:72–8. doi: 10.1007/s1016200 10060
31. Rosengren SM, Colebatch JG, Young AS, Govender S, Welgampola MS. Vestibular evoked myogenic potentials in practice: Methods, pitfalls and clinical applications. *Clin Neurophysiol Pract.* (2019) 4:47–68. doi: 10.1016/j.cnp.2019.01.005
32. IBM SPSS Statistics for Windows. Version 25.0 ed. Armonk, NY: IBM Corp (2017).
33. GraphPad Prism for Windows. *GraphPad Software. Version 9.0.0 ed.* San Diego, CA.
34. Smeds H, Eastwood HT, Hampson AJ, Sale P, Campbell LJ, Arhatari BD, et al. Endolymphatic hydrops is prevalent in the first weeks following cochlear implantation. *Hear Res.* (2015) 327:48–57. doi: 10.1016/j.heares.2015.04.017
35. Tien H-C, Linthicum FH. Histopathologic changes in the vestibule after cochlear implantation. *Otolaryngology-Head Neck Surg.* (2002) 127:260–4. doi: 10.1067/mhn.2002.128555
36. Handzel O, Burgess BJ, Nadol JBJ. Histopathology of the peripheral vestibular system after cochlear implantation in the human. *Otol Neurotol.* (2006) 27:57–64. doi: 10.1097/01.mao.0000188658.36327.8f
37. West N, Klokker M, Caye-Thomasen P. Vestibular screening before cochlear implantation: clinical implications and challenges in 409 cochlear implant recipients. *Otol Neurotol.* (2021) 42:e137–44. doi: 10.1097/MAO.0000000000002898
38. Abramides PA, Bittar RSM, Tsuji RK, Bento RF. Caloric test as a predictor tool of postural control in CI users. *Acta Oto-Laryngol.* (2015) 135:685–91. doi: 10.3109/00016489.2015.1020395

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