Magnetic Resonance Imaging Evaluation for Predictive Factors of Cochlear Nerve Deficiency in Pediatric Cochlear Implant Candidates

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ABSTRACT

The presence of a functioning cochlear nerve fiber is a crucial issue in the preoperative evaluation of pediatric cochlear implant candidates. Correlations between cochlear nerve deficiency and bony abnormalities of the labyrinth or internal acoustic canal (IAC) have not been well elucidated. The purpose of this study was to determine whether an inner ear or IAC anomaly could serve as a reliable predictive factor for the presence of cochlear nerve deficiency.

We retrospectively reviewed magnetic resonance imaging (MRI) images of 88 patients with sensorineural hearing loss (SNHL) for the presence of cochlear nerve deficiency, cochlear, vestibular or semicircular canal (SCC) anomalies, endolymphatic duct enlargement, and IAC stenosis. Generalized estimating equations (GEE) logistic regression models were used to determine the predictive factors of cochlear nerve deficiency.

MRI demonstrated inner ear or IAC anomalies in 60 of 149 ears (40%) with SNHL, among which 37 presented with cochlear nerve deficiency, 16 had cochlear anomaly, 10 had vestibular/SCC anomaly, 28 demonstrated IAC stenosis, and 18 presented with endolymphatic duct enlargement. Multivariate GEE model demonstrated IAC stenosis and cochlear dysplasia to be positive predictive factors for cochlear nerve deficiency with odds ratios of 23.0 and 16.0, respectively. We concluded that most ears with cochlear nerve deficiency have concurrent anomaly of the bony labyrinth or IAC. In those children with IAC stenosis or cochlear dysplasia which may be detected by CT in advance, MRI should be performed for evaluation of cochlear nerve deficiency.

Children with sensorineural hearing loss (SNHL) often present to otolaryngologists before adolescence. Early diagnosis and correction of the cause of SNHL are important in speech and language development for young children [1]. Cochlear implantation is an effective treatment for selected patients with SNHL [2]. The presence of a functioning cochlear nerve becomes a crucial issue in the preoperative evaluation of pediatric cochlear implant candidates. Cochlear nerve deficiency implies an absence or hypoplasia of the cochlear nerve. A hypoplastic cochlear nerve is considered a relative contraindication for cochlear implantation. Previous studies have shown that a reduction in the diameter of the cochlear nerve may be associated with a reduced number of spiral ganglion cells [3]; although the residual cochlear nerve fibers may still be effective, the extent of functioning nerve fiber is uncertain and needs...
to be evaluated [4]. The absence of the cochlear nerve is considered an absolute contraindication for cochlear implantation. Lack of a visible cochlear nerve on magnetic resonance imaging (MRI) has been shown to be related to poor outcome of cochlear implantation [5].

The preoperative evaluation for cochlear implantation includes CT and MRI. High-resolution CT has been recommended by many authors as the imaging modality of choice for the initial work-up of children with SNHL [6, 7]. CT may provide good resolution for abnormalities of the bony labyrinth, internal acoustic canal (IAC), ossicular chain, facial nerve canal, and jugular bulb, and can assist in the planning of the operative route [8]. To detect cochlear nerve deficiency, MRI provides better soft tissue resolution and direct visualization of the cochlear nerve [9, 10], but has a higher cost and a longer examination time.

Some authors have suggested that there may be a correlation between cochlear nerve deficiency and bony abnormalities of the labyrinth or IAC, which can be detected by CT [11-13], while others have suggested that the correlation is unreliable [14, 15]. Most of these studies were case series or of small patient numbers utilizing descriptive statistical methods. To the best of our knowledge, there have been no previous large-scale reports of multifactorial analysis for the predictive factors of cochlear nerve deficiency, especially imaging variables on MRI and CT.

**Figure 1.** Normal and hypoplastic cochlear nerves seen in 3DFT-CISS images through the IAC of a 6-year-old boy. 

**Figure 1a.** Axial image showing the right cochlear nerve (arrow) in the right IAC with normal dimension. The left cochlear nerve (arrow) was poorly visualized in the left IAC.

**Figure 1b.** Oblique sagittal image through the right IAC showing that the right cochlear nerve (arrow) lay in the anteroinferior portion of the IAC. The diameter of the cochlear nerve was the same or larger than that of the adjacent facial nerve, suggesting a normal right cochlear nerve.

**Figure 1c.** Oblique sagittal image through the left IAC showing that the left cochlear nerve (arrow) was markedly smaller than the facial nerve, suggesting severe hypoplasia of the left cochlear nerve.
The present study was performed to determine whether there are significant correlations between cochlear nerve deficiency and bony anomalies of the inner ear or IAC. The endpoint was to determine whether an inner ear or IAC anomaly could serve as a reliable predictive factor for the presence of cochlear nerve deficiency.

MATERIALS AND METHODS

Subjects

A retrospective review of the medical records of pediatric cochlear implant candidates during the period from June 2002 to June 2010 at our center was performed. A total of 111 patients with MRI examinations for SNHL were identified. Complete audiological data were available for 88 of the 111 patients, and these cases were included in this study.

Imaging Acquisition

MRI was performed with a pediatric vestibulocochlear nerve protocol on two 1.5-T scanners. The protocol included axial unenhanced spin-echo (SE) T1-weighted imaging, axial and coronal T2-weighted imaging, and high-resolution three-dimensional Fourier transformation-constructive interference in steady state (3DFT-CISS) imaging through the temporal bones as well as axial fluid-attenuated inversion recovery imaging of the entire brain. Parameters for the CISS sequence varied by MR scanners (TR/TE/NEX, 5.42–12.25 ms/2.42–5.9 ms/1–2; FA, 50°–80°; FOV, 120–160 mm; matrix size, 512), with near-isotropic voxel sizes of 0.5 mm in length. Oblique coronal and oblique sagittal CISS images of IAC were reformatted by the multiplanar reconstruction (MPR) procedure.

Image Analysis and Data Collection

MR images were reviewed on a PACS station by a board-certified neuroradiologist with 20 years of experience, who was blinded to the side of hearing loss. Diameters of cochlear nerve, facial nerve, IAC, and endolymphatic duct were measured on PACS and recorded. The reviewer examined the images and recorded data for the presence of cochlear nerve deficiency, cochlear, vestibular, or semicircular canal (SCC) anomalies, endolymphatic duct enlargement, and IAC stenosis.

Cochlear nerve deficiency implied an absence or hypoplasia of the cochlear nerve (Fig. 1). The cochlear nerve was considered hypoplastic if it was smaller in diameter than that of the adjacent facial nerve at the level of the middle to lateral third of the IAC. The cochlear nerve was considered aplastic if it was not visible on any plane of the MR images. The morphology of the cochlea was also assessed, which was categorized as normal or dysplastic (including aplasia and hypoplasia) (Fig. 2). Cochlear hypoplasia was defined as morphological malformation of the cochlea or a cochlear duct with less than 2.5 turns. Common cystic anomaly was included in the category of cochlear hypoplasia. If the cochlea was not visible, the case was considered to be a

Figure 2

2a

2b

Figure 2. Cochlear anomalies seen on axial 3DFT-CISS images through the IAC. a. Cochlear hypoplasia (arrow) was seen as a cochlea with smaller size. A dilated endolymphatic duct (arrowhead) was also noted. b. No visualization of cochlear turns in the temporal bone, suggesting cochlear aplasia (arrow). A severely stenotic IAC, deformed vestibule (arrowhead), and absence of semicircular canals were also noted.
**Figure 3.** Cochleovestibular anomalies seen on axial 3DFT-CISS images through the IAC. **a.** Cystic dilatation of the cochlea and vestibule (arrow). **b.** Absence of cochlear and cystic dilatation of the vestibule (arrow), suggesting cochlear aplasia and vestibular hypoplasia.

**Figure 4.** Axial 3DFT-CISS images through the IAC showing decreased diameter of the right IAC (arrow) < 3 mm and a normal-sized left IAC, suggesting right IAC stenosis.

**Figure 5.** Axial 3DFT-CISS images through the level of the vestibular aqueduct showing dilatation of the bilateral endolymphatic ducts (arrows).
cochlear aplasia. Vestibular or SCC anomaly was considered in cases with any morphological malformation of the vestibule or SCC (Fig. 3). IAC was considered stenotic if its narrowest dimension on axial or parasagittal oblique images was less than 3 mm [16, 17] (Fig. 4). Endolymphatic duct dilatation was defined as a midpoint diameter larger than 1.5 mm (Fig. 5).

Statistical Analysis
Descriptive statistical analyses of the ears with cochlear nerve deficiency, inner ear anomalies, and IAC stenosis were performed. Categorical data were calculated with frequency measurements. To determine the predictive factors of cochlear nerve deficiency, generalized estimating equations (GEE) logistic regression models were used, taking into account the dependence between both ears of the same individual. The outcome of interest (i.e., the dependent variable) was cochlear nerve deficiency. Covariates (i.e., the predictor variables) included cochlear dysplasia, vestibular/SCC anomaly, endolymphatic duct dilatation, and IAC stenosis. First, each of the possible predictors was subjected to univariate analysis with a GEE model. Then a multivariate GEE model was adopted with respect to statistically significant results from univariate analyses. Statistical analyses were performed using SPSS Version 18.0 (SPSS, Chicago, IL). In all analyses, P < 0.05 was taken to indicate statistical significance.

RESULTS
Among the 111 patients with SNHL undergoing temporal bone MRI over the 8-year study period, 23 were excluded due to incomplete audiological data. Therefore, 88 patients were included in the analysis (44 males and 44 females). The patients ranged in age from 6 months to 18 years (mean age, 7.8 years). Among these 88 patients (176 ears), 61 (69%) had bilateral SNHL and the other 27 (31%) had unilateral SNHL, comprising a total of 149 ears with SNHL. MRI demonstrated inner ear or IAC anomalies in 60 of 149 ears (40%) with SNHL and IAC stenosis in only 2 of the 27 (7%) asymptomatic ears. Of the 62 ears with inner ear or IAC anomalies, 30 (48%) had at least one coexisting anomaly. The specific type of anomaly, number and percentage of ears, and concurrent anomalies are summarized in Table 1.

Of note, 10 ears (from 9 patients) had cochlear nerve deficiency but were not associated with any other anomaly of the inner ear or IAC, considered isolated cochlear nerve deficiency, which represented 6.7% of ears with SNHL.

As 10 (37%) of the 27 patients with cochlear nerve deficiency presented with bilateral ear involvement, potential correlations between the left ear and right ear of the same individual were considered. With respect to the presence of cochlear nerve deficiency, the Pearson’s correlation coefficient between the bilateral ears was calculated to be 0.42 (P < 0.001), indicating a medium positive correlation.

In the univariate GEE models (Table 2), after adjusting for the sidedness of the ears, the presence of cochlear dysplasia, vestibular/SCC anomaly, and IAC stenosis showed significant associations with cochlear nerve deficiency, with calculated odds ratios for prediction of 38.0, 31.7, and 30.2, respectively. Endolymphatic duct dilatation could not be evaluated by logistic regression analysis as there were no concurrent cases of cochlear nerve deficiency and endolymphatic duct dilatation in our study population.

In the multivariate GEE model (Table 3), after adjustment for the sidedness of the ears, both cochlear dysplasia and IAC stenosis showed significant correlations with cochlear nerve deficiency. The odds ratios of cochlear dysplasia and IAC stenosis for prediction of cochlear nerve deficiency were 16.0 and 22.8, respectively. The odds ratio of vestibular/SCC anomaly was 1.4 and was not statistically significant.

| Table 1. Inner Ear and IAC Anomalies Detected by Magnetic Resonance Imaging in 149 Ears of Children with Sensorineural Hearing Loss |
|---------------------------------|-----------------|----------------|-----------------|-----------------|-----------------|-----------------|
| Anomaly Type                    | Anomalies, No/Total (%) | Concurrent Anomalies, No/Total (%) | Type of Concurrent Anomalies, No/Total (%) |
|                                 | Cochlear nerve deficiency | Cochlear anomaly | Vestibule/SCC anomaly | IAC stenosis | Endolymphatic duct dilatation |
| Cochlear nerve deficiency       | 37/149 (25) | 27/37 (73) | - | 13/37 (35) | 9/37 (24) | 23/37 (62) | 0/37 (0) |
| Cochlear anomaly                | 16/149 (11) | 16/16 (100) | 13/16 (81) | - | 9/16 (56) | 10/16 (63) | 2/16 (13) |
| Vestibule/SCC anomaly           | 10/149 (7) | 10/10 (100) | 9/10 (90) | 9/10 (90) | - | 8/10 (80) | 0/10 (0) |
| IAC stenosis                    | 28/149 (19) | 24/28 (86) | 23/28 (82) | 10/28 (36) | 8/28 (29) | - | 0/28 (0) |
| Endolymphatic duct dilatation   | 18/149 (12) | 2/18 (11) | 0/18 (0) | 2/18 (11) | 0/18 (0) | 0/18 (0) | - |
DISCUSSION

IAC stenosis and cochlear dysplasia were positive predictive factors for cochlear nerve deficiency. In addition, the odds ratio for success of predicting cochlear nerve deficiency was larger in the presence of IAC stenosis than for cochlear dysplasia.

To the best of our knowledge, there have been no previous reports of multivariate regression models for predictors of cochlear nerve deficiency. In addition, the potential correlation between both ears of the same individual has not been mentioned in previous reports. Our study demonstrated that there is a positive correlation among the bilateral ears of the same individual with respect to cochlear nerve deficiency. The GEE models were used with correction for this within-subject variable. Future studies should be performed to elucidate for potential correlations among the ears of the same individual.

In multivariate GEE analysis, both IAC stenosis and cochlear dysplasia showed significant odds ratios for predicting cochlear nerve deficiency. Compared to normal IAC, the presence of IAC stenosis had 23 times greater odds of success for predicting cochlear nerve deficiency. In contrast, the presence of cochlear dysplasia had 16-fold greater odds of successful prediction for cochlear nerve deficiency than its normal counterpart. Therefore, IAC stenosis demonstrated a larger odds ratio than cochlear dysplasia, suggesting that it might be the most important predictor among all of the variables.

In univariate GEE analyses, cochlear anomaly, vestibular/SCC anomaly, and IAC stenosis showed possible correlations with cochlear nerve deficiency. However, in multivariate GEE analysis, the odds ratio of vestibular/SCC anomaly dropped and became statistically insignificant. One possible explanation is that the weighting of correlation of vestibular/SCC anomaly with cochlear nerve deficiency is far smaller than those of either cochlear anomaly or IAC stenosis, so its influence is suppressed by the other two variables in multivariate analysis. Another possible explanation is that there may be multicollinearity among the predictor variables. However, no significant multicollinearity was found in our study, because the value of variance inflation factor (VIF) between the predictor variables was less than 10 (just slightly greater than 1).
The overall incidence of inner ear or IAC anomaly was 40% in the ears with SNHL, falling at the high-end value of the previously reported range of 20-41% [6, 7, 18]. The most common inner ear anomaly identified in our study was cochlear nerve deficiency (25%), the incidence rate of which was higher than the values of 12–18% reported previously [10, 18].

Embryonic development of the inner ear begins with the formation of the otic vesicle into a vestibular pouch and a cochlear pouch (the future utricle and saccule), which occurs between the fourth and fifth gestational week in humans [6, 19, 20]. The cochlear duct begins to extend from the cochlear pouch late in the fifth gestational week, further developing into cochlear turns in the seventh gestational week. The semicircular canals develop from the vestibular pouch in the seventh gestational week. The developing inner ear elicits a trophic effect on cochlear neurons with nerve growth factor released from the otic vesicle, which is necessary for neuronal survival [9]. Disturbance of this neurotrophic effect may lead to cochlear nerve hypoplasia, which may explain the positive predictive value of cochlear dysplasia for cochlear nerve deficiency observed in the present study.

As embryonic development of the vestibule precedes that of the cochlea, vestibular anomaly suggests an earlier embryological disturbance which may affect both the developing vestibule and cochlea with resultant more severe labyrinthine malformation. Previously, vestibular dysplasia was thought to be almost always in association with other inner ear anomalies [21]. Our study also demonstrated that there was no isolated vestibular anomaly in our patients with SNHL. In addition, all the ears with vestibular anomaly were also associated more than two other types of inner ear or IAC anomaly.

The development of IAC occurs by inhibition of cartilage formation at the medial side of the otic vesicle during fetal life. Previous studies have suggested that an inhibitory substance may be induced by the presence of the vestibulocochlear nerve [21, 22]. Glastonbury et al. further suggested that the degree of vestibulocochlear nerve hypoplasia may be related to the severity of IAC stenosis [11]. The results of the present study indicate that IAC stenosis is the strongest statistically significant positive predictor of cochlear nerve deficiency, which supports the developmental theory of the cause-effect relationship between the cochlear nerve and IAC.

There are four nerves contained in IAC, including cochlear nerve, superior and inferior vestibular nerves, and facial nerve. The presence of a normal cochlear nerve within a stenotic IAC may be explained by deficiency of cartilage inhibitory substance resulting from hypoplasia of facial nerve or vestibular nerves in the IAC [21].

The finding of isolated cochlear nerve deficiency is of interest, which means a hypoplastic cochlear nerve within a normal IAC and without any labyrinthine deformity. Previously, this was considered very rare [9, 13]. The development of isolated cochlear nerve deficiency may be due to disturbance of the neuronal growth of cochlear nerve after formation of the bony labyrinth and IAC. In the present study, the incidence of isolated cochlear nerve deficiency was 6.7% in the ears with SNHL. Clinically, ENT surgeons and radiologists should keep in mind that there is a small percentage of cochlear nerve deficiency that cannot be suggested by CT findings of abnormal bony labyrinth or IAC, but can be determined by MRI.

In the present study, endolymphatic duct dilation had an incidence of 12%, comparable to the previously reported incidence of 10-15% [18, 21]. In those both ears with combined endolymphatic duct dilatation and cochlear anomaly, the cochlear anomaly was presented with the milder form of cochlear deformity (cochlear hypoplasia) rather than the more severe form (cochlear aplasia). This observation was consistent with previous findings [23]. We did not find any deficient cochlear nerve in the ears with endolymphatic duct dilatation, although one such case was reported previously [11]. The vestibular aqueduct grows throughout fetal life and continues postnatally until age 3 or 4 years [24], which is different from the development of the otic capsule and cochlear nerve early in embryonic development. The difference in developmental chronicity of cochlear nerve and vestibular aqueduct may explain the lack of concurrent endolymphatic duct dilatation and cochlear nerve deficiency observed in our study.

In this study, most ears with cochlear nerve deficiency had concurrent structural anomaly that can be detected by both CT or MRI. However, there were ten ears with isolated cochlear nerve deficiency that could only be detected by MRI, which represented 27% of ears with cochlear nerve deficiency. Clinically, children with SNHL who are candidates for cochlear implantation usually undergo MRI before final pretreatment evaluation. However, at times ENT surgeons may prefer to order a HRCT of temporal bone first for an overall evaluation. Besides, parents may concern about the risk of sedation for their children, and some children are not suitable for sedation due to medical issues. CT has a number of advantages, including ready availability, lower cost, faster scan time that reduces the need for sedation of children, and better cortical delineation of the ossicles, bony labyrinths, facial nerve canal, and jugular fossa. CT findings can assist the surgeon in choosing the appropriate type and size of cochlear implant. This study suggests that if IAC stenosis or cochlear malformation is detected by CT, there is a higher risk of cochlear nerve deficiency, and MRI is indispensable for definite results and more cost-effective treatment in such cases. In contrast, if an enlarged vestibular aqueduct is detected by CT, there is a better chance of the presence of a normal cochlear nerve.

In terms of choosing which ear for implantation, the ear without IAC stenosis or cochlear malformation is preferred due to lower risk of cochlear nerve deficiency,
leading to a higher likelihood of successful implantation. In the presence of cochlear nerve deficiency, the diameter of nerve fibers is also of clinical importance, which represents a disease spectrum ranging from nerve hypoplasia to aplasia and correlates with the number of spiral ganglion cell count [3]. It is important to remind the clinician of the different extent of disease severity in the imaging report for better outcome of cochlear implantation. Further study to elucidate the relationship between severity of cochlear nerve deficiency and degree of congenital malformations may be considered.

CONCLUSIONS

Congenital anomalies of the inner ear and IAC represent a spectrum of diseases that may be attributed to disturbance of the embryological development of the inner ear. Most ears with cochlear nerve deficiency have concurrent anomaly of the bony labyrinth or IAC. IAC stenosis and cochlear dysplasia were shown to be positive predictive factors for cochlear nerve deficiency with significant odds ratios of 23.0 and 16.0, respectively. In those children with IAC stenosis or cochlear dysplasia which may be detected by CT in advance, MRI should be performed for evaluation of cochlear nerve deficiency.

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