

3D-fluid-attenuated inversion recovery MR images in sudden hearing loss: audio vestibular correlations.

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Abstract

Objective This study aimed to investigate correlation between 4-hour delayed-enhanced 3.0 Tesla (3T) 3D-fluid-attenuated inversion recovery (FLAIR) MR images and audio-vestibular function in idiopathic sudden sensorineural hearing loss. **Setting** Tertiary center **Methods** All patients underwent 4-hour delayed-enhanced 3D-FLAIR MR imaging for identifying lesion-side laterality and enhanced labyrinth patterns. Audiologic and vestibular function tests were performed. Vestibular function test sum scores were additionally calculated by summing the scores on each test and defining normal as 0 and abnormal as 1. The hearing recovery was evaluated according to the American Academy of Otolaryngology-Head and Neck Surgery Criteria at 3 months after the end of treatment. **Results** Lesion-side laterality was identified in 31 (40.8%) of the 76 patients with ISSNHL and these patients had a lower hearing recovery rate ($P<0.05$). Furthermore, patients with a lower initial hearing threshold (dB), word recognition score, and lesion-side posterior semicircular canal gain displayed poorer hearing recovery ($P<0.05$). Initial hearing threshold and word recognition score did not change significantly as the extent of the enhancement in the labyrinth increased; however, the probability of being accompanied by vertigo and the total score on the vestibular function tests did increase ($P<0.05$). **Conclusions** Lesion-side laterality of the labyrinth in ISSNHL can be identified on 4-hour delayed-enhanced 3D-FLAIR MR images. The extent of enhancement in the labyrinth is associated with clinical findings such as impaired audio-vestibular function, and also with the prognosis of ISSNHL. **Keywords:** Idiopathic sudden sensorineural hearing loss, 4-hour delayed 3D FLAIR MRI, Audiovestibular function, Prognosis. **Level of Evidence;** 4

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Conclusions

Lesion-side laterality of the labyrinth in ISSNHL can be identified on 4-hour delayed-enhanced 3D-FLAIR MR images. The extent of enhancement in the labyrinth is associated with clinical findings such as impaired audio-vestibular function, and also with the prognosis of ISSNHL.

Keywords : Idiopathic sudden sensorineural hearing loss, 4-hour delayed 3D FLAIR MRI, Audio-vestibular function, Prognosis.

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Key Points

1. Sudden sensorineural hearing loss (SSNHL) is an emergent disease and significance of 4-hour delayed-enhanced 3D-FLAIR MR imaging for diagnosis or prognostic factor has not been studied thoroughly.
2. This retrospective study of the 76 patients with ISSNHL aimed to investigate correlation between 4-hour delayed enhanced 3D-FLAIR MRI and audio-vestibular function.
3. Lesion-side labyrinth lesions can be identified by 4hr delayed 3D-FLAIR MRI in patients with idiopathic sudden sensorineural hearing loss.
4. The extent of labyrinthine enhancement on 4hr delayed 3D-FLAIR MRI is related to the results of hearing and vestibular function tests.
5. As the extent of labyrinthine enhancement on 4hr delayed 3D-Flair MRI increased, vertigo became more common, and the sum of the vestibular function tests increased significantly.

Introduction

Idiopathic sudden sensorineural hearing loss (ISSNHL) is defined as sensorineural hearing loss that occurs suddenly with no clear cause, and involves hearing loss [?] 30 dB at [?] 3 consecutive frequencies in pure tone audiometry within 3 days from the onset of the symptom.(1) Although many underlying causes have been suggested such as vascular insufficiency, viral infection, auditory nerve tumors, ototoxic drugs, trauma, autoimmune diseases, and congenital anomalies, the exact cause and mechanism have not been elucidated. (2, 3) ISSNHL is frequently accompanied by ear fullness, tinnitus, and vertigo. Since vertigo is a subjective symptom related to the functioning of the inner ear, patients are generally given vestibular function tests. Once the video-head impulse test (vHIT) had been developed, all the vestibular end organs, including the three semicircular canals (SCCs), could be evaluated.(4) Steroids are widely used as standard treatment worldwide because of their effectiveness in restoring hearing; they are generally given orally or in combination with intratympanic administration of dexamethasone.(5, 6) Rapid diagnosis and treatment are required because if treatment is delayed, the prognosis may be affected, and the quality of life of the patient may decrease.(3)

It is crucial to divide patients with sensorineural hearing loss into cochlear and retro-cochlea pathologies. There are various hearing tests, notably the auditory brainstem response (ABR), for differentiating retro-cochlea pathologies. With the development of radiological examination, magnetic resonance imaging has come to be used to diagnose retro-cochlear lesion-induced hearing losses, such as those due to auditory nerve tumors. Currently magnetic resonance imaging is recognized as an accurate test for identifying retro-cochlea

pathologies rather than for detecting pathological changes of the lesion side inner ear.(7, 8) However, recent studies emphasize the usefulness of 4-hour delayed-enhanced 3.0 Tesla (3T) 3D-FLAIR MR images with double-dose intravenous gadolinium (Gd) for prognosis of ISSNHL and have suggested that focal contrast enhancements in the inner ear are due to breakdown of the blood-labyrinth barrier.(9, 10) Various MRI protocols have been introduced to identify subtle changes in the inner ear from the contrast enhancement period. There is a recent report that 4-hour delayed enhanced images can identify efficiently neuroinflammatory conditions in the inner ear. In contrast, 10-minute delayed enhanced images may be better at identifying non-neuroinflammatory findings.(11) Therefore, the aim of this study was to investigate the correlation between focal enhancement of the affected inner ear on 4-hour delayed-enhanced 3D FLAIR MRI and audio-vestibular function in ISSNHL, and to analyze its utility for prognosis.

Materials and methods

Study populations and subjects

A total of 323 patients with unilateral hearing loss visited our hospital from June 2016 to November 2020. The diagnostic criterion for idiopathic sudden hearing loss was sensorineural hearing loss \geq 30 dB at \geq 3 consecutive frequencies in pure tone audiometry without apparent cause within 3 days from the onset of the symptom. Patients with conductive hearing loss of \geq 10 dB and hearing loss due to trauma or retro-cochlear pathologies were excluded from the analysis. 76 patients were eventually diagnosed with ISSNHL and completed the study protocol; their medical records were retrospectively analyzed following STROBE guidelines, and all were treated with high-dose oral steroid for 5 days. If their hearing improved, the dose was gradually reduced over 7 days. If there was no improvement in hearing, the steroid dose was reduced, and intratympanic steroid was injected 4 times over 2 weeks. The study was reviewed and approved by the Institutional Review Board of “Blinded for review” (IRB FILE No: 2021-10-008).

Audio - vestibular tests

Audiologic and vestibular function tests, including the video-head impulse test (vHIT), cervical vestibular-evoked myogenic potential test (cVEMP), ocular vestibular-evoked myogenic potential test (oVEMP), and caloric test, were performed for diagnosis and evaluation. A single senior audiologist performed the tests. For all three semicircular canals, high-frequency vestibulo-ocular reflex (VOR) gains were measured by vHIT using an ICS Impulse (GN Otometrics, Taastrup, Denmark). VOR-gain abnormality was defined as VOR-gain <0.8 for horizontal canals or <0.7 for vertical canals.(12) The cVEMP testing saccule and the oVEMP testing utricle were used to evaluate otolith function, employing an auditory evoked potential system, the Biologic Navigator Pro (Biologic System Corp., IL). If the response was absent or the P1-N1 amplitude differed by $>30\%$ on the two sides, it was considered abnormal.(13) The horizontal canals were evaluated with the caloric test using a Visual Eyes 4-channel VNGTM (Micromedical Technologies, Illinois, USA) or an ICS Chartr 200 (GN Otometrics, Denmark). According to Jongnkee’s formula, if the canal paresis (CP) value was $\geq 30\%$, it was defined as abnormal.(14) Also, the vestibular function test was recalculated by summing the scores on each test including vHIT, o-cVEMP and the caloric test, and by defining normal as 0 and abnormal as 1 for each test.

Pure tone audiometry was performed at first visit and 3 months after the end of treatment to assess hearing recovery. The average hearing threshold was calculated by the hexadecimal method of 500, 1000, 2000, and 4000 Hz, and hearing recovery was evaluated according to the AAO-HNS hearing classification. Complete recovery was defined as hearing improvement with a difference of less than 10dB from the unaffected side, partial recovery as the hearing threshold improved by 10dB or more, and no recovery as the hearing threshold improved by less than 10dB.

3D-FLAIR MRI

4-hour delayed-enhanced 3D-FLAIR MRI using double-dose IV gadolinium was performed in all cases before treatment was started. All scans involved 3 Tesla MRI (Achieva 3T; Philips Healthcare, Best, The Netherlands) using a receive-only 32-channel phased array coil. 3D-FLAIR imaging was performed before

and after intravenous administration of a double dose of Gd-DTPA at 0.2 mmol/kg. Contrast-enhanced 3D-FLAIR was initiated 4 hours after Gd administration. Two head and neck radiologists evaluated the MR images visually and recorded them separately as positive or negative in terms of lesion-side laterality. The extent of enhancement in the inner ear was also assessed. Lesion-side laterality was defined when the MR image of the inner ear structure including cochlea, vestibule and semicircular canals showed obvious contrast enhancement and clear asymmetry compared to the unaffected ear (Figure 1). In our study, the extent of enhancement in the inner ear was classified as E0, E1 or E2. E0 was defined as the absence of lesion-side laterality; E1 as focal enhancement of the cochlea only, on the lesion side, and E2 as enhancement of the cochlea and other inner ear structures including vestibule and/or semicircular canals (Figure 2).

Statistics

Statistical analysis was performed using SPSS version 19.0 (IBM Corp., Armonk, NY, USA). Continuous variables were expressed as mean \pm standard deviation, and categorical variables as frequencies and ratios. Independent t-tests and one-way ANOVA were used for comparisons of continuous variables, and Pearson's chi-square test for categorical variables. P values <0.05 were considered statistically significant.

Results

Demographics

Of the total of 76 patients, 30 (39.5%) were male, and the mean age was 53.0 (± 14.3) years. In terms of underlying disease, 20 patients (26.3%) had hypertension, 22 (28.9%) diabetes mellitus, and 5 (6.6%) cardiovascular or cerebrovascular disease. The affected ear was on the right in 24 cases (31.6%), and there was no case where both sides were affected. The mean time to start treatment after symptom onset was 4.7 ± 10.5 days. At the time of admission, average hearing was 72.1 (± 9.3) dB on pure tone audiometry. Associated symptoms included vertigo (23, 30.3%), tinnitus (49, 64.5%), and ear fullness (52, 68.4%). Fifteen patients (19.7%) received only high-dose oral steroid therapy; since no hearing recovery was detected in the remaining 61 patients (80.3%) after administration of oral steroids, intratympanic steroid injection was added to the treatment. No patients received only intratympanic steroid. Thirty-six (47.4%) patients recovered their hearing completely according to AAO-HNS guidelines, 19 (25%) recovered their hearing partially, and 21 (27.6%) patients showed no improvement in hearing.

Factors associated with hearing recovery

Based on the AAO-HNS hearing classification, the patients were classified into three groups: complete, partial, and no hearing recovery. Table 1 compares certain characteristics of these groups. A history of cardiac or cranial vascular disease was significantly associated with recovery rate ($P=0.024$). Also, patients with normal oVEMP ($P=0.006$), high posterior semicircular canal gain in vHIT ($P=0.006$), a low initial hearing threshold ($P=0.000$) and better speech discrimination ($P=0.008$) had a better hearing prognosis.

Lesion-side laterality on 3D-FLAIR MRI

All 76 patients underwent 4-hour delayed-enhanced 3D-FLAIR MRI, and 31 (40.8%) had an obviously asymmetric enhancement of the inner ear structures. In all the latter cases, the asymmetry was in the affected ear. A comparison of clinical parameters according to presence or absence of lesion-side laterality is presented in Table 2. The recovery rate of patients with lesion-side inner ear enhancements was significantly lower than that of patients without such enhancement ($P=0.028$).

Extent of the enhancement in the labyrinth on 3D-FLAIR MRI

According to the extent of enhancement in the inner ear we divided the patients into groups E0, E1 and E2, corresponding to absence of lesion-side laterality, focal enhancement of cochlea only and enhancement of cochlea and other inner ear structures, respectively. Table 3 shows the associations between clinical parameters and extent of inner ear enhancement. There was no difference in sex, age, or comorbidity between these groups. Initial hearing in the three groups was 68.93 ± 23.14 dB in E0, 72.79 ± 25.17 dB in E1, and 82.67 ± 24.73 in E2, with no statistically significant difference between them. Speech discrimination

was 48.21+-40.41, 32.44+-39.57 29.82+-42.42, respectively, in the three groups, again with no statistically significant difference between them. Furthermore, the results of the vestibular function tests were not related to the extent of inner ear enhancement. However, as the extent of enhancement of the inner ear increased, vertigo became more frequent ($P=0.011$) and lateral canal gain declined or became abnormal ($P=0.030$, $P=0.020$).

Vestibular function test SUM scores

All patients underwent vestibular function tests including vHIT, a caloric test, oVEMP and cVEMP. Each test was scored as 0 for normal and 1 for abnormal. After summing the results of different combinations of tests, the resulting groups were compared in terms of the extent of inner ear enhancement. Table 4 shows that, for all the combinations of VHT tests (except oVEMP+cVEMP) the extent of abnormality of the test results increased significantly as the extent of lateral hyperintensity increased.

Discussion

We have studied the relationship between 4hr delayed 3D FLAIR MRI findings and audio-vestibular function in patients with idiopathic sudden sensorineural hearing loss (ISSNHL). Our results can be summarized as follows; (1) of 76 patients, 31 (40.4%) showed focal enhancement in the affected inner ear and the patients had a significantly lower hearing recovery rate than those without focal enhancement. (2) Hearing recovery was better when the initial hearing threshold was higher. (3) The lower the PSCC gain in vHIT, the poorer the hearing recovery rate. (4) While the individual vestibular function test results were not significantly correlated with the extent of enhancement in the labyrinth, the *sum* of the vestibular function tests was significantly correlated with the extent of enhancement.

ISSNHL is a medical emergency that lasts for several hours to several days without any specific cause, and its etiology has not been elucidated. Many factors are associated with the etiology and treatment of the disease, and for this reason we needed to evaluate a variety of aspects of the patients.

3D FLAIR MRI, which we used as a diagnostic tool for evaluating inner ear structure, is a routine type of brain MR imaging. It yields an image of the lesion restricted by water signal suggesting local hemorrhage and concentrated protein material due to an increase in permeability.(10) Additionally, after gadolinium injection, if there is breakdown of the blood labyrinth barrier (BLB) in the affected ear, the MRI identifies any contrast enhancement in the labyrinth. The breakdown of the blood labyrinth barrier (BLB) causes disruption of inner ear homeostasis and damages the inner ear structure. It can be associated with many pathological conditions such as infections, inflammation, hypoxia, and noise exposure, which resemble the causes of ISSNHL. Hence, focal enhancement and high-intensity signals on 3D-FLAIR images after injection of gadolinium are important findings in indicating various pathologic conditions of the inner ear.(15) 3D FLAIR MRI is also emerging as a clinical indicator of the prognosis of the disease after treatment, not only as a way to detect retro-cochlear lesion-induced hearing loss such as that due to auditory nerve tumors. There have been several studies of the usefulness of 3D FLAIR images in ISSNHL. In one study, a comparison was made between cases showing focal enhancement of the cochlear base only of the affected inner ear, those with enhancement of the whole inner ear including semicircular canals, and those with no inner ear enhancement.(16) It demonstrated that the greater the contrast enhancement in the labyrinth, the poorer the hearing prognosis..

In this study, we examined the correlation between the results of 4hr delayed 3D-Flair MRI with double-dose intravenous Gd and auditory-vestibular function in patients with ISSNHL, and assessed the value of 3D-Flair MRI as a prognostic factor. The percentage of patients with lesion-side laterality was 40.4%, which was similar to that in previous studies, and cases with lesion-side laterality had a significantly lower hearing recovery rate than those without laterality. Blood-labyrinth barrier breakdown, which affects inner ear homeostasis and structure, is thought to influence the prognosis for hearing recovery. One previous study of the relationship between the degree of hearing loss before treatment and hearing recovery after treatment reported that the prognosis was good when the average hearing threshold was below 45 dB between 500 and 2000 Hz.(17) Another study demonstrated that the greater the initial hearing loss, the poorer the prognosis.

(18) We confirmed the latter finding, with a statistically significant difference in recovery between the two groups. Another report suggested that abnormal vHIT gain in the posterior SCC is a specific predictor of incomplete hearing recovery in ISSNHL,(19) and we confirmed that the lower the PSCC gain in vHIT the poorer the hearing recovery after treatment. Furthermore, it has been reported that unilateral vestibular enhancement on 3D FLAIR MRI is not only associated with hearing prognosis but also with abnormal findings in vestibular function tests.(20) We were unable to confirm a significant association between the results of the individual vestibular function tests and the extent of lateral hyperintensity. However, we found that as the extent of labyrinthine enhancement on 4hr delayed 3D-Flair MRI increased, vertigo became more common, and the sum of the vestibular function tests increased significantly.

The limitations of this study are that it was a retrospective study also that the vestibular function of the patients could not be compared after treatment because the vestibular function tests were not repeated, since the vestibular function of the patients generally adjusted over time. In addition, two head and neck radiologists read the FLAIR MR images and there may have been subtle differences in the way they interpreted the images as there were no objective guidelines for radiologic interpretation. A prospective study with more cases and a maximum interval between the onset of ISSNHL and the beginning of treatment would be desirable, and would allow more accurate assessment of the clinical value of 4hr delayed 3D FLAIR MRI.

Despite these limitations, this report is noteworthy in that it discusses the relationship between 4hr delayed 3D FLAIR MRI, the prognosis of hearing after treatment and the results of vestibular function tests in ISSNHL. Although the results do not point to a change in treatment, they may be useful for developing a unified MR imaging protocol, and for making treatment decisions in the clinic.

Conclusions

In conclusion, we have shown that lesion-side labyrinth lesions can be identified by 4hr delayed 3D FLAIR MRI in patients with idiopathic sudden sensorineural hearing loss, and that the extent of labyrinthine enhancement is related to the results of hearing and vestibular function tests and prognosis of the disease.

Conflicts of interest

None of the authors have any conflicts of interest.

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