Lesion-specific prognosis by magnetic resonance imaging in sudden sensorineural hearing loss

Background: High signals in the inner ear of idiopathic sudden sensorineural hearing loss (ISSNHL) on MRI have been reported, but no quantitative evaluation has yet been done.

Objectives: To evaluate hearing outcomes and cochlear signal intensities on 3-T heavily T_2-weighted three-dimensional fluid-attenuated inversion recovery magnetic resonance imaging (hT_2W-3D-FLAIR) in patients with ISSNHL.

Materials and Methods: Twenty-nine patients with ISSNHL were included. Patients underwent hT_2W-3D-FLAIR with intravenous gadolinium injection and pure tone audiometry (PTA) at initial visits and three months later. Signal intensity ratios (SIRs) were measured in the basal or apical-middle turns of the affected cochlea. A statistical analysis of relationships between SIRs and the average hearing levels (HLs) at low (125, 250, and 500 Hz) and high (2, 4, and 8 kHz) tone frequencies was performed.

Results: Hearing improvements at high-tone frequencies in ears with HLs ≥60dB were significantly worse in those with high SIRs at the basal turns on pre-contrast images. Similarly, hearing improvements at low-tone frequencies in ears with HLs ≥60dB were significantly worse in those with high SIRs at the apical-middle turns on post-contrast images.

Conclusions and Significance: High SIRs on hT_2W-3D-FLAIR indicate cochlear disturbances with severe ISSNHL and could provide lesion-specific prognostic information.

Keywords: idiopathic sudden sensorineural hearing loss, heavily T_2-weighted 3D-FLAIR, quantitative analysis

Introduction

The pathogenesis of idiopathic sudden sensorineural hearing loss (ISSNHL) remains to be elucidated, but epidemiological studies have shown that a poor prognosis is related to age over 60 years, severe initial hearing loss, longer duration from onset of the disease to initial treatment, flat or down-sloping pattern on pure tone audiometry (PTA), presence of vertigo, and high signals in the cochlea on magnetic resonance imaging (MRI) [1,2]. High signals in the inner ear of ISSNHL on MRI were reported in 27%–53% of cases [3-5]. In our previous study, about 50% of patients with ISSNHL showed high signals in the affected inner ear on pre-contrast three-dimensional fluid-attenuated inversion recovery (3D-FLAIR) MRI [6], suggesting that the presence of high signals is associated with a poor hearing prognosis [6]. A meta-analysis reported that patients with high signals had a significantly lower chance of hearing recovery than those without them [1]. The presence of high signals on pre-contrast 3D FLAIR is considered to indicate the presence of minor haemorrhage or proteinaceous exudate, with an increased concentration of protein in the inner ear [3,6]. On the other hand, high signals on post-contrast 3D FLAIR are consistent with blood-labyrinth barrier breakdown, which indicates increased permeability due to inflammation occurring in the lateral wall of the cochlea [6-8]. The findings of previous MRI studies were based on qualitative analyses, but no quantitative evaluation has been done for ears with ISSNHL.

Systemic or local steroid administration has been widely used as treatment for ISSNHL. Steroids have a significant mineralocorticoid function, as demonstrated by increased function of ion homeostasis genes, implicating their ionic and fluid regulatory properties as a mechanism for their therapeutic effects [9]. Treatment including steroids is not effective for all cases with ISSNHL, and inner ear disturbances are different among cases with the disease.

A recent paper demonstrated that heavily T_2-weighted 3D-FLAIR (hT_2W-3D-FLAIR) was more sensitive to signal alterations in the cochlea with ISSNHL [10] than regular 3D-FLAIR. In the present study, signal intensities of inner ears with ISSNHL were quantitatively evaluated on hT_2W-3D-FLAIR to identify lesion-specific disturbances and their prognoses. The results may provide an additional clue to elucidating the pathogenesis of ISSNHL.

Materials and Methods

Subjects

A total of 49 patients with ISSNHL recruited at our department from January 2017 to June 2020 were evaluated. ISSNHL is defined as loss of 30 dB or more in at least three contiguous frequencies within 72 hours [11]. The study population consisted of 31 male and 18 female patients (average age 54 years; age range 14-90 years). Patients were treated within one week from presentation with intravenous systemic steroid therapy (hydrocortisone 200 mg per day for 4 days and then 100 mg for 3 days). If hearing recovery was insufficient, intratympanic steroid administration (dexamethasone 4 mg/ml, 0.4-0.6 ml) was given a maximum of 3 times at weekly intervals. During or after treatment, pre- and post-contrast examinations with intravenous gadolinium hT_2W-3D-FLAIR were performed. The exclusion criteria were acoustic neuroma, psychogenic HL, progressive HL, prior medical history of HL, other known causes of HL, or insufficient follow-up.

Pure tone audiometry (PTA)

PTA was performed at the initial visit and at the final hearing evaluation almost 3 months later using an Audiometer (Model AA-78; Rion, Tokyo, Japan). If the patients did not respond to the maximum level of sound, 5dB were added to each threshold.

According to the criteria for grading of hearing loss in ISSNHL proposed by the Research Committee of the Ministry of Health and Welfare for Acute Profound Deafness in Japan [12], the cases were divided into 4 grades (mean hearing level (HL) of the five frequencies: 250, 500, 1000, 2000, and 4000 Hz): grade 1, HL< 40 dB; grade 2, 40 dB ≤ HL< 60 dB; grade 3, 60 dB ≤ HL < 90 dB; and grade 4, HL ≥ 90 dB. In each ear, the average HLs for low-tone (125, 250, and 500 Hz) and high-tone (2, 4, and 8 kHz) frequencies were calculated. All patients were classified into a grade 1-2 group or a grade 3-4 group. To evaluate hearing outcomes, hearing recovery rates (HRRs) of low and high tone frequencies were calculated based on Siegel's criteria [13]: (initial hearing levels - final hearing levels) / (initial hearing levels – opposite ear hearing levels) ×100 (%) [14]. Ears with HRRs ≥ 80% were defined as those with better hearing recovery, and others were defined as having worse hearing recovery.

MRI

Imaging evaluation with hT_2W-3D-FLAIR was performed on a 3-T scanner (Verio, Siemens, Erlangen, Germany) using a 32-channel array head coil, according to the protocol [10]. All patients underwent hT_2W MR cisternography (MRC) for anatomical reference of the fluid space, and hT_2W-3D-FLAIR for evaluating labyrinthine fluid alterations in 7 minutes with a 2250 msec inversion time (TI) after MRC images using variable flip angle 3D turbo spin echo technique (SPACE, sampling perfection with application-optimized contrasts using different flip angle evolutions) and repetition time (TR) of 9000 msec. Immediately after intravenous administration of contrast agent (gadobutrol 0.1 mmol/kg; Gadovist; Bayer AG, Leverkusen, Germany), patients underwent T1-weighted 3D-volumetric interpolated breath-hold examination (VIBE) in 3 minutes and hT_2W-3D-FLAIR in 7 minutes again. These methods have been described in previous reports [6,10].

Qualitative evaluations of signal intensities in the cochlea on imaging were reported by radiologists who were blinded to clinical information. Calculations of signal intensities in the basal and apical-middle turns of each affected cochlea were quantitatively performed as follows: after obtaining images on SPACE of a region of interest (ROI), its copy was precisely pasted on images of hT_2W-3D-FLAIR, as shown in Figure 1A and B. On images visually containing the largest cochlear modiolus, the largest cochlear ROI was selected. Using the signal value of the cerebellar hemisphere as a control (Figure 1C), each signal intensity ratio (SIR) was calculated as signal intensity of the ROI / signal intensity of the cerebellar hemisphere.

Statistical analysis

The grade 1-2 and grade 3-4 groups were compared, with SPSS statistics 27 software (SPSS Inc., Chicago, IL, USA) used for the statistical analyses. The Mann-Whitney U test and Fisher's exact test were used, as appropriate, for the comparisons. The significance level was 5%.

The medical ethics committee of our institution approved this retrospective study (No. 2019-0504) with a waiver of written, informed consent from the patients.

Results

Two patients with acoustic neuroma, 1 with psychogenic HL, 2 with progressive HL, 6 with a prior medical history of HL, 6 with other known causes of HL, and 3 with insufficient follow-up were excluded. The characteristics of the subjects are summarized in Table 1. Ten patients in the grade 1-2 group (mean age 45 years, 30% female) and 19 patients in the grade 3-4 group (mean age 55 years, 21% female) were finally included in the study. Average durations from onset of the disease to initial treatment in the grade 1-2 group and the grade 3-4 group were 1.9 days and 2.2 days, respectively; the difference was not significant. Average durations from onset of the disease to MRI evaluations in the grade 1-2 group and the grade 3-4 group were 5.8 days and 7.8 days, respectively; the difference was not significant. Average HLs on the initial PTA at low- and high-tone frequencies in the grade 3-4 group were 75.0 dB and 83.9 dB, respectively, significantly higher than in the grade 1-2 group (52.0 dB and 49.2 dB, respectively) (both $p<0.01$). Average HLs on the final PTA at low- and high-tone frequencies in the grade 3-4 group were 36.2 dB and 54.0 dB, respectively, significantly higher than in the grade 1-2 group (18.5 dB and 31.0 dB, respectively) (both $p<0.05$). One patient in grade 1 and four patients in grade 2 who were given initial systemic steroid treatment recovered completely without intratympanic steroid. A 90-year-old patient classified as grade 4 was treated with intratympanic steroid for initial treatment because of his age. Others were given both systemic and intratympanic steroid administration.

In the grade 1-2 group, average pre-contrast SIRs in the basal and apical-middle turns were 1.98 (1.23-4.99) and 2.42 (1.74-3.95), respectively; average post-contrast SIRs in the basal and apical-middle turns were 2.32 (1.31-5.46) and 2.48 (1.83-4.87), respectively. In the grade 3-4 group, average pre-contrast SIRs in the basal and apical-middle turns were 2.84 (1.18-7.89) and 3.62 (1.10-8.19), respectively; average post-contrast SIRs in the basal and apical-middle turns were 3.38 (1.15-7.26) and 4.28 (1.33-8.40), respectively.

In the grade 1-2 group, 4 patients recovered with better hearing (HRRs ≥ 80%), and 6 patients had worse hearing at high-tone frequencies on the follow-up PTA. Similarly, at low-tone frequencies, 8 patients recovered with better hearing, and 2 patients had worse hearing. Concerning the comparison of SIRs between ears with better and worse hearing recoveries, pre-contrast SIRs of the basal turn and apical-middle turn were not significantly related to hearing recovery at high-tone frequencies (*p*=0.762, *p*=0.476) and at low-tone frequencies (*p*=0.178, *p*=0.089**)**. Post-contrast SIRs of the basal turn and apical-middle turn were not significantly related to hearing recovery at high-tone frequencies (*p*=0.114, *p*=0.762) and low-tone frequencies (*p*=0.400, *p*=0.711). In the grade 3-4 group, 4 patients recovered with better hearing and 15 patients had worse hearing at high-tone frequencies on the follow-up PTA. Similarly, 12 patients recovered with better hearing and 7 patients had worse hearing at low-tone frequencies. The SIRs were compared between those with better and worse hearing recovery (Figure 2). Pre-contrast SIRs of the basal turns in the group with worse hearing recovery at high-tone frequencies were significantly higher than in those with better hearing recovery (*p*=0.037). At high-tone frequencies, pre-contrast SIRs of the apical-middle turn were not significantly related to hearing recovery (*p*=0.062, *p*=0.643), and neither were post-contrast SIRs of the basal turn and of the apical-middle turn (*p*=0.152, *p*=0.062). Post-contrast SIRs of the apical-middle turn were significantly higher in the group with worse hearing recovery at low-tone frequencies than in those with a better hearing recovery (*p*=0.017). At low-tone frequencies, pre-contrast SIRs of the basal turn and apical-middle turn were not significantly related to hearing recovery (*p*=0.083, *p*=0.068), and neither were post-contrast SIRs of the basal turn (*p*=0.056).

Discussion

In the present study, signal intensities in the cochlea were evaluated with hT_2W-3D-FLAIR, which provides higher signal sensitivity than regular 3D-FLAIR [10]. In the grade 3-4 group, pre-contrast SIRs were significantly higher in the group with worse hearing recovery than in those with better hearing recovery at high-tone frequencies. This finding is consistent with our previous study [6], though a frequency-specific analysis was not performed in that study. Moreover, post-contrast SIRs of the apical-middle turn were significantly higher in the group with worse hearing recovery at low-tone frequencies than in those with better hearing recovery. This new finding has not been previously reported, including our previous study.

Concerning the clinical course of ears with ISSNHL, hearing recovery is generally better at lower frequencies than at higher frequencies. The reason for this is still to be elucidated. Animal studies by Wu and Hoshino [15,16] demonstrated that localized damage in the basal turn led to depression of apical endocochlear potentials (EPs), with eventual EP recovery without morphological changes. Degeneration of fibrocytes in the lateral wall causing a decrease in EPs may lead to hearing loss [7], and remodelling of the lateral wall may be associated with EP recovery [17].

The present study showed that high post-contrast SIRs in the apical-middle turns, not in the basal turns, were related to worse hearing recovery at low-tone frequencies in the grade 3-4 group. This result may indicate irreversible changes with breakdown of the blood-labyrinth barrier in the apical-middle turns. In addition, low post-contrast SIRs in the apical-middle turns were related to better hearing recovery at low-tone frequencies, and this finding may indicate reversible changes, with temporary damage of the lateral wall by EP depression in the apical-middle turns.

The end portion of the basal turn may be the most vulnerable to damage in ears with ISSNHL [18]. In the present study, high pre-contrast SIRs in the basal turns were related to worse hearing recovery at high-tone frequencies in the grade 3-4 group. These results demonstrate an association between high signals and their physiology in the corresponding lesions of the affected cochlea. The cases in the grade 1-2 group were not likely to show high signals in the cochlea compared to those with severe hearing loss.

This tendency matched the meta-analysis that showed that the presence of high signals in the inner ear indicated more severe initial hearing loss [1].

There are some limitations in this study. The sample size was unexpectedly quite small, partially due to the strict selection criteria for ISSNHL, and selection bias may have existed because of the retrospective nature of the study. We are planning a further study to investigate lesion-specific prognosis in detail with a larger number of cases by means of such sensitive MRI evaluations in patients with ISSNHL.

Conclusions

The presence of high SIRs on hT_2W-3D-FLAIR indicates cochlear disturbances in ears with ISSNHL. The results showed that quantitative evaluation on MRI provides lesion-specific prognostic information for diseased ears and clues to elucidate the pathogenesis of ISSNHL.

Disclosure statement

The authors report no conflict of interest.

References

[1] Gao Z, Chi FL. The clinical value of three-dimensional fluid-attenuated inversion recovery magnetic resonance imaging in patients with idiopathic sudden sensorineural hearing loss: a meta-analysis. Otol Neurotol. 2014;35(10):1730-1735.

[2] Kuhn M, Heman-Ackah SE, Shaikh JA, et al. Sudden sensorineural hearing loss: a review of diagnosis, treatment, and prognosis. Trends Amplif. 2011;15(3):91–105.

[3] Conte G, Di Berardino F, Sina C, et al. MR imaging in sudden sensorineural hearing loss. Time to talk. AJNR Am J Neuroradiol. 2017;38(8):1475-1479.

[4] Lee JI, Yoon RG, Lee JH, et al. Prognostic value of labyrinthine 3D-FLAIR abnormalities in idiopathic sudden sensorineural hearing loss. AJNR Am J Neuroradiol. 2016;37(12):2317–2322.

[5] Berrettini S, Seccia V, Fortunato S, et al. Analysis of the 3-dimensional fluid-attenuated inversion-recovery (3D-FLAIR) sequence in idiopathic sudden sensorineural hearing loss. JAMA Otolaryngol Head Neck Surg. 2013;139(5):456-464.

[6] Yoshida T, Sugiura M, Naganawa S, et al. Three-dimensional fluid-attenuated inversion recovery magnetic resonance imaging findings and prognosis in sudden sensorineural hearing loss. Laryngoscope. 2008;118(8):1433-1437.

[7] Mizutari K. Spontaneous recovery of cochlear fibrocytes after severe degeneration caused by acute energy failure. Front Pharmacol. 2014;5:198.

[8] Sugiura M, Naganawa S, Teranishi M, et al. Three-dimensional fluid-attenuated inversion recovery magnetic resonance imaging findings in patients with sudden sensorineural hearing loss. Laryngoscope. 2006;116(8):1451–1454.

[9] MacArthur C, Hausman F, Kempton B, et al. Intratympanic steroid treatments may improve hearing via ion homeostasis alterations and not immune suppression. Otol Neurotol. 2015;36(6):1089-1095.

[10] Naganawa S, Kawai H, Taoka T, et al. Heavily T2-weighted 3D-FLAIR improves the detection of cochlear lymph fluid signal abnormalities in patients with sudden sensorineural hearing loss. Magn Reson Med Sci. 2016;15(2):203-211.

[11] Wilson WR, Byl FM, Laird N. The efficacy of steroids in the treatment of idiopathic sudden hearing loss. A double-blind clinical study. Arch Otolaryngol. 1980;106(12):772-776.

[12] Nakashima T, Sato H, Gyo K, et al. Idiopathic sudden sensorineural hearing loss in Japan. Acta Otolaryngol. 2014;134(11):1158-1163.

[13] Siegel LG. The treatment of idiopathic sudden sensorineural hearing loss. Otolaryngol Clin North Am. 1975;8(2):467-473.

[14] Wilkins SA Jr, Mattox DE, Lyles A. Evaluation of a “shotgun” regimen for sudden hearing loss. Otolaryngol Head Neck Surg. 1987;97(5):474-480.

[15] Wu R, Hoshino T. Changes in off-lesion endocochlear potential following localized lesion in the lateral wall. Acta Otolaryngol. 1999;119(5):550–554.

[16] Wu R, Hoshino T. Long-term changes in off-lesion endocochlear potential after induction of localized lesions in the lateral wall. Ann Otol Rhinol Laryngol. 2001;110(3):271-276.
[17] Kitao K, Mizutari K, Nakagawa S, et al. Recovery of endocochlear potential after severe damage to lateral wall fibrocytes following acute cochlear energy failure. Neuroreport. 2016;27(15):1159–1166.
[18] Psillas G, Rizou A, Rachovitsas D, et al. Hearing outcome of low-tone compared to high-tone sudden sensorineural hearing loss. Int Arch Otorhinolaryngol. 2019;23(1):65-69.

Table 1. Characteristics of Patients with Idiopathic Sudden Sensorineural Hearing Loss

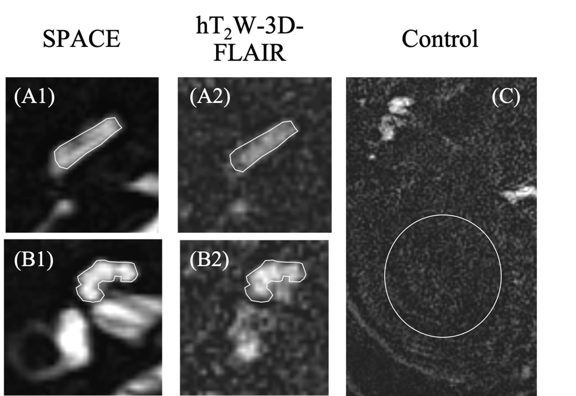
Figure 1. Example images to calculate the region of interest on hT_2W-3D-FLAIR. We draw the shape of each basal turn (A1) and apical-middle turn (B1) of the cochlea for the region of interest on the SPACE sequence, then copy both shapes (A2) (B2) to draw the region of interest on hT_2W-3D-FLAIR, using the signal value of the cerebellar hemisphere in the drawn circle (C) as a control. The image was obtained from a case with grade 3 right ear hearing loss. hT_2W-3D-FLAIR = heavily T_2-weighted three-dimensional fluid-attenuated inversion recovery; SPACE = sampling perfection with application-optimized contrasts using different flip angle evolutions.

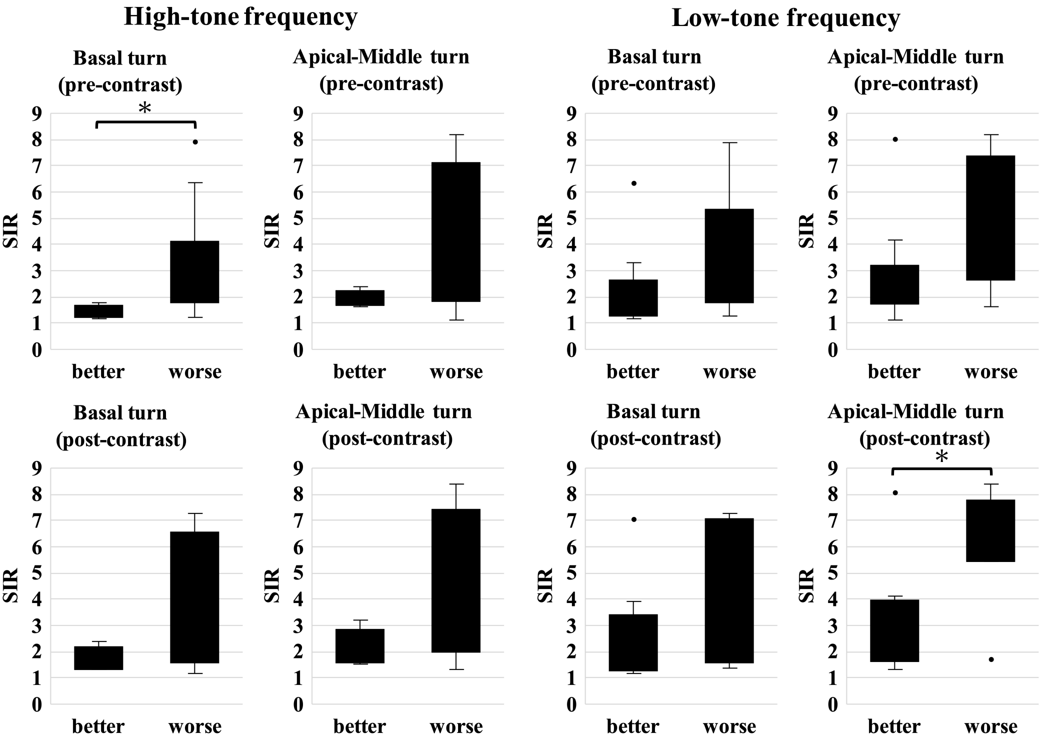
Figure 2. Comparison of SIRs between ears with better and worse hearing recoveries in the grade 3-4 group. Pre-contrast SIRs of the basal turns in the group with worse hearing recovery at high-tone frequencies are significantly higher than in those with better hearing recovery. Post-contrast SIRs of the apical-middle turn in the group with worse hearing recovery at low-tone frequencies are significantly higher than in those with better hearing recovery. SIRs = signal intensity ratios.

TABLE 1. Characteristics of Patients with Idiopathic Sudden Sensorineural Hearing Loss

Characteristic	Grades 1-2 n= 10 (±SD)	Grades 3-4 n= 19 (±SD)	*P* Value
Sex (female / male)	3 / 7	4 / 15	NS
Affected ear (right / left)	4 / 6	4 / 15	NS
Initial HL at high-tone frequencies (dB)	49.2 (±16.5)	83.9 (±14.7)	< .001**
Initial HL at low-tone frequencies (dB)	52.0 (±16.3)	75.0 (±13.9)	.004**
Final HL at high-tone frequencies (dB)	31.0 (±25.2)	54.0 (±19.2)	.024*
Final HL at low-tone frequencies (dB)	18.5 (±10.4)	36.2 (±24.1)	.031*
Duration from onset to initial treatment (days)	1.9 (±0.8)	2.2 (±1.5)	NS
Duration from onset to MRI (days)	5.8 (±2.6)	7.8 (±3.9)	NS

HL = hearing level; SD = standard deviation; MRI = magnetic resonance imaging; NS = non-significant; *p<0.05 **p<0.01


SPACE
hT2W-3D-FLAIR
Control
(A1)
(A2)
(B1)
(B2)
(C)


High-tone frequency
Low-tone frequency
Basal turn
(pre-contrast)
Apical-Middle turn
(pre-contrast)
Basal turn
(pre-contrast)
Apical-Middle turn
(pre-contrast)
Basal turn
(post-contrast)
Apical-Middle turn
(post-contrast)
Basal turn
(post-contrast)
Apical-Middle turn
(post-contrast)
SIR
better
worse
*
0
1
2
3
4
5
6
7
8
9