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ORIGINAL RESEARCH

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Perilymphatic enhancement and endolymphatic hydrops: MRI findings and clinical associations

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Abstract

Objective: In this study, we aimed to summarize magnetic resonance imaging (MRI) findings of perilymphatic enhancement (PE) and endolymphatic hydrops (EH) of the inner ear, which are associated with vestibular and cochlear symptoms.

Methods: We analyzed data on ears with definite Meniere's disease (MD), sensorineural hearing loss (SNHL), vertigo, and listening difficulties (LiD) from 508 ears of 254 patients who underwent contrast-enhanced 3-Tesla MRI between April 2021 and March 2023. We evaluated the degree of endolymphatic hydrops (EH), signal intensity ratios (SIRs) between the basal turns of the cochlea and cerebellum, and hearing levels for all ears. Ears with definite MD were also assessed for changes in vestibular and cochlear symptoms within 6 months.

Results: Ears with definite MD exhibited significantly higher percentages of EH in both the vestibule and cochlea compared with ears with other diseases. Furthermore, ears with MD or sensorineural hearing loss (SNHL) had significantly higher SIRs of PE compared with ears with other diseases or asymptomatic ears. Among patients with definite MD, those experiencing hearing fluctuations or vertigo attacks within the last 6 months had significantly higher SIRs of PE compared with those who did not experience any symptoms.

Conclusion: Significant EH in the vestibule and cochlea was a major finding for the imaging diagnosis of definite MD. A high SIR of PE was a good indicator for assessing MD activity, reflecting vestibular and cochlear symptoms and fluctuations.

Level of Evidence: 4.

KEYWORDS
endolymphatic hydrops, Meniere's disease, perilymphatic enhancement

1 | INTRODUCTION

Endolymphatic hydrops (EH), in which endolymph accumulates in the inner ear for various reasons, is known to cause symptoms such as vertigo attacks, hearing loss, and tinnitus. EH is a characteristic sign of Meniere's disease (MD) and is also found in other atypical MD, such as the cochlear or vestibular type; sensorineural hearing loss (SNHL)[1]; and listening difficulties (LiD).[2] The pathogenesis of MD is considered

to be idiopathic EH, and secondary EH can also develop after an infection or other inner ear disease.[1] The effect of EH on the symptoms of MD remains unelucidated, although several hypotheses have been proposed. These hypotheses include the drainage hypothesis, in which debris is retained in the vestibular aqueduct, resulting in EH and causing attacks attributed to the changes in pressure[3]; the rupture of Reissner's membrane hypothesis[4]; and K + intoxication theory.[5] EH can be visualized using 3-Tesla magnetic resonance imaging (MRI) performed 4 h after intravenous administration of gadolinium-based contrast agents (GBCA).[6,7]

Recently, heavily T2-weighted three-dimensional fluid-attenuated inversion recovery (hT2W-3D-FLAIR), which has a higher sensitivity to pathological signal changes in the cochlea than conventional contrast-enhanced 3D-FLAIR, has emerged. This imaging method displays greater sensitivity to subtle T1 changes in lymph fluid and more pronounced contrast effects.[8] The signal intensity ratio (SIR) of the cochlea and cerebellum in hT2w-3D-FLAIR in idiopathic sudden SNHL was associated with a frequency-specific hearing prognosis and could be a good indicator of blood labyrinthine barrier impairment.[9] A combined evaluation of the degree of vestibular EH and cochlear perilymphatic enhancement (PE) is reportedly useful for diagnosing MD.[10] However, we had experienced a case in which high PE appeared before symptoms and EH on MRI, suggesting that alterations of vascular permeability in the blood labyrinthine barrier (BLB) may have led to the formation of EH.[11] Thus, in this study, we aimed to evaluate the signal intensity of PE on hT2W-3D-FLAIR and EH on MRI in cases with vestibular and cochlear symptoms to elucidate the inner ear pathophysiology.

2 | MATERIALS AND METHODS

The study included cases of definite MD, SNHL, vertigo, and LiD from 508 ears of 254 patients who underwent contrast-enhanced 3-Tesla MRI between April 2021 and March 2023. Ears with the following conditions were excluded from the present study: a medical history of otitis media, postoperative cases, otosclerosis, probable MD, fluctuating hearing loss, and delayed endolymphatic hydrops (DEH). We used the diagnostic and staging criteria of MD and DEH according to the criteria proposed by the Japan Society for Equilibrium Research (JSER),[12] that is, cases with recurrent vertigo attacks accompanied by fluctuating hearing symptoms were diagnosed as MD. Cases with nonrecurrent (one-time) sensorineural hearing loss of unknown cause were diagnosed as SNHL, and cases with only vestibular symptoms and no cochlear symptoms were diagnosed as vertigo. Patients with normal hearing but complaining of listening difficulties and without vestibular symptoms were considered to have LiD.[2] All ears were evaluated for the degree of EH, SIRs of PE, hearing levels on pure tone audiometry (PTA), and change of vestibular and cochlear symptoms within 6 months.

2.1 | Hearing level

Hearing thresholds on PTA, at frequencies of 125–8000 Hz, were measured using an audiometer (AA-79, Rion, Tokyo, Japan), and the average values of thresholds at 500, 1000, and 2000 Hz in each ear of the participants were calculated. Hearing changes in MD were defined as an average ≥10 dB variation in the three lowest (125, 250, and 500 Hz) or three middle frequencies (500, 1000, and 2000 Hz) on PTA.

2.2 | MRI

Ears were evaluated using an MRI performed 4 h after intravenous injection of a standard GBCA dose (0.1 mL/kg body weight). All scans were performed using a 3-T MRI scanner (Trio or Verio; Siemens, Erlangen, Germany, or Vantage Centurian; Canon Medical Systems, Tochigi, Japan) equipped with a receive-only, 32-channel, phased-array coil. The presence of EH was investigated on a hybrid of a reversed image of the positive endolymph signal and a native image of the positive perilymph signal (HYDROPS), a hybrid of a reversed image of magnetic resonance cisternography and the positive perilymph signal observed using hT2w-3D-FLAIR, and three-dimensional real inversion recovery sequences.[13] The degrees of EH in the cochlea and vestibule using three grades (none, mild, and significant), according to the criteria described previously,[14] by at least two radiologists blinded to the patients' clinical courses. They also measured the ratio of the area of endolymphatic space to the vestibular space (sum of the endolymphatic and perilymphatic spaces).

2.3 | SIRs of PE in the cochlear

In hT2w-3D-FLAIR, the cochlear signal value of PE was measured at the basal turn of the scala tympani, whereas the cerebellar signal value was set as a 10 mm diameter circle in the ipsilateral cerebellar white matter (Figure 1). Each SIR of PE between the cochlea and cerebellum was calculated using the signal value of the cerebellum as a control.

All statistical analyses were performed using SPSS IBM Statistics version 28 (IBM Corporation, Armonk, NY). The χ^2 test, Kruskal-Wallis's test, and Mann–Whitney *U* test were used for statistical analyses. All procedures performed in studies involving human participants were in accordance with the ethical standards of our institutional research committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards, and informed consent has been obtained for the study. The study was approved by the ethics review committee of Nagoya University School of Medicine, Nagoya, Japan (approval number 2023-0152).

3 | RESULTS

Table 1 shows a summary of diseases, number of ears, and sex and age of patients for each ear. Definite MD was more common in men, whereas other diseases were more common in women. Most patients were middle-aged, with a median age of approximately 60 years, except for LiD patients. Figure 2 shows the EH evaluation for each case; EH in the entire vestibule was significantly higher in ears with

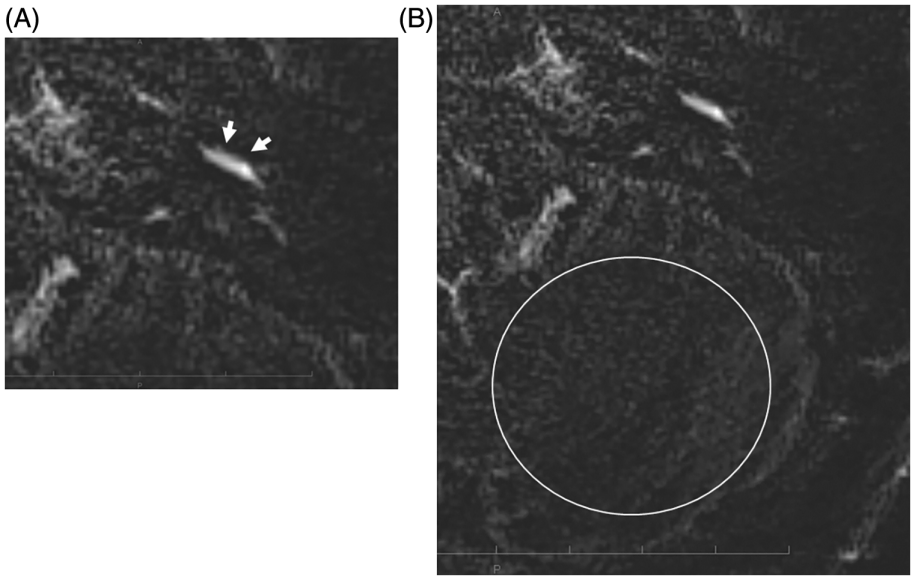

FIGURE 1 Representative image showing the measurement of signal intensity (SI) in regions of interest in the most artifact-free areas of (A) the basal turn of the scala tympani (arrows), and (B) cerebellum (white circle).

TABLE 1 Shows summary of diseases, number of cases, gender, and age of each ear.

Case	Ear	Sex		Age (average)
		Male	Female	
Affected ear of definite MD	53	38	15	60
Affected ear of sensorineural hearing loss	35	14	21	63
Vertigo	20	8	12	51
Listening difficulties	51	16	35	23
Contralateral asymptomatic ear	51	29	22	59

Abbreviation: MD, Meniere's disease.

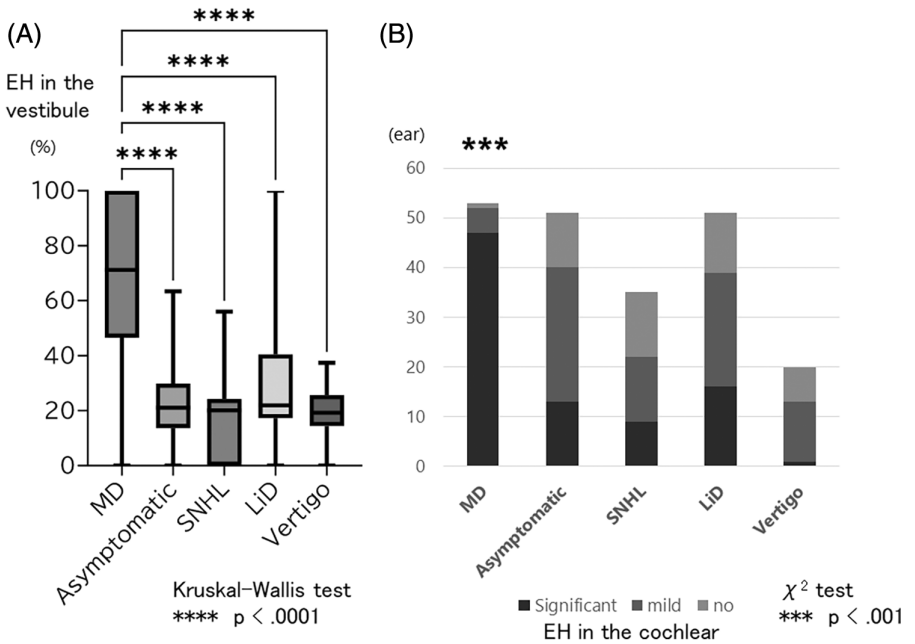

FIGURE 2 (A) The percentage of endolymphatic hydrops (EH) in the vestibule of ears with Meniere's disease (MD), sensorineural hearing loss (SNHL), listening difficulty (LiD), vertigo, and an asymptomatic ear is shown. Ears with MD had a significantly higher ratio of vestibular EH than ears with other diseases. (B) The degree of EH in the cochlea of ears with MD, SNHL, LiD, vertigo, and asymptomatic ear is shown. Ears with MD had a significantly higher cochlear EH than ears with other diseases.

definite MD than in ears with other diseases (p <.0001). Moreover, ears with definite MD showed more significant EH in the cochlea than ears with other diseases (p<.001).

Comparing the hearing level and SIR value for each case, ears with MD and SNHL had significantly worse hearing than ears with other diseases and asymptomatic contralateral ears (p <.0001).

Case	Hearing (dB) (average)		SIR (average)	
Affected ear of definite MD	51.8	****	9.71	***
Affected ear of sensorineural hearing loss	51.5	****	9.6	**
Vertigo	17.3		6.98	
Listening difficulties	10		6.8	
Contralateral asymptomatic ear	18.4		7.59	

TABLE 2 Shows the average hearing level and SIR of each case.

Note: Ears with Meniere's disease (MD) and sensorineural hearing loss (SNHL) had significantly worse hearing than ears with other diseases and asymptomatic contralateral ears (p <.0001). Furthermore, the SIR value of ears with MD and SNHL was significantly higher than that of ears with other diseases and asymptomatic contralateral ears (p <.001, .01).
Abbreviations: MD, Meniere's disease; SIR, Signal intensity ratio.
Kruskal-Wallis test: ****p <.0001; ***p <0.001; **p <.01.

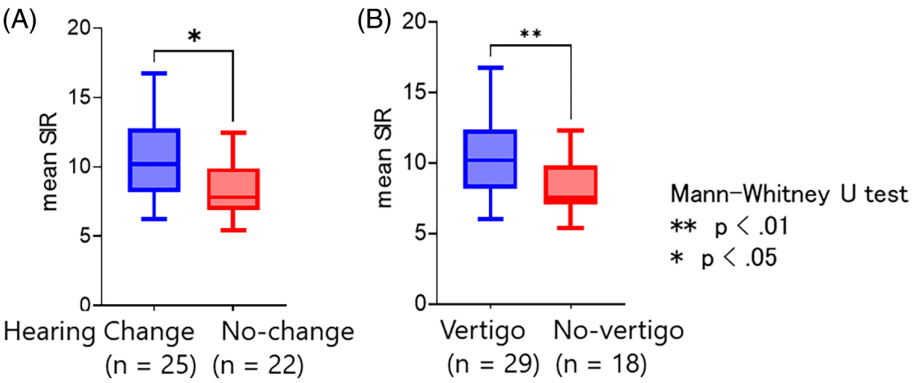

FIGURE 3 The relationship between the signal intensity ratio (SIR) of PE and hearing changes (A) and vertigo attacks (B) within 6 months in patients with MD is shown. SIR was significantly higher in the group experiencing changes within 6 months compared with the group that did not experience change.

Furthermore, the SIR value of ears with MD and SNHL was significantly higher than that of ears with other diseases and asymptomatic contralateral ears (p <.001, .01) (Table 2).

The relationship between MRI findings and hearing changes and vertigo attacks within 6 months in patients with MD was investigated. The SIR value in ears with MD was significantly higher in those with hearing changes than in those without ($p = .011$). The SIR value was significantly higher in patients with vertigo attacks than in those without ($p = .006$) (Figure 3). In addition, changes in hearing and vertigo attacks were unrelated to the percentage of cases with EH in the vestibule. Nine cases were diagnosed with bilateral MD, of which four had vertigo attacks and hearing changes on only one side of the ear within 6 months. In those four cases, SIRs were higher in the ear with hearing change than in the contralateral ear.

4 | DISCUSSION

In this study, we evaluated PE and EH in cases with definite MD, SNHL without hearing fluctuations and vestibular symptoms, vertigo without auditory symptoms, and LiD without hearing loss and vestibular symptoms. Because contralateral ears, often compared in previous reports, have been reported to harbor asymptomatic EH potentially, we classified them as asymptomatic ears in this study and chose LiD patients as a reference for normal ears without hearing impairment or vestibular symptoms. We found that, as in previous studies, significant vestibular and cochlear EH was present on the MRI of ears with a definite MD diagnosed based on the symptoms.[15] In addition, ears with definite MD and SNHL, that is, ears with auditory symptoms, had higher SIRs of PE in the cochlear basal turn than ears with vertigo, LiD, and asymptomatic contralateral ears, that is, ears without auditory symptoms. A previous study demonstrated that older people had higher PE than younger people[16]; in the present study, SIRs of ears with definite MD and SNHL were significantly higher than in other groups regardless of age because, on average, patients other than those with LiD were around the same age. Although definite MD and SNHL were classified based on vestibular symptoms and hearing fluctuations, both showed high SIR values on average and did not significantly differ, indicating that SIR could not be used to distinguish definite MD from SNHL. Therefore, these results showed that ears with hearing loss have higher SIR values, and we reconfirmed that the presence of significant EH was a major indicator for a definite MD diagnosis, whereas PE can be a corroborating indicator. Therefore, in facilities where EH cannot be evaluated, patients with SNHL ears with high SI values should pay attention to the appearance of cochleovestibular symptoms in the future.

High signal on precontrast 3D-FLAIR imaging of the inner ear in patients with sudden deafness was associated with a poor hearing prognosis, suggesting that high signal reflected minor hemorrhage, increased vascular permeability, and an elevated concentration of protein originating from disrupted cells.[17] Postcontrast high signal may indicate disruption of the BLB, which primarily functions in the stria

vascularis and cochlear spiral ligament in the cochlea, resulting in increased passage of GBCAs and proteins into the perilymph.[18] Owing to disrupted vascular integrity in the stria vascularis and disturbed endolymph ion homeostasis, BLB disruption would eventually result in hearing impairment.[19] Thus, the high signal observed in the hT2w-3D-FLAIR image of ears with hearing impairment due to MD and SNHL was considered to indicate inner ear impairment due to BLB disruption.

High cochlear PE in definite MD was associated with recent hearing fluctuations and vertigo attacks, and such findings on MRI obtained near the attack phase in definite MD may help elucidate the mechanism of MD attacks. In MD, EH grade was significantly correlated with the contrast effect, suggesting BLB impairment in MD.[20] Pathological degeneration of the BLB was associated with edematous changes within the vestibular stroma.[21] Thus, an MD attack may be caused by dysfunctional inner ear blood flow, which is exacerbated by the pathological increase in vascular permeability of the BLB owing to increased endolymphatic pressure or Reissner's membrane rupture. From a therapeutic perspective, definite MD cases with significant vestibular EH and high cochlear PE signal intensity were considered to have symptomatic EH; such cases require treatment and necessitate a careful follow-up.

In the present study, the signal value of PE was measured at the basal turn of the scala tympani. Although the signal value at the vestibule might be high in ears with vestibular symptoms due to inner ear damage, we did not measure the signal value of the vestibule. Previous studies showed that significant EH, which occupied almost the entire vestibule, was common in ears with definite MD, thereby making accurate measurement of signal value impossible.[10] In our study, not only changes in cochlear symptoms but also changes in vestibular symptoms were shown to be related to the SI value of the basal cochlear rotation. Though vestibular SI values were difficult to measure in the presence of EH, vestibular symptoms were shown to be related to the SI value at the basal turn of the scala tympani, which could estimate the activity of vestibular symptoms. Our findings could be particularly useful in selecting treatment for a definite MD. It is the first study to evaluate the signal intensity of PE using hT2W-3D-FLAIR for each inner ear disease. In the future, we would like to evaluate changes in SI values sequentially to assess the relationship between the treatment effect of MD and vascular permeability. In addition, in ears without vestibular EH but with vestibular impairment, we hypothesized that calculating the SI values of the vestibule could provide insights into the degree, activity, and prognostic implications of vestibular impairment when compared with vestibular function. Comparing cochlear and vestibular PE signal intensities may further help elucidate the mechanisms of vertigo.

5 | CONCLUSIONS

Significant EH in the vestibule and cochlea was a major finding in the imaging diagnosis of definite MD, with high postcontrast signal intensity in the cochlea as an additional finding. High postcontrast signal intensity was common in ears with hearing loss, indicating that BLB disruption reflects the recent symptoms, particularly in cases of definite MD.

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CONFLICT OF INTEREST STATEMENT

The authors have no conflicts of interest to disclose.

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