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3D-real IR MRI of Meniere's disease with partial endolymphatic hydrops

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ABSTRACT

Objectives: A three-dimensional inversion-recovery sequence with real reconstruction (3D-real IR) sequence 4 h after intravenous gadolinium injection (IV) has been used to visualize the endolymphatic hydrops (ELH) in Meniere's disease (MD). This study was designed to explore the pathology of MD with partial ELH.

Methods: We collected 338 patients with definite MD, all of whom underwent the IV method. Patients who were found to have partial ELH (vestibular or cochlear) were enrolled. The hearing thresholds of the enrolled patients were analyzed, the regions of interest of the cochlear perilymph and the cerebellum white matter were determined, and the signal intensity ratio in the former to the latter (CC ratio) for both sides in the patients was subsequently evaluated.

Results: Of the 338 collected patients with definite MD, 19 patients (5.6%) had unilateral vestibular ELH ($N = 18$) or cochlear ELH (N = 1), and 4 patients (1.2%) with bilateral ELH had contralateral cochlear ELH. The CC ratio of the affected side (1.44 ± 0.46) was higher than that of the unaffected side (1.15 ± 0.33, $P < 0.05$) in the 19 patients with unilateral ELH. Conversely, there was no difference between the ratio of the contralateral side (1.18 ± 0.16) and the unaffected side ($P > 0.05$) in the 4 patients with bilateral ELH.

Conclusions: Partial vestibular ELH was more common than partial cochlear ELH in MD. Moreover, vestibular ELH, rather than cochlear ELH, may correlate with the elevated contrast effect in the affected side, which may better reflect the pathologic mechanism of MD.

1. Introduction

Meniere's disease (MD) is a poorly understood inner ear disorder characterized by spontaneous vertigo attacks, fluctuating hearing loss, tinnitus and aural fullness. Its pathological hallmark is underlying endolymphatic hydrops (ELH) [1]. Recently, extensive use of gadolinium (Gd) contrast-enhanced MRI has enabled the depiction of ELH [2,3]. MRI following intratympanic Gd injection (IT method) [4] or intravenous Gd injection (IV method) [5] has been used to visualize ELH in MD. The IV method is less invasive, is independent of the condition of the round window membrane [6], and results in more uniformly distributed Gd [7] compared to the IT method. Moreover, the IV method allows the simultaneous visualization of the bilateral labyrinth [5], enabling MRI to ascertain bilateral blood-labyrinth-barrier permeability.

To our knowledge, MD remains a mysterious disease with an unclear pathogenesis; thus, investigating detailed MR images may contribute to illustrating the pathology of MD. The intensity ratio in the cochlea to the cerebellum white matter (CC ratio) can better reflect the change in the signal intensity of the cochlea. In a recently published study, the CC ratio of the affected side (1.39 ± 0.37) was higher than that of the unaffected side (1.18 ± 0.29, $P < 0.01$) in 115 patients with unilateral MD. However, the relationship between elevated contrast effect and vestibular or cochlear ELH remains unclear.

Therefore, patients with definite MD confirmed by the proposed diagnostic criteria were included in our study, all of whom underwent the IV method, and MRI images were used to analyze the grade of ELH. Ultimately, patients with vestibular or cochlear ELH were enrolled, and the characteristics of perilymphatic enhancement were analyzed by combing our previous study.

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2. Materials and methods

2.1. Patients

Of the 338 patients with definite MD, all of whom conformed to the diagnostic criteria of definite MD [8], patients with partial ELH were included from March 2016 to January 2019. Neurotologic evaluations were performed, including electro-otoscopy, audiometry and tympanometry. The study obtained permission from the medical ethics committee of the Eye, Ear, Nose, and Throat Hospital of Fudan University (Shanghai, China), and all patients signed an intravenous Gd contrast operation consent form.

2.2. Pure tone audiometry test

Hearing thresholds were tested regularly, including not > 7 days before Gd intravenous injection in all patients. Low-frequency (125, 250, 500 Hz), median-frequency (1 kHz, 2 kHz) and high-frequency (4 kHz, 8 kHz) hearing thresholds were evaluated to analyze the hearing threshold in each patient's partial ELH ear.

2.3. IV Gd injection and MRI acquisition

All patients underwent an IV injection of a double dose (0.4 mL/kg body weight) of Gd-HP-DO3A; 4 h later, MRI was performed on each patient. For the IV method, all scans were performed on a 3 T MRI scanner (Verio; Siemens Healthcare, Erlangen, Germany) using a 32-channel phased array receive-only coil. Three-dimensional sampling perfection with application optimized contrasts using different flip angle evolution (3D-SPACE) and three-dimensional inversion-recovery sequence with real reconstruction (3D-real IR) sequence MRIs were applied for collecting images. The parameters for the 3D-SPACE sequence were as follows: slice thickness = 0.6 mm; repetition time = 1000 ms; echo time = 132 ms; flip angle (FA) = 120°; field of view = 200 × 100 mm^2; and scan time = 2 min and 44 s. The parameters for the 3D-real IR sequence were as follows: voxel size = 0.17 × 0.17 × 0.6 mm; scan time = 15 min and 20 s; repetition time = 6000 ms; echo time = 181 ms; inversion time = 1850 ms; slice thickness = 0.6 mm; field of view = 160 × 160 mm; and matrix size = 768 × 768.

2.4. Image evaluation

T2-space imaging was used to rule out vestibular schwannoma or other causes of vertigo and hearing loss. The grades of ELH were evaluated according to the expansion of the vestibule and cochlea, which were classified into three stage gradings: none or mild, moderate and significant by the Nakashima grading standard [9] (Table 1). The ELH stage gradings were judged by two experienced radiologists who were blinded to the diagnosis of all patients. The 2 radiologists conducted their assessments independently in the radiology department. For each patient with partial vestibular or cochlear ELH, we randomly determined three points on both the basal turns of the cochleae and on a coplanar circular 50-mm^2 region of interest in the cerebellum white matter on 3D-real IR images (Fig. 1). The intensity ratio of the cochlea to cerebellum white matter (CC ratio) was calculated. The data were analyzed with the blinding of clinical diagnosis status. Moreover, Photoshop CS4 (Adobe Systems, San Jose, CA) was used to calculate the area ratio of the endolymphatic space to the vestibular space.

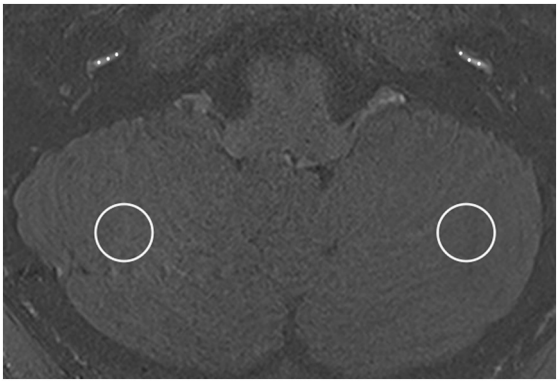


Fig. 1. A 3D-real IR image at the level of the cochlear basal turns after IV gadolinium injection with left MD is presented. On this image, three points of interest on the scala tympani of both cochlear basal turns and a 50-mm^2 circular region of interest on the cerebellar white matter coplanar with the basal turn of both cerebellar hemispheres were set.

2.5. Statistical analysis

Statistical analyses were performed using the SPSS Statistics 17 software package (IBM, Chicago, IL, USA). Data are shown as the mean ± SD. A paired *t*-test was used to compare differences in the CC ratio between the affected and unaffected sides in patients with cochlear or vestibular ELH. Differences were considered statistically significant when $P < 0.05$.

3. Results

3.1. Demographics

The group consisted of 19 patients (female = 7, male = 12) with partial ELH and with an age at presentation of 55.3 ± 10.5 (range, 40–78) years, an onset age of 51.1 ± 9.6 (range, 32–67) years, and a disease duration of 22.9 ± 41.7 months. Additionally, 4 patients with bilateral ELH (female = 1, male = 3) who had contralateral cochlear ELH, an age at presentation of 44.8 ± 22.4 (14–67) years, an onset age of 30 ± 26.9 (11–49) years, and a disease duration of 42 ± 8.5 months were included. Of the 23 individuals, no patients had morbidity.

3.2. Clinical characteristics

A total of 338 patients were diagnosed as having definite MD according to the diagnostic criteria, presenting with episodic vertigo and fluctuating sensorineural hearing loss. In patients with unilaterally vestibular ELH, the low-frequency, median-frequency and high-frequency hearing thresholds in the affected ear were 39.4 ± 20.5 dB, 37.2 ± 22.4 dB and 51.8 ± 21.0 dB, respectively, during the last hearing threshold measurement before the MRI was conducted. In the

Table 1
Three-stage grading of ELH using MRI.

Degree	Vestibule (area ratio)[a]	Cochlea
None or mild hydrops	≤1/3	No displacement of Reissner's membrane
Moderate hydrops	1/3 < , ≤1/2	Displacement of the Reissner's membrane, but the area of the endolymphatic space didn't exceed the area of the scala vestibule
Significant hydrops	1/2 <	The area of the endolymphatic space didn't exceed the area of the scala vestibule

[a] The area ratio of the endolymphatic space to the vestibular fluid space (sum of the endolymphatic and perilymphatic space).

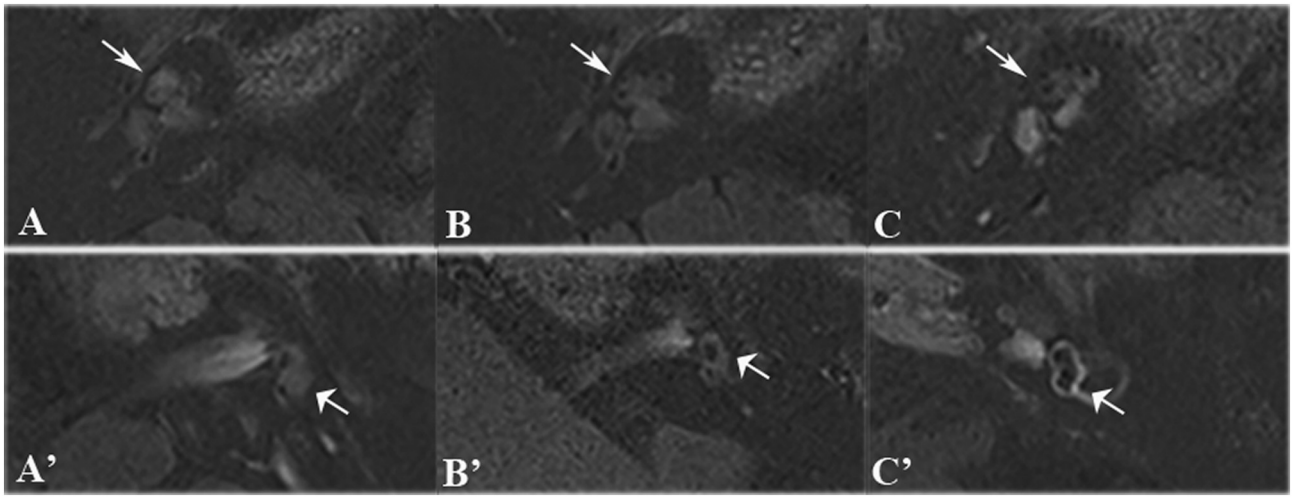


Fig. 2. 3D-real IR MRI scans of patients with different degrees of ELH. A–C, images of cochlear ELH. A, No ELH in cochlea, B, moderate ELH in cochlea, C, significant ELH in cochlea; A′–C′, images of cochlear ELH. A′, No ELH in vestibule, B′, moderate ELH in vestibule, C′, significant ELH in vestibule. Cochlea (thin arrows) and vestibule (broad arrows).

patient that had unilateral cochlear ELH for one year, the disease manifested as recurrent dizziness, accompanied by aural fullness and tinnitus, and hearing thresholds of 45.0 ± 10.0 dB, 25.0 dB and 60.0 ± 14.1 dB in all frequencies. Conversely, the hearing thresholds in the contralateral ear of the 4 patients with bilateral ELH were 20.4 ± 0.83, 20.6 ± 3.1; 34.4 ± 15.3 dB did not show an apparent decrease.

3.3. Imaging findings

Of 338 MD patients, 19 patients (5.6%) had unilateral vestibular (N = 18) or cochlear ELH (N = 1), while 4 patients (1.2%) with bilateral ELH had contralateral cochlear ELH. The ELH grading was based on the Nakashima grading standards (Fig. 2). Among the 19 patients with unilateral partial ELH, the moderate and significant grades of ELH accounted for 26.3% (5/19) and 68.4% (13/19) in patients with vestibular ELH, while only one patient [5.3% (1/19)] had moderate cochlear ELH. Four patients (1.2%) with bilateral ELH had contralateral significant cochlear ELH.

The CC ratio of the affected side (1.44 ± 0.46) was higher than that of the unaffected side (1.15 ± 0.33, P < 0.05) in the 19 patients with unilateral ELH (Fig. 3A, C), and according to an analysis of 115 patients with unilateral MD in our previous study, there was no difference compared to the affected side (1.39 ± 0.37, P > 0.05). Meanwhile, the CC ratio of the contralateral silent side in cochlear ELH (1.18 ± 0.16) (Fig. 3B, C) showed no difference when compared with the unaffected side (1.15 ± 0.33) in 4 patients with bilateral ELH (P > 0.05). The CC ratio of the affected side and unaffected side of the patient with unilateral cochlear ELH was 1.23 vs 1.02.

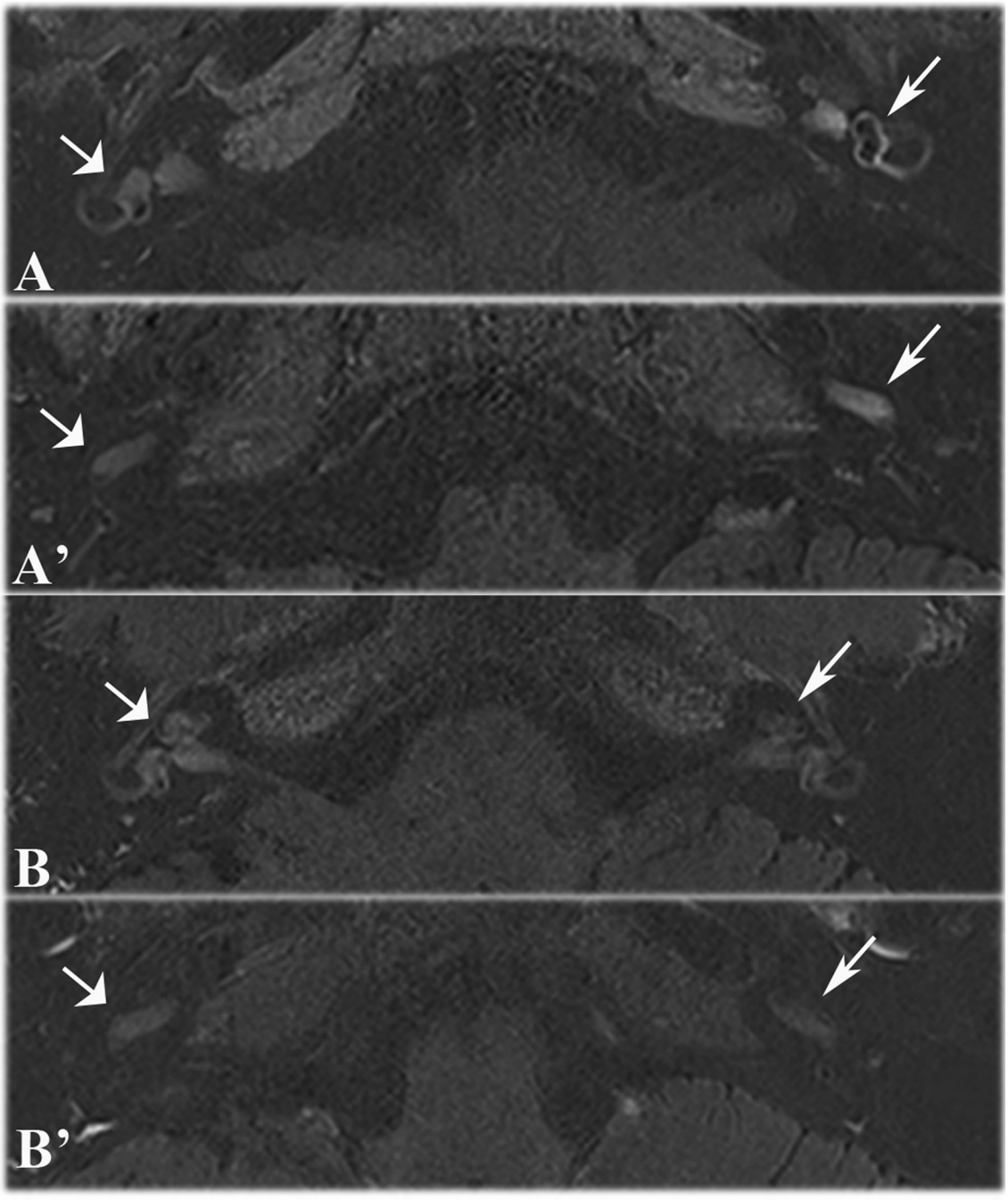
4. Discussion

All patients enrolled were diagnosed with definite MD according to clinical diagnostic criteria. The IV method was used in our study, as it has recently been applied to the in-depth investigation of ELH clinically, and it rendered the function of the blood-perilymph barrier visible [10,11].

Partial ELH was rarely demonstrated in previous studies [12,13]. In our study, only 19 patients (5.6%) had unilateral vestibular (N = 18) or cochlear (N = 1) ELH, and 4 patients (1.2%) with bilateral ELH had contralateral cochlear ELH in 338 patients. The data indicated that vestibular ELH predominated the cases of partial ELH, while cochlear ELH was common in the silent side in patients with bilateral ELH. The phenomenon may indicate that vestibular ELH can contribute to the symptoms of MD, including fluctuating hearing loss, while cochlear ELH may form in the early stages of MD but rarely induces symptoms. The CC ratio of the affected side (1.44 ± 0.46) was higher than that of the unaffected side (1.15 ± 0.33, P < 0.05) in the 19 patients with unilateral ELH. According to an analysis of 115 patients with unilateral MD in our previous study, the ratio of the affected side and the unaffected side was 1.39 ± 0.37 vs 1.18 ± 0.29 (P < 0.01) by [14]. Although there was significant overlap between the patients in this study and in the previous study, partial ELH was first evaluated in this study. There was no difference in the intensity ratio of the affected side between vestibular ELH and classical ELH (P > 0.05). While the CC ratio of the contralateral silent side in 4 patients with bilateral ELH showed no difference when compared to the unaffected side (1.18 ± 0.16 vs 1.18 ± 0.29). The elevated ratio may suggest a potential relationship with vestibular ELH, as a cause or consequence, rather than a consequence of the concentration of perilymph fluid caused by cochlear ELH. The hearing threshold in patients with unilateral vestibular ELH was decreased, which may indicate that the elevated signal intensity in the basal turn of the cochlea may contribute to hearing loss even in the absence of cochlear ELH.

While unclear in origin, the alteration in signal intensity is thought to be due to three possible causes: (1) impaired blood-perilymph barrier [15,16], (2) blockage of neuroaxonal transport mechanisms [17], and (3) cellular immune reaction [18]. The alteration in signal intensity may reflect the pathology of MD. Moreover, vestibular ELH is more closely associated with this elevated signal intensity. On the other hand, the early stages of cochlear ELH had no effect on the blood-perilymph barrier or neuroaxonal transport. However, the elevated signal was less apparent in MD than that in sudden sensorineural hearing loss [19], so it was easily overlooked.

The limitations of the present study were that the signal intensity measurement was conducted only in the regional basal turn of the cochlea, which cannot represent the entire cochlea or vestibule. Because the regional areas of other parts of the cochlea were small and unrecognizable, the signal intensity was susceptible by other structures in the same section, the other parts of the cochlea were not measured. The unilateral cochlear ELH was insufficient because only 1 patient with unilateral cochlear ELH was involved. The intravenously administered Gd agent distributes into the perilymph space of the scala tympani through the blood–perilymph barrier, and the elevation of the cochlear basal turn signal intensity is most easily observed 4 h after IV Gd injection on 3D-real IR in human subjects [5,20]. Therefore, we selected



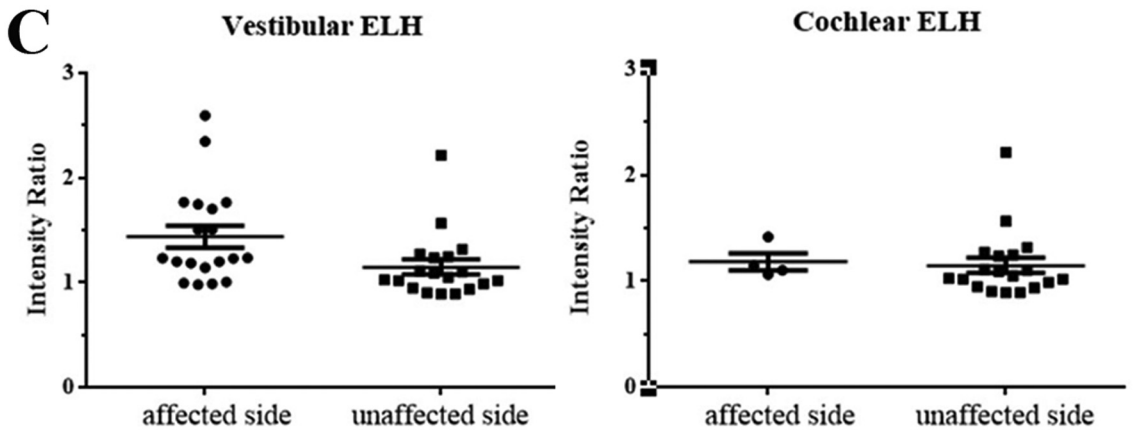


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Fig. 3. MRI scans of patients with partial ELH. A, a patient with left significant ELH in vestibule, A′, The signal intensity of basal turn of the cochlear basal turn in the affected side (thin arrows) was higher than that in the unaffected side (broad arrows). B, A patient with left moderate ELH in cochlea, B′, The signal intensity of basal turn of the cochlear basal turn in the affected side (thin arrows) had no significant difference with that in the unaffected side (broad arrows). C, The CC ratio in the affected side was higher than that in the unaffected side ($P < 0.05$) in vestibular ELH, whereas there was no apparent elevation in patients with cochlear ELH.

the basal turn of the cochlea and the cerebellum white matter for reference to enable the statistical comparison of the cochlear signal intensity of both sides with the IV method. To ensure the reliability of the signal intensity measured in the region of interest of the cochlea and to diminish the measurement error, we determined three points in every region of interest and averaged the signal intensities for analysis. Moreover, it lacked follow-up for patients with partial ELH.

5. Conclusion

In conclusion, partial vestibular ELH was more common than partial cochlear ELH. Moreover, the elevated contrast effect in the affected side may correlate with vestibular ELH rather than cochlear ELH, which may better reflect the pathologic mechanism of MD.

Declaration of Competing Interest

The authors have no other funding, financial relationships, or conflicts of interest to disclose.

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