The etiologies of hearing loss in Meniere's disease:Impairment of internal auditory canal barrier

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Abstract

Objective: The aim of this investigation was to explore the potential correlation between signal intensity ratio (SIR) at internal auditory canal (IAC) bottom and hearing impairment in MD, thereby providing a foundation for further comprehension of the underlying mechanisms contributing to hearing loss. **Design**: Fifty patients diagnosed with unilateral definited MD were enrolled in the study. 3D-FLAIR MRI was conducted four hours after intravenous administration of gadobutrol to determine the SIR of bilateral IAC bottom. The difference of SIR of IAC bottom was assessed between affected and unaffected sides, followed by an analysis of its correlation with low-, middle-, and high-tone hearing thresholds. Additionally, correlation analysis was conducted between the degree of EH in vestibular and cochlea and the SIR on the affected side. **Results:** The degree of EH in MD can be clearly visualized through 3D-FLAIR MRI. The SIR on the affected side was significantly higher than that on the unaffected side (P=0.000). Furthermore, a positive correlation was observed between the SIR at the affected and low (r=0.692, P=0.000), middle (r=0.615, P=0.000) and high-tone (r=0.440, P=0.001); the SIR showed no significant correlation with cochlear (r=0.315, P=0.088) or vestibular hydrops (r=0.215, P=0.244). **Conclusion**: 3D-FLAIR MRI can observe the degree of EH in MD; impairment of the internal auditory barrier may be one of the factors of hearing loss in MD.

Introduction

Meniere's disease (MD) is a multifaceted disorder of the inner ear, characterized by fluctuating sensorineural hearing loss, episodic vertigo, tinnitus and aural fullness [1]. It is commonly regarded as a midlife disorder, with an average onset age of 40 to 50 years and an incidence rate of about 513/100,000[2]. Its etiology and pathogenesis remain unknown and may be associated with autoimmune, genetic, neurophysiological, cellular, and molecular mechanisms. Currently, endolymphatic hydrops(EH) is generally considered its pathological hallmark[3].

According to the 2015 diagnostic criteria, all patients with definited MD exhibit varying degrees of hearing loss[4]. A wealth of clinical data has demonstrated that low-frequency hearing declines in the early stages of MD, while middle- and high-frequency hearing gradually deteriorate as the condition progresses[5]. The sound is transmitted to the cochlea via the auditory pathway, where it causes eardrum vibration and activates auditory receptors in the cochlea. These receptors convert acoustic vibrations into nerve impulses that travel along the auditory nerve to reach the brain's auditory center. Disruption of any aspect within this process may result in hearing loss. The bipolar cells located in the spiral ganglion serve as the primary neurons for auditory conduction. Their peripheral processes are distributed among inner ear hair cells, while their central processes form the cochlear nerve responsible for transmitting auditory signals to the brain. Research has demonstrated a strong correlation between EH and degeneration of spiral ganglion cells within the cochlea[6]; Megerian et al. discovered a significant reduction in the maximum diameter of the auditory nerve in mice with EH[7]. We hypothesize that EH plays a significant role in the development of hearing loss in patients with

MD. However, it remains unclear whether other factors contribute to this condition and further investigation is warranted.

With the continuous advancement of magnetic resonance technology in recent years, visualization of EH has gradually become feasible and is now being applied in clinical practice. Intravenous administration of contrast agents enables simultaneous imaging of bilateral inner ear structures while also reflecting blood-labyrinth barrier permeability through signal intensity ratio of cochlear basal tur[8]. Therefore, the signal intensity ratio can serve as a reliable indicator for permeability estimation and barrier integrity assessment at specific locations.

The internal auditory canal (IAC) is a crucial component of the inner ear, characterized by intricate anatomical architecture. It houses vital blood vessels (labyrinthine artery) and nerves (facial nerve, vestibulocochlear nerve). In patients with non-sudden sensorineural hearing loss, Three-dimensional fluid-attenuated inversion recovery (3D-FLAIR) MRI scanning after intravenous injection of gadolinium contrast agent reveals higher signal intensity in the IAC bottom on the affected side compared to the normal side[9]; this may be related to the patient's hearing loss. We hypothesize that a potential obstruction exists at the IAC bottom, and its destruction may result in hearing impairment.

All patients diagnosed with definited MD exhibit hearing loss. Our hypothesis suggests that the IAC bottom may be compromised in these individuals, yet no research has specifically examined the signal intensity of this region and its correlation to hearing loss; The objective of this investigation was to examine whether the signal intensity of the IAC bottom alters in MD patients following intravenous administration of gadolinium contrast agent, and to investigate its correlation with hearing loss.

Materials and Methods

The patient

This study was observational study(cross-sectional study). According to the diagnostic criteria established by the American Academy of Otolaryngology, Head and Neck Surgery in 2015[4], a total of 50 patients with unilateral definited MD at the Department of Otolaryngology in the First Hospital of China Medical University from November 2020 to December 2021 were included. There were 21 male and 29 female patients, aged between 28 to 74 years old, with an average age of 56 years old. Among them, there were 31 cases of left ear and 19 cases of right ear. All patients underwent physical examination and medical history collection by professional otologists. They all presented with varying degrees of hearing loss in the affected ear, persistent tinnitus and intermittent vertigo.

None of the patients had a history of gadolinium contrast allergy, neurogenic deafness or otitis media, or ear surgery. This study was approved by the Medical Ethics Committee of our Hospital (2018-298-2), and all patients provided informed consent for MRI enhancement.

MRI image scanning

All patients received a double dose (0.2ml/kg) of gadobutrol intravenously (Bayer Pharmaceuticals, specifications: 7.5ml/ tube, 1.0mol/L), 3D-FLAIR sequence scan was performed after a 4-hour delay using a 3T MR Scanner (GE signa pioneer 3.0T) and matching 21-channel head coil.

Before the contrast agent is injected, whole-brain T2 FLAIR scan (TE 95ms, TR 9000ms, Slice Thickness 5mm, FOV 24*0.9, TI 2468ms, Matrix Size 256*256, Echo Train Length 22, Acceleration Factor 1, Scan Time 1 min and 57 sec), inner ear scanning 3D FIESTA C Shim (TE 95ms, TR 6.6ms, Acceleration Factor 2, TI 3.1ms, Matrix Size 256*256, FOV 18*1, Slice Thickness 0.8mm, Scan Time 3 min and 37 sec) were performed. After an injection of gadolinium, 3D-FLAIR sequence scan (TE 189ms, TR 9000ms, Acceleration Factor 4, TI 2134ms, Slice Thickness 1mm, FOV 22*0.8, Matrix Size 320*320, Echo Train Length 180, Scan Time 10 min and 52 sec) was performed.

Image analysis

The routine sequence is utilized for the purpose of excluding neoplastic lesions of the brain and inner ear, as well as malformations of the inner ear. According to Kim's method of measuring signal intensity[9], we selected a 4 mm2 region of interest located at the optimal display position of the bilateral inner auditory canal bottom, we conducted three measurements and calculated the average value. A 50mm2 region of interest (ROI) was selected from the bilateral cerebellar white matter at the same level (**Figure1a**). The signal intensity ratio between the average signal intensity at the IAC bottom on the affected side and unaffected side were calculated. The signal intensity ratio served as an indicator of the extent of enhancement at the IAC bottom, while our previous measurements were utilized to evaluate the degree of cochlear and vestibular hydrops[8, 10]. The images of all patients were assessed in a double-blind manner by two experienced imaging diagnostic physicians with 30 years of expertise, and the mean value of their measurements was calculated.

Statistical Analysis

SPSS 22.0 software was used for data analysis, and data conforming to normal distribution were expressed as mean ± standard deviation. Paired sample T test was used to analyze the difference in the signal intensity of the IAC between the affected and unaffected sides. Pearson correlation was utilized to examine the association between low, middle, and high tone hearing thresholds, cochlear and vestibular hydrops, as well as signal intensity of the IAC on the affected side. A statistical difference was observed when $P<0.05$.

Results

No other abnormal lesions were detected in the brain or inner ear. The images of all patients were clear, and structures such as the cochlea, vestibule, semicircular canal, and IAC could be distinctly identified. In all cases, there was enhancement of the perilymphatic space with a clear demarcation between endolymph and perilymph; furthermore, varying degrees of EH were observed in each patient (**Figure1b**). The signal intensity at the IAC bottom is illustrated in **Figure 2** . The low, middle, and high tone were 57.72±16.10 dB, 56.16±19.87 dB, 66.20±17.56 dB, respectively. Cochlear and vestibular hydrops were 0.39±0.20 and 0.44±0.17, respectively. The signal intensity ratios of the affected and unaffected internal auditory channels were 4.72±0.70 and 3.76±0.80, respectively.

The signal intensity ratio of the IAC on the affected side exhibited a statistically significant increase compared to that on the unaffected side (**Figure3**). The Pearson correlation analysis revealed a significant positive correlation between the hearing threshold of low, middle and high tones and the signal intensity ratio of the IAC bottom (**Table 1**). The scatter diagram depicting this relationship is presented in **Figure 4** . The signal intensity of the IAC bottom did not show a significant correlation with cochlear and vestibular hydrops (**Table 1**).

Discussion

According to the 2015 diagnostic criteria, hearing loss is a necessary component for definitive clinical diagnosis of MD, highlighting its pivotal role in the pathogenesis of this condition. However, the underlying mechanisms leading to hearing loss remain poorly understood. After intravenous administration of gadolinium, the 3D-FLAIR sequence offers distinct advantages in visualizing EH and plays a pivotal role in diagnosing MD[11, 12]. In this study, a 3D-FLAIR scan was conducted four hours after double-dose gadobutrol injection, revealing varying degrees of EH among all patients. However, our study also revealed a statistically significant enhancement in signal intensity at the IAC bottom on the affected side of the patient compared to the unaffected side. This suggests that the contrast agent permeates more deeply into IAC bottom of the affected than the unaffected side, potentially due to compromised barrier integrity on the affected side. So, does it affect hearing? Therefore, further investigation is necessary to determine its impact on hearing.

In this study, we further investigated the correlation between the signal intensity ratio of the IAC and hearing levels. Our analysis revealed a significant correlation between signal intensity at the IAC bottom and low, middle, and high-tone hearing loss. The IAC contains vital anatomical structures such as nerves and blood vessels, whose integrity is crucial for optimal hearing function. Disruption of the IAC barrier can result in nerve damage, leading to hearing loss; the severity of hearing loss is directly proportional to

the extent of damage to the IAC barrier. Similar to our study, in patients with neurogenic deafness, the signal intensity at the IAC bottom was observed to be higher on the affected side than on the unaffected side[9], which is believed to be associated with hearing loss on the affected side; Labyrinthitis is a prominent etiology of sensorineural hearing loss[13], and certain investigations have demonstrated that patients with labyrinthitis exhibit conspicuous enhancement of the labyrinth and IAC bottom on enhanced MRI, implying an association with hearing impairment[14, 15]. Therefore, we hypothesize that a barrier exists at the IAC bottom, and its disruption results in hearing impairment in the affected ear.

Studies indicate that EH can result in significant loss of spiral ganglion cells located at the cochlea apex, and this loss is closely associated with the severity of EH[6]; Other studies have demonstrated a consistent pattern of spiral ganglion cell loss progressing from the cochlear apex to the base, which aligns with the progression of EH[16]; Currently, numerous studies have demonstrated a positive correlation between the degree of EH and hearing loss in patients diagnosed with MD[10, 17, 18]. Therefore, it is our belief that EH may serve as a contributing factor to hearing loss among individuals afflicted with this condition.

We observed a positive correlation between the signal intensity of the inner auditory canal bottom and hearing loss on the affected side in patients with MD. However, there was no significant correlation found between this signal intensity and the degree of cochlear and vestibular hydrops. Therefore, we hypothesize that the changes in signal intensity at the affected side's IAC bottom are not directly associated with EH, but rather caused by destruction of the barrier within the canal. In conclusion, it is postulated that the disruption of the IAC barrier in MD patients may contribute to hearing impairment. The destruction of this barrier can potentially harm the auditory nerve traversing through it, ultimately leading to hearing loss.

Limitation

Our study has several limitations.

1. Because EH cannot be detected pathologically in vivo, the presence of EH cannot be confirmed through pathological means in this study. Therefore, animal experiments are necessary to further validate our hypothesis.

2. Our study was limited by the absence of a healthy control group, and previous research has indicated that unilateral MD may progress to bilateral involvement over time[19]. Although no EH or hearing loss were detected in the unaffected side of our patients, it is possible that some microscopic structures have undergone changes, which could potentially impact the precision of our findings.

Conclusion

Intravenous administration of a double dose of gadobutrol is a viable method for assessing EH in MD. The disruption of the internal auditory barrier may be one contributing factor to hearing loss in MD.

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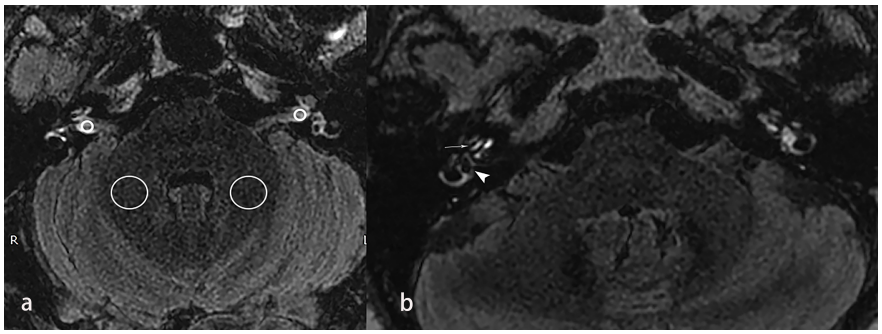
Figure1 a : The optimal layer was shown at the bilateral internal auditory canal bottom on 3D-FLAIR image. A 4mm^2 ROI was drawn on the bilateral internal auditory canal bottom and a 50mm^2 ROI was drawn on the cerebellar hemisphere of the corresponding layer.

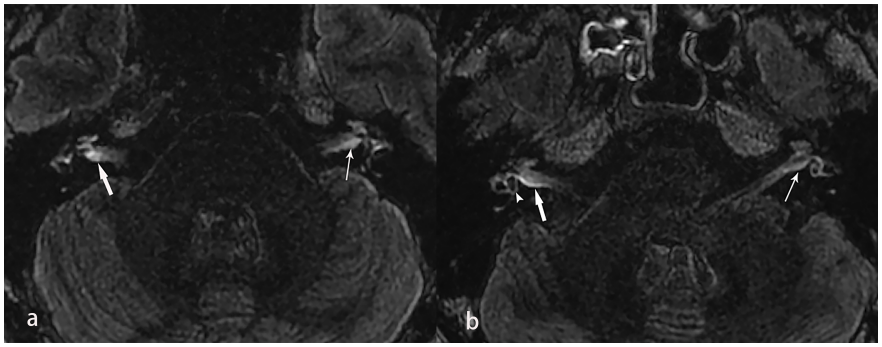
b : Endolymphatic hydrops in patients with Meniere's disease on the right side. Arrow: cochlear hydrops; Triangle: vestibular hydrops.

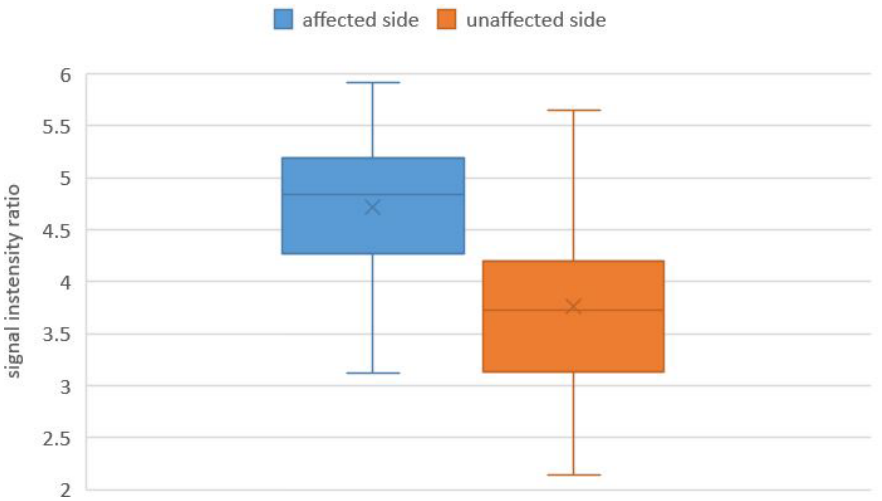
Figure2 : Endolymphatic hydrops in patients with Meniere's disease on the right side. Thick arrow: affected side (signal intensity ratio: 5.18); Thin arrow: unaffected side (signal intensity ratio: 2.7).

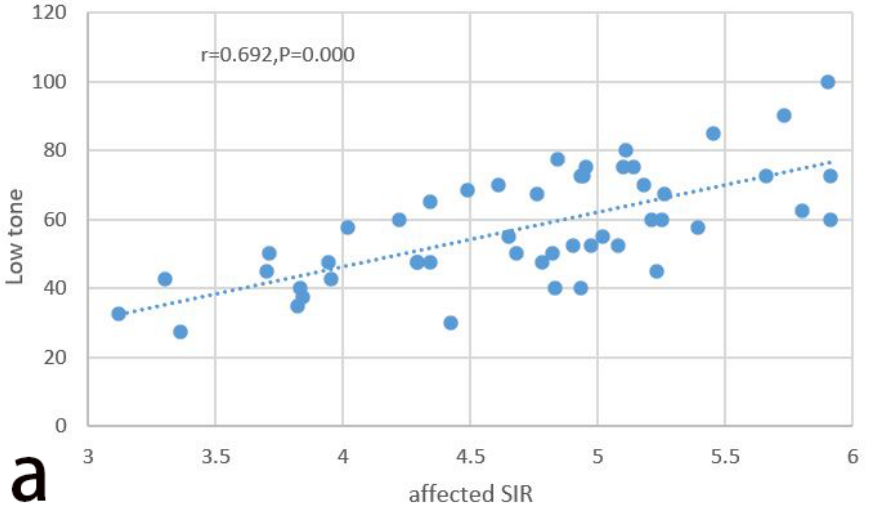
Figure3 : The signal intensity ratio at the auditory canal bottom on the affected side was significantly higher than that on the unaffected side (P=0.000).

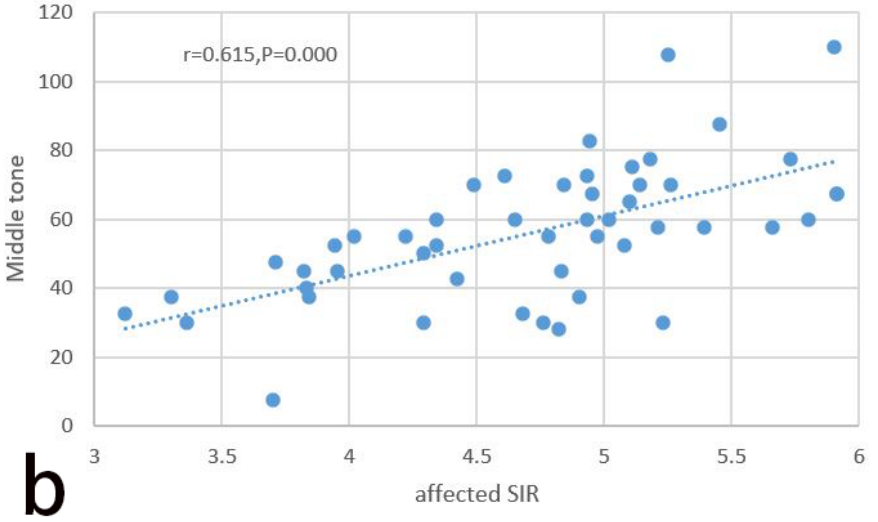
Figure4: Correlation of signal intensity ratio of internal auditory canal and low, middle and high tone hearing thresholds in patients with Meniere's disease.

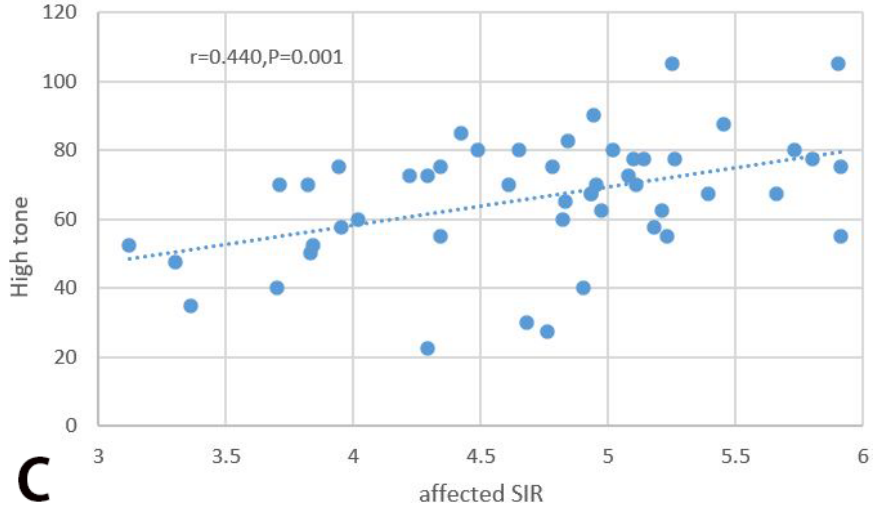












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