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Chronic cerebrospinal venous insufficiency in Ménière disease

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Abstract

Objectives: The aim of this study was to focus on patients suffering from cochleo-vestibular disorder with and without Ménière disease (MD) in order to verify whether chronic cerebrospinal drainage abnormalities could play a role in the etiopathogenesis of endolymphatic hydrops.

Methods: Fifty-two volunteers were enrolled and subdivided into two groups: 24 definite MD and 28 not-MD. Both magnetic resonance venography imaging with contrast-enhanced imaging of the venous cerebrospinal system (MRV) and venous echo-color Doppler (ECD) were performed.

Results: MRV showed abnormalities in 83% of MD and 57% of not-MD subjects ($p < 0.001$). Asymmetrical cervical venous flow, assessed by MRV, was confirmed by ECD in 62.5% of MD but in only 21.5% of not-MD subjects ($p < 0.001$).

Conclusion: Chronic cerebrospinal venous insufficiency might be the anatomical background, which provides a pre-disposing factor for the development of endolymphatic hydrops in MD patients.

Keywords

Chronic cerebrospinal venous insufficiency, Ménière disease, vertigo, hearing loss

Introduction

Chronic cerebrospinal venous insufficiency (CCSVI) is a syndrome characterized by stenosis of the internal jugular veins (IJVs) and/or azygos vein with disturbed flow, insufficient drainage, and the opening of collateral venous channels.¹ It was initially described as being strongly associated with multiple sclerosis (MS),² and can be diagnosed by means of magnetic resonance venography (MRV) and dynamic extracranial color-coded duplex sonography (duplex examination of the cerebral and cervical vein systems).^{3,4} As reported in the literature, MS patients demonstrate a higher prevalence of CCSVI (mean 71%, $n = 1336$) upon ultrasound and venographic examination in comparison with normal controls and patients without MS (mean 7.1%, $n = 505$).⁵ Recently, other pathologies such as migraine⁶ and sudden sensorineural hearing loss⁷ have been associated with CCSVI.

Ménière disease (MD) is a multifactorial condition^{8,9} associated with histopathological evidence of endolymphatic hydrops, partially explained in the literature by an insufficient drainage of the vein of the cochlear

aqueduct.¹⁰ In 1983, Gussen¹¹ firstly reported that abnormal venous drainage of the vestibular organs through the vein of the paravestibular canaliculus may be crucial to inner ear fluid mechanics in MD.

Since CCSVI would seem to be responsible for causing an abnormal outflow of the inner ear,^{7,12–14} we chose to

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focus our study on patients suffering from cochleo-vestibular disorder and MD to verify whether abnormalities of cerebrospinal drainage could play a role also in the etiopathogenesis of endolymphatic hydrops.¹⁵

Methods

Fifty-two patients suffering from cochleo-vestibular disorders were studied.

We divided the subjects into two groups:

- MD: Twenty-four subjects (9 males and 15 females, mean age: 41.6 years) affected by definite unilateral MD according to the criteria of the American Academy of Otolaryngology-Head and Neck Surgery Committee on Hearing and Equilibrium (AAO-HNS CHE),¹⁶
- Not-MD: Twenty-eight subjects (12 males and 16 females, mean age: 44.7 years) suffering from a unilateral cochleo-vestibular deficit revealed by bithermal caloric test according to the Hallpike technique using Jongkees' formula.

The exclusion criteria comprised:

- external, middle, or internal acute or chronic ear pathologies such as tympanosclerosis, otosclerosis, and noise-induced hearing loss (excluding definite MD for the second group),
- retrocochlear lesion or other known anatomic/structural lesions of the ear, and temporal bone or head trauma; syndromic features or congenital otological abnormalities, and
- active alcohol and/or drug dependence or history of alcohol and/or drug dependence within the last year, psychological illness such as major depressive disorder or taking over-the-counter or prescribed medication administered for the treatment of any psychiatric or neurologic disorder or any other known central nervous system active drugs, including herbal, over-the-counter, and homeopathic medications.

The complete audio-vestibular investigation was performed on all subjects by the same audiologist and the diagnosis was made by the same otoneurologist. All subjects were willing to participate and informed consent was obtained from all of them before enrolment in the study.

This study was approved by the Ethical Committee of the Fondazione Don Gnocchi. The work was carried out in accordance with the Declaration of Helsinki, including, but not limited to there being no potential harm to participants, guaranteed anonymity of participants, and informed consent.

All subjects underwent a routine magnetic resonance imaging (MRI) of the brain during which contrast-enhanced imaging of the venous cerebrocervical system was also performed in order to assess the condition of the IJVs and vertebral veins (VVs).

MRI and MRV were performed and evaluated by the same neuroradiologist who had no knowledge of the otoneurological diagnosis (MD vs. not-MD) of the subjects.

MRI was performed using a 1.5 T scanner with a standardized imaging protocol consisting of axial and coronal fast spin-echo T2-weighted imaging and axial and sagittal spin-echo T1-weighted imaging. The intracranial and cervical venous systems were investigated using computer-based MRV performed in three standard orientations (transverse, coronal, and sagittal). A maximum-intensity projection algorithm was used to display three-dimensional MRV reconstruction angiograms. The subjects underwent contrast-enhanced MRV in the supine position and the right and left cross-sectional areas (CSAs) of the IJVs and VVs were compared.¹⁷

Asymmetrical venous flow in the IJVs and VVs was also investigated using venous echo-color Doppler (ECD) (Esaote MyLab and General Electric Logiq P5 with the same probes and settings), randomly carried out by two well-trained specialists, both of whom were unaware of the neuro-otological diagnosis but not of the MRV findings. ECD was performed at 0° and 90° according to the CCSVI protocol¹³⁻¹⁵ and was considered confirmation of MRV findings when at least two of the five CCSVI criteria were satisfied.^{18,19}

Statistical analysis was carried out by an independent well-trained audiologist. MD versus not-MD results were compared by means of Student's t-test, whereas MRV versus ECD concordance was examined using the Fischer exact test. Values of $p < 0.05$ were considered statistically significant.

Results

MRV showed cerebrocervical drainage abnormalities in 20/24 (83.3%) MD and in 16/28 (57.1%) not-MD subjects ($p < 0.001$). Figure 1 shows an example of asymmetrical venous flow in the right IJV. The arrow indicates a reduced CSA of the right IJV with respect to the left IJV in a right-side MD patient (female, 43 years old). Moreover, the right jugular bulb is restricted, the IJV is coiled, and the VVs are hypertrophic.

ECD confirmed an asymmetrical venous flow in IJVs and/or VVs found using MRV in 15/24 (62.5%) MD patients and in 6/28 (21.4%) not-MD subjects (Figure 2) ($p < 0.001$). Figure 3(a) and (b) shows the ECD of the same patient as in Figure 1. The arrow

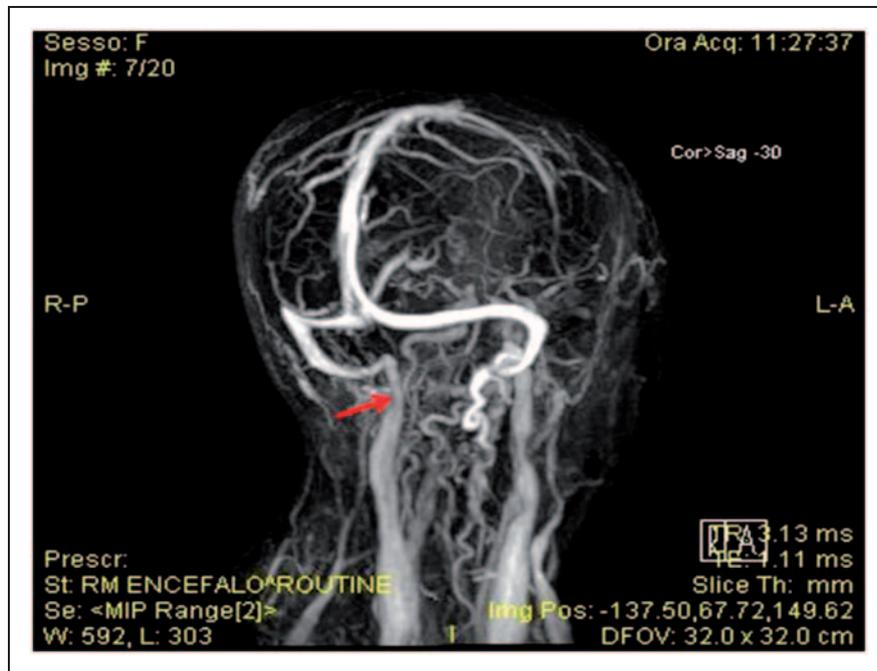


Figure 1. An example of MRV in a patient with right side MD: asymmetrical venous flow in the left IJV.

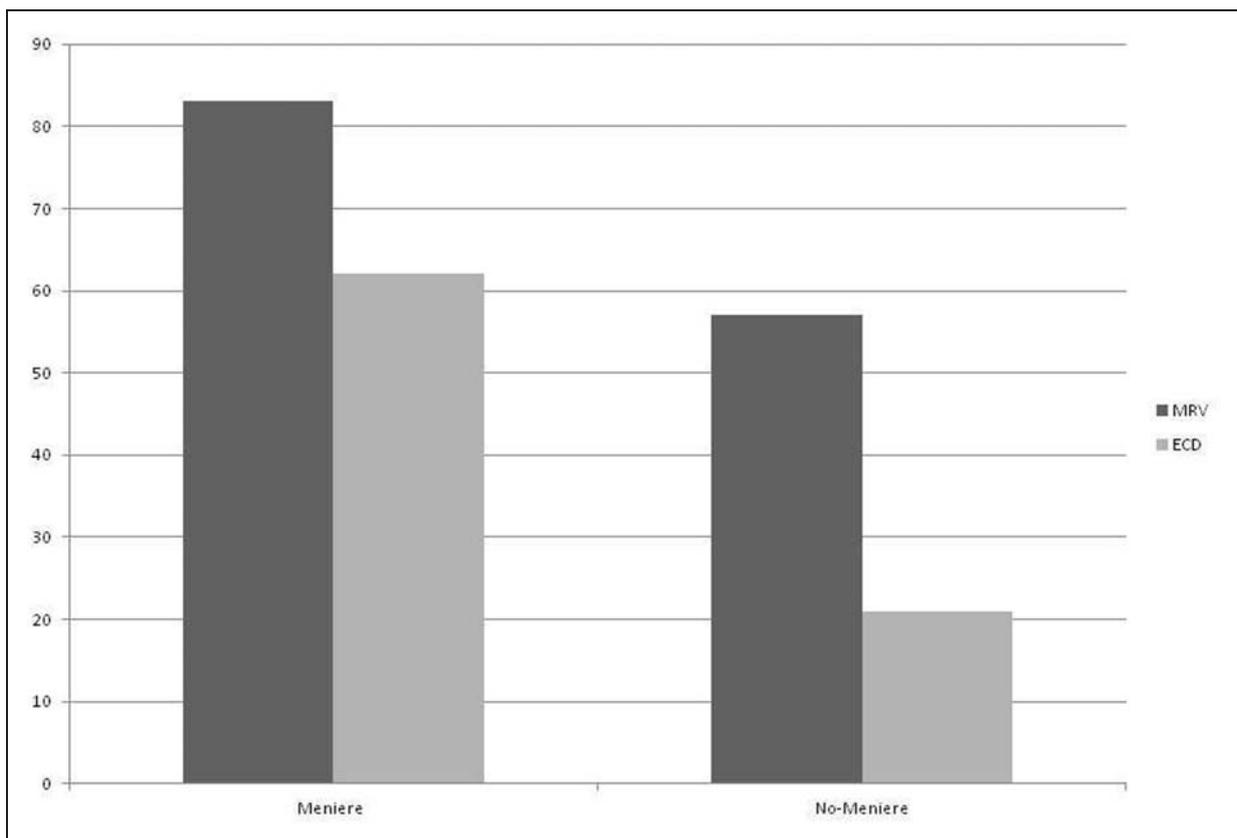


Figure 2. ECD confirmed an asymmetrical venous flow in IJVs and/or VVs found using MRV in 15/24 (62.5%) MD patients and in 6/28 (21.4%) not-MD subjects ($p < 0.001$). MRV: magnetic resonance venography; ECD: echo-color Doppler.

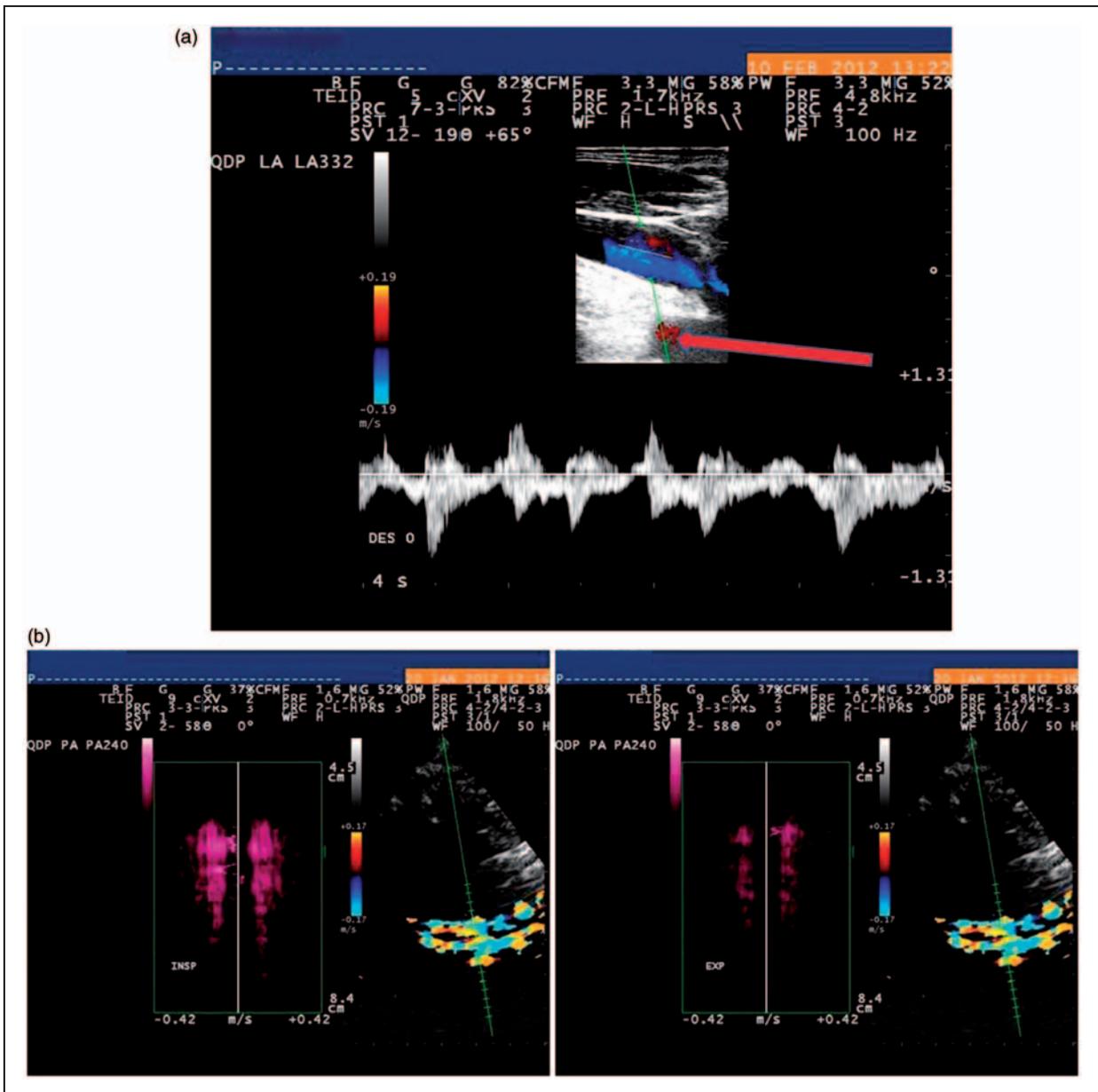


Figure 3. (a, b) An example of ECD (as reported in Figure 1): the arrow indicates a septum in the lumen of the left IJV and blood flow inversion during breathing.

indicates a septum in the lumen of the left IJV and blood flow inversion during breathing.

MRV and ECD findings were concordant in MD subjects (75%, $p < 0.05$) but not in not-MD subjects (37.5%, $p = 0.1$).

While the sensitivity was 83.3% for MRV and 62.5% for ECD, ECD was more specific than MRV (78.6% vs. 42.9%). The positive predictive values of MRV and ECD were 55.6% and 71.4%, respectively, while the negative predictive values were 75.0% for MRV and 70.9% for ECD.

Discussion

MD is a chronic illness that affects a substantial number of patients every year all over the world. The disease is characterized by intermittent episodes of vertigo lasting from minutes to hours, with fluctuating sensorineural hearing loss, tinnitus, and aural pressure.⁹ It has been considered closely correlated with endolymphatic hydrops caused by an obstruction near the endolymphatic sac or duct, leading to a backlog of endolymphatic fluid.⁸ This anatomical condition may

be responsible for triggering the effect of other suggested causes of MD such as trauma, viral infections, metabolic disorders, allergies,²⁰ autoimmune factors, and genetic variations.²¹ Furthermore, among the various cited causes that have been ascribed to MD, the relevance of atopy has recently been highlighted since almost all MD patients have been found to be atopic subjects.²²

Although the pathophysiology of MD remains controversial, Minoda et al.²³ have demonstrated that repeated antigen challenge in the inner ear mimics recurrent MD symptoms in actively sensitized animal models and can be reduced by drugs that limit mast cell reactions. This observation is confirmed by the fact that patients with significant and chronic symptoms, including those with labyrinthine symptoms of allergy, will respond well to specific immunotherapy and/or dietary elimination.²²

It is well known that the induction of ICAM-1 on epithelial cells is the hallmark of allergic inflammation and marks the affected site of the allergic response. It is also common knowledge that the same adhesion molecule is among those overexpressed in the microangiopathic changes associated with chronic venous insufficiency.²⁴ This microscopic condition might explain the tropism of the allergic response in the inner ear, a protected site.

CCSVI is a three-dimensional structure that is often asymmetric and has a considerably more variable pattern than the arterial anatomy; the cerebral veins collect blood in the dural sinuses and in turn redirect it toward the main extracranial venous outflow routes, that is, the IJVs and VV.²⁵

In our study, MRV showed asymmetrical right versus left CSA of IJVs and VVs to be more frequent in MD than in not-MD subjects. Furthermore, ECD showed a dynamic alteration of cerebrospinal venous flow, in which venous drainage depends on position and breathing. In our patients, CCSVI was confirmed mainly in the MD group.

Isildak et al.²⁶ described spontaneous intracranial hypotension as a curable cause of hearing loss, tinnitus, and vertigo. According to the authors, modification of cerebral fluid pressure may cause MD-like symptoms, including fluctuation of hearing loss with positional changes. Similar observations have been highlighted by Koc and Sanisoğlu²⁷ and Kuhn et al.²⁸ In 2007, Shim et al.²⁹ reported a case of unilateral profound sensorineural hearing loss due to a venous malformation of the internal auditory canal. In a previous case report, we observed a relationship between CCSVI and bilateral sudden sensorineural hearing loss.⁷

Our results support the hypothesis that CCSVI could be responsible for causing an abnormal outflow of the inner ear.^{30–32}

The fact that CCSVI was also observed in a small percentage of not-MD subjects with cochlea-vestibular disorders suggests that these subjects may have a fragility of the inner ear that might subsequently lead to MD. Further longitudinal studies are needed in order to investigate the mechanisms of the correlation between inner ear diseases and CCSVI.

Abnormalities of cerebrospinal drainage in the static supine position assessed by MRV proved to be very frequent (approximately 80%), whereas the dynamic alteration of venous flow confirmed by ECD was less frequent but more MD specific. This may depend on the fact that, during ECD, the subject can be turned rapidly with the help of a tilt chair in order to investigate the significance of gravitational gradient in ensuring venous return, whereas this cannot be done during MRV.³³

Therefore, MRV should perhaps be added to the standard MRI protocol for the investigation of audio-vestibular disorders as an initial examination that is inexpensive and relatively easy to carry out, whereas ECD remains a more specific tool for the assessment of dynamic cerebrospinal drainage abnormalities.³⁴

To the best of authors' knowledge, the association between MD and CCSVI has never been reported before. CCSVI might be the anatomical background, which provides a predisposing factor for the development of endolymphatic hydrops in MD patients.

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Conflict of interest

None declared.

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