CLINICAL STUDY

The Prevalence of Chronic Cerebrospinal Venous Insufficiency in Meniere Disease: 24-Month Follow-up after Angioplasty

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ABSTRACT

Purpose: To evaluate relationship between Meniere disease (MD) and chronic cerebrospinal venous insufficiency (CCSVI) using ultrasound, magnetic resonance (MR) imaging, and venography and to evaluate the effectiveness of angioplasty of the internal jugular vein (IJV) and azygos vein (AV) in reducing symptoms of MD.

Materials and Methods: Patients with a confirmed diagnosis of MD unresponsive to standard treatment underwent duplex ultrasound and MR imaging to diagnose CCSVI. Healthy volunteers were also studied to evaluate CCSVI in asymptomatic subjects. Patients with CCSVI and MD underwent venography and percutaneous transluminal angioplasty (PTA) of IJV and AV.

Results: There were 182 patients with no clinical benefit from standard treatments evaluated. CCSVI was diagnosed in 175 (87.5%) patients with MD. Venography was performed in 69 patients to confirm the diagnosis of CCSVI. In 80% of these patients, PTA of the IJV and/or AV was effective for treating signs and symptoms of MD. In the healthy cohort, CCSVI was observed in only 12% of subjects.

Conclusions: These results suggest a possible etiologic relationship between CCSVI and MD that warrants further investigation.

ABBREVIATIONS

AV = azygos vein, CCSVI = chronic cerebrospinal venous insufficiency, IJV = internal jugular vein, MD = Meniere disease

Meniere disease (MD) affects the inner ear and is characterized by dizziness, hearing impairment, tinnitus, and a sensation of fullness in the ear (1,2). The disease occurs in approximately 0.5 per 100,000 people (1,2). Although Ménière described the disease for the first time in 1861 (3), the mechanism leading to MD to date still is not fully understood. Diagnostic guidelines from the American Academy of Otology in 1985 and 1995 defined MD as an idiopathic syndrome of endolymphatic hydrops (1,2,4). Several factors have been advocated to contribute to the etiology of MD, including genetic predisposition, autoimmune disease, inflammation, blocked drainage and increased endolymphatic fluid production, endocrine system abnormalities, viral infection, dietary deficiencies, vascular system abnormalities,

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and trauma (2,4,5). These factors, individually or in various combinations, may lead to endolymphatic hydrops (2,4–6). MD is associated with a recurrent clinical course characterized by acute attacks of vertigo and fluctuations in hearing ability that are more obvious in the early stages of the disease and can negatively affect the patient's quality of life, particularly during acute episodes (5–7). The diagnosis is usually simple; the most common differential diagnosis is neuroma of the eighth cranial nerve (1,2,7). At the present time, there is no definitive treatment for MD (8–11). In the last decade, morphologic changes in the veins draining blood from the brain and spinal cord of patients with multiple sclerosis have been observed, with consequent slowing of the blood flow and the development of collateral circulation. This condition has been identified as chronic cerebrospinal venous insufficiency (CCSVI) (12–14). Blood flow alterations also could represent a concurrent etiologic factor for MD onset. This hypothesis derives from previously reported vascular histologic abnormalities affecting the stria vascularis (15,16) and endolymphatic sac (17,18) of patients with MD.

The aim of the present study was to evaluate whether CCSVI could be a predisposing factor for developing MD. Duplex ultrasound in combination with transcranial Doppler is considered to be the most suitable method for diagnosis of CCSVI (12,19–21). In 2009, an endovascular angioplasty protocol was proposed for the treatment of these lesions to improve cerebral venous outflow (22); however, the efficacy of the procedure is still debated in the scientific community (23). Therefore, a secondary purpose of the present study was to assess the effectiveness of percutaneous transluminal angioplasty (PTA) for treating symptoms of MD.

MATERIALS AND METHODS

This experimental study was approved by the Ethics Committee of the Italian National Health Service, "Comitato Etico Campania Nord," and it was performed in accordance with the guiding principles of care. From April 2013 to December 2015, patients with a confirmed diagnosis of MD were enrolled; patients included 109 women and 72 men with a mean age of 46 years (range, 34–76 y) (**Table 1**). MD was diagnosed according to the 1995 and 2015 American Academy of Otology criteria. The onset of MD in patients ranged from 28 years to 2 years prior. All patients underwent duplex ultrasound of the neck veins and intracranial venous circulation according to the criteria of the International Society for Neurovascular Disease Consensus of 2011 (20) and modified by guidelines published in 2014 (21). Duplex ultrasound was also performed on healthy volunteers (mean age, 49 y; range, 30–75 y) who did not have a neurologic or audiovestibular disease (control population). In patients with MD and positive CCSVI by ultrasound evaluation, magnetic resonance (MR) imaging was performed with a 1.5T clinical MR imaging system (Brivo MR355; GE Healthcare, Fairfield, Connecticut). Venography of the internal jugular vein (IJV) and azygos vein (AV) was also performed in patients with CCSVI.

Table 1. Demographic Data of Enrolled Patients with MD

Characteristic	Value
Mean age, y (range)	46 (34–76)
Women	109
Men	72
Smokers	48 (26.5%)
Body mass index > 25	34 (18.7%)
Alcohol intake	51 (28.1%)
Oral contraception	18 (0.9%)

MD = Meniere disease.

The main criterion adopted to define stenosis of the IJV or AV at venography was at least 50% stenosis of the vein compared with the diameter of an adjacent segment of the vein. Stenosis was confirmed if ≥ 2 of the following additional criteria were met: (*i*) emptying time of > 6 seconds in all vein projections; (*ii*) intraluminal abnormalities (web, septa, valvular abnormalities); (*iii*) collateral veins with a faster emptying time compared with IJV or AV. When a stenosis was diagnosed, endovascular treatment (PTA) was performed. The following PTA protocol was applied (22): (*i*) percutaneous right/left femoral access under local anesthesia; (*ii*) administration of 2,500 IU of heparin sodium; (*iii*) selective venography of the IJV in 3 views using a 100-cm 4-F Ber 2 hydrophilic catheter (Cordis Corporation, Miami Lakes, Florida) and selective venography for the AV using a 100-cm 4-F Cobra catheter (Cordis Corporation), both mounted on a 0.035-inch hydrophilic guide wire (Cordis Corporation). Drainage time of the IJV and AV was evaluated. Dilation was performed with a low-compliance PTA catheter and a 10- to 20-mm balloon (Maxi LD; Cordis Corporation) for the IJV and a 10- to 12-mm balloon (Maxi LD) for the AV using inflations assisted by an inflation device for 120 seconds at 4–8 atm.

At discharge, low-molecular-weight heparin was prescribed at a therapeutic dosage (6,000 IU 2×/d) for 20 days followed by mesoglycan at a dosage of 100 mg/d for 12–24 months. The following criteria were adopted to define the resolution of stenosis after PTA: resolution or marked improvement (> 80%) of vein stenosis, normal outflow, and disappearance of collateral venous circulation. Regular follow-up visits, including laboratory assays (vitamin B, vitamin D, folic acid, and homocysteine plasma levels), duplex ultrasound, and ear, nose, and throat examination at the Audiology and Vestibular Disease Center of one of the referral enrolling centers, were scheduled 1 month after treatment and once every 3 months thereafter. Dizziness was