MENIERE’S DISEASE:
AN HETERODOX APPROACH

President: R. Filipo
Chairman: L. Califano
Panelists: A. Bruno, V. Giugliano, G. Attanasio
The Research of Truth will never end.

There are very few certainties for building our weak knowledge.
The «shadow» zone

Endolymphatic Hydrops

The «causative» zone

Genetic
Infection
Vascular
Dietary
Allergy
Autonomic
Endocrine
Autoimmune

Episodic vertigo
Fluctuating hearing loss
Tinnitus
Fullness

The «fixed» zone

Merchant, 2005 (da Kiang, 1989 modificata)
• Genetics
• Autoimmunity
• Flogosis
• Altered endolymph flow (radial vs longitudinal flow)
• ADH- Aquaporins system
• Autonomic responses
• Viral infections
• Dietary deficiency
• Vascular factors /either arterial and VENOUS)
• Trauma

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Citotoxicity (Iron??)  
ROS  
Modified idro-ionic omeostasis  
Modified endocochlear potentials

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Endolymphatic Hydrops
Episodic vertigo
Fluctuating Hearing loss
Tinnitus
Fullness
Pathophysiology of Ménière’s Syndrome: Are Symptoms Caused by Endolymphatic Hydrops?

Saumil N. Merchant, Joe C. Adams, and Joseph B. Nadol, Jr.

Otology & Neurotology Laboratory, Department of Otolaryngology, Massachusetts Eye and Ear Infirmary, Department of Otolaryngology and Laryngology, Harvard Medical School, Boston, Massachusetts, U.S.A.

Searching for Ménière’s Syndrome
28 clinical cases: each case had hydrops in the affected ear (26- idiopathic hydrops; 2-secondary hydrops)

Searching for Endolymphatic Hydrops
79 cases with hydrops in at least one ear

Idiopathic Hydrops (35 cases)
26 cases with Ménière symptoms
9 cases without Ménière symptoms

Secondary Hydrops (44 cases)
2 cases with Ménière symptoms
42 cases without Ménière symptoms

FIG. 2. Results of searches of database containing temporal bone records.
OTHER, THAT IS AN HETERODOX POINT OF VIEW?
Menière’s disease (MD) is a multifactorial disorder where the combined effect of genetics and environmental factors probably determine the onset of the disease. It is associated with the accumulation of endolymph in the cochlear duct and the vestibular organs in histopathological studies [1], although endolymphatic hydrops (EH) per se does not explain all clinical features, including the progression of hearing loss or the frequency of attacks of vertigo [2]. Menière’s disease is a clinical syndrome that consists of episodes of spontaneous vertigo usually associated with unilateral fluctuating sensorineural hearing loss (SNHL), tinnitus and aural fullness. Cochlear symptoms may also occur between vertigo episodes. The episodes of vertigo are usually much more common in the first years of the disease, but hearing loss and vestibular hypofunction show a great variability among patients, making the phenotyping of MD difficult. A taxonomy of MD subtypes is needed to help categorize individuals who manifest what may be incomplete phenotypes. Moreover, subsets of patients have been described who develop bilateral SNHL and other co-morbidities such as migraine, benign paroxysmal positional vertigo and systemic autoimmune diseases, further complicating the diagnosis and management in these cases.
Vascular syndrome characterized by stenosis of the internal jugular veins and/or azygos veins, with opening of collaterals and insufficient cerebrospinal venous drainage.

Histological examination of the veins involved shows peri-venous iron deposits and fibrin residues, typical of chronic venous insufficiency of the lower limbs.

Zamboni, 2006

CCSVI was included in the Consensus Document of the International Union of Phlebology on Venous Malformations, 2009.
INNER EAR ENDOLYMPHATIC DRAINAGE

The endolymphatic sac keeps inner ear fluid at a constant level.
The balance canals collect balance information.
The hearing canal collects sound information.

DRAINAGE
VESTIBULAR AQUEDUCT VENA

By Courtesy of ALDO MESSINA
Inner ear venous drainage

- Internal auditory vein
- Vestibular aqueduct vein
- Cochlear aqueduct vein
- Superior petrosal sinus
- Inferior petrosal sinus
- Transverse sinus
- Sigmoid sinus

Internal Jugular Vein
An elevation of the hydrostatic pressure at the arterial level of stria vascularis will increase the force which drives fluid from the capillaries into the endolymphatic space. In this case, the hydrostatic pressure of the endolymph will rise if the excess fluid is not eliminated at an equal rate back to the venous end of the stria vascularis.

In other terms, several causes (inflammatory, infectious, immunological, traumatic, with or without associated emotional factors) can modify the balance between perilymph hydrostatic pressure and venous drainage.

An impaired venous drainage could cause EH in MD.


Vascular mechanisms in Meniere's disease. Theoretical considerations.
Gussen R.

Abstract
Unimpeded venous drainage of the vestibular organs via the paravestibular canaliculus (PVC) vein is crucial to inner ear fluid mechanisms. With increased venous pressure, insufficient drainage may result in endolymphatic hydrops, unless collateral veins develop. Different mechanisms cause venous insufficiency in different cases of Meniere's. One suggested mechanism is alteration of the intermediate endolymphatic sac (IES) microcirculation with decreased regulation of blood held within subepithelial capillaries of the sac. Increased blood may thus drain into the veins, with increased venous pressure and inadequate vestibular drainage. Altered microcirculation may be morphological as in fibrosis or shortening of the IES, or physiological where the microcirculation receives abnormal stimuli or reacts abnormally to normal stimuli. Venous insufficiency may result from PVC vein anomalies. Variations in venous pattern whereby vestibular organs preponderantly drain through the PVC vein may predispose to Meniere's disease.


Vascular mechanisms in Meniere's disease.
Gussen R.

Abstract
Normal venous drainage of the vestibular organs through the vein of the paravestibular canaliculus (PVC) may be crucial to inner ear fluid mechanics. It is proposed that increased venous pressure, with resultant venous insufficiency of the vestibular organs, may result in endolymphatic hydrops unless collateral venous circulation develops. Certain variations in pattern of venous drainage where the vestibular organs drain predominantly through the PVC vein may be a predisposing factor. In patients with Meniere's disease, different mechanisms can cause venous insufficiency. One suggested mechanism is morphologic change in the microcirculation of the intermediate portion of the endolymphatic sac. Microcirculation changes may be associated with fibrosis of the perisac tissues or shortening of the intermediate sac region or might be physiologically determined. Venous insufficiency may also result from anomalies of the PVC vein.
Cochlea and receptorial vestibular organs venous drainage is in the inferior cochlear vena

Vestibular Aqueduct Vein (Also called Paravestibular canaliculus vein, PCV) drains receptorial areas of the vestibulus including the dark cells area and it receives tributary veins from the endolymphatic sac region.

In 25% of cases, PCV receives venous blood from some vestibular areas usually affering into the inferior coochlear vein.

In such a case, the venous pressure raises causing an insufficient endolymphatic drainage.

If PCV is congenitally missing, E. H. could happen.

(Could the raise of the venous pressure and the insufficient venous drainage provoke cellular toxicity in the E.S and/or in Stria vascularis?)
Why an impaired drainage by PCV?
- Temporal Bone in MM → Perisaccular Fibrosis and shortening of perisac region could have caused an impaired microcirculation in vivo.
- Fibrosis could be caused through a persistent of the perisaccular region caused by an impended venous drainage
- Normally in perisacuclar region the microcirculatory system controls the blood volume drained toward PV

Unimpeded venous drainage of the vestibular organs via the paravestibular canaliculus (PVC) vein is crucial to inner ear fluid mechanisms. With increased venous pressure, insufficient drainage may result in endolymphatic hydrops, unless collateral veins develop.
Vascular occlusion in the endolymphatic sac in Meniere's disease.

Frtberg U, Rask-Andersen H.

Department of Otorhinolaryngology-Head and Neck Surgery, Uppsala University Hospital, Sweden.

Hystopathological evidence of occlusion of the Vestibular aqueduct vein associated to the occlusion of many small perisaccular vessels in the perisaccular region and evidence of perisaccular fibrosis.

These alterations could affect the normal venous drainage leading to EH.

Figure 6: ES human subepithelial tissue. A capillary vessel is totally occluded by amorphous material. A thrombus-like formation is also evident.
THE DESCRIBED SPECIMENS REPRESENT PATHOLOGIC CHANGES THAT OCCUR AFTER A PROLONGED DISEASE. A THROMBUS MAY RECANALIZE, LYSE, PROPAGATE, OR BECOME ORGANIZED; ACCORDINGLY, A REVERTED FLOW CAN BE TEMPORARY OR CHRONIC. IN THE CASES REPORTED HERE, THE THROMBUS APPEARED AS ORGANIZED AND HENCE INDICATES A LONGSTANDING PROCESS, WHICH IS CONSISTENT WITH MD FOR SEVERAL YEARS.

IN THEORY, REPEATED MICROTHROMBOSIS COULD REVERSE THE FLOW OVER AND OVER AND CAUSE FLUCTUATING SYMPTOMS AS SEEN IN MD.
Abstract

Objectives/Hypothesis: The aim of the present study was to visualize the flow direction of blood in the extraosseous part of the vein of the vestibular aqueduct (VVA) and to explore the effect of an induced obstruction in the distal part of the VVA before it merges with the sigmoid sinus. The endolymphatic sac has been implicated as a potential endocrine gland, which venules drain to the VVA. A reversal of the direction of flow in the VVA toward the inner ear could, through vestibular arteriovenous anastomosis, cause portal circulation in the inner ear.

Study Design: The authors conducted an experimental animal study using in vivo fluorescence microscopy.

Results: Obstructing the distal part of the VVA just before it empties into the sigmoid sinus immediately reverses the flow of blood in the VVA toward the inner ear.

Conclusions: After an obstruction of the VVA, the drained venous blood from the endolymphatic sac may enter a portal circulation in the inner ear, which could cause disturbances in the endolymph homeostasis and potentially symptoms as seen in Meniere disease.
VENOUS BLOOD REFLUX IN VVA DUE TO VENOUS THROMBOSIS DISTAL TO THE ENDOLYMPHATIC SAC
The occlusion, or the congenital absence, of VVA could cause a local Venous Hypertension, leading to an anomalous Portal Flow in the Inner ear.
Conclusions: After an obstruction of the VVA, the drained venous blood from the endolymphatic sac may enter a portal circulation in the inner ear, which could cause disturbances in the endolymph homeostasis and potentially symptoms as seen in Menière disease.

In caso di ostruzione della Vena dell’Acquedotto Vestibolare il sangue venoso refluo dal sacco endolinfatico può invertire il suo flusso, entrando in un circolo di tipo portale che può determinare alterazioni dell’omeostasi dell’endolinfà e potenzialmente sintomatologia di tipo menierico.

SE produces ADH which, in a little amount, through the anomalous portal flow of the inner ear, could affect the idro-ionic metabolism of the inner ear fluids.
A decreased microvascular circulation in the ES, including impaired venous drainage from the duct and sac through the PVV, may lead to morphologic changes that alter normal ES function and may theoretically result in impaired regulation of fluid balance and disturbance of inner ear pressure control (2). It is suggested that those patients with drainage predominantly through the PVV may be more prone to developing EH when there is insufficiency of this vein (3).
Stria vascularis gets an important role in Endolymph production, reabsorption and metabolism and it is very probable its involvement in pathological events leading to Endolymphatic Hydrops in Menière’s disease.

Remember: stria vascularis has the only not avascular epithelium.
Stria vascularis gets an important role in Endolymph production, reabsorption and metabolism and it is very probable its involvement in pathological events leading to Endolymphatic Hydrops in Menière’s disease

- Stria vascularis is severely atrophic and degenerated in patients with MD.
  Paparella et al., 2007
- The number of vessels in the stria vascularis in ears with MD are smaller than in normal controls in all cochlear turns.
  Paparella et al., 2009
• Fibrocytes are essential, due to their of gap junctions and enzymes, to maintain the inner ear fluids. Hystological and cytochemical alterations of fibrocytes and other nonsensory cells in the spiral ligament in an experimental model precede and do not follow the Hydrops.

• EH would be caused by the rupture of the cellular and ultrastructural mechanisms controlling the endolymphomeostasis in the Stria Vascularis.

• These events could be provoked by cytotoxic events from unknown causes.

**CONCLUSION**

Endolymphatic hydrops should be considered as a histologic marker for Ménière’s syndrome rather than being directly responsible for its symptoms.
CCSVI AND MENIERE’S DISEASE

Could CCSVI give us one of the *unknown causes* invoked by Merchant in 2005 to explain the pathophysiological events of Menière’s disease?
Is it possible to hypothesize that CCSVI for congenital, anatomical alterations or for functional acquired alterations represents a predisposing factor for developing inner ear disorders like MD?
Chronic cerebrospinal venous insufficiency (CCSVI) in Meniere Disease, Case or Cause?

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(2) Dept Otolaryngol, Med Ctr, University of Washington, Seattle, WA, USA

Objective: To explore the possibility that CCSVI could be central in Meniere disease.

Methods: The study was prospective and involved 60 patients with Meniere disease, diagnosed by the criteria of the American Academy of Otolaryngology-Head and Neck Surgery. CCSVI was evaluated using a Magnetic Resonance Imaging (MRI) protocol, which included T1-weighted and T2-weighted imaging of the brain and cervical spine. The images were analyzed for the presence of venous abnormalities.

Results: The results showed a high prevalence of CCSVI in the group of patients with Meniere disease, with a significant difference compared to a control group of healthy individuals. The presence of CCSVI was associated with a higher incidence of vertigo attacks and hearing loss in Meniere disease patients.

Conclusion: The findings suggest a potential link between CCSVI and Meniere disease, highlighting the need for further research to understand the mechanisms underlying this association.
CCSVI PREVALENCE IN MENIERE DISEASE
AND PRELIMINARY RESULTS OF BALLOON
VENOUS ANGIOPLASTY

Authors: A. Bruno, L. Califano, G Attanasio, M Viccaro, E Masci, D Mastrangelo, F Salafia, S. Mazzone, V Giugliano, PP Cavazzuti, B. Bernardo, L Cagnoni and R Filipo
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Bologna
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Telese T. (BN)
Clinica Gepos, Vascular Department and Neuroradiology Department

ECD, MRI, PTA
Our group worked both on diagnosis and on therapy of CCSVI
The diagnostic phase:
Venous ultrasonography, Venous System MRI
# MATERIAL and METHODS

March 2013 - June 2016

- **281 PATIENTS WITH DEFINITE MENIERE’S DISEASE**
  - 121 MEN AND 160 WOMEN
  - Age 58 +/- 18.3 years

- **Definite Meniere's disease**
  - Two or more definite spontaneous episodes of vertigo 20 minutes or longer
  - Audiometrically documented hearing loss on at least one occasion
  - Tinnitus or aural fullness in the treated ear
  - Other cases excluded

- **102 healthy subjects**
  - 48 men and 54 women
  - Age 49.3 +/- 7.8
• All the patients enrolled in the study have been already treated (medical therapy, intratympanic therapies) at the ENT/AudioLOGY reference centers.

• Some of them have undergone to surgical therapy (endolympHathic sac surgery, selective vestibular neurotomy).
**Ethics**

The experimental study was approved by the local authority and was in accordance with the guiding principles in the care
Neck veins to be examined within the CCSVI Examination Protocol

**IJVs** – Internal Jugular Veins
(examined side Left and Right both sitting 90° and supine 0° position)

**VVs** – Vertebral Veins
(examined side Left and Right both sitting 90° and supine 0° position)
IJVs – Internal Jugular Veins (examined Left and Right sides both sitting 90° and supine 0° position)

VVs – Vertebral Veins (examined Left and Right sides both sitting 90° and supine 0° position)
<table>
<thead>
<tr>
<th>ECD-TCCS PARAMETERS</th>
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<tbody>
<tr>
<td><strong>1.</strong> Bidirectional flow in one or both the IGV and / or the VV in both positions</td>
</tr>
<tr>
<td>or bi-directional flow in one position with absence of flow in the other (65%)</td>
</tr>
<tr>
<td><strong>2.</strong> Bidirectional flow in the intracranial veins and sinuses (80%).</td>
</tr>
<tr>
<td><strong>3.</strong> Intraluminal defects (flaps, septa or valves) associated with hemodynamic</td>
</tr>
<tr>
<td>changes (blocks, reflux or acceleration) and / or reduction of the area of the</td>
</tr>
<tr>
<td>IGV in the supine position to 0.3 cm /sq (90%)</td>
</tr>
<tr>
<td><strong>4.</strong> Absence of flow in the IGV and / or VV and / or absence of flow in one</td>
</tr>
<tr>
<td>position and bidirectional flow in the other (45%)</td>
</tr>
<tr>
<td><strong>5.</strong> IGV DCSA increased or unchanged both at 90° to 0° (3%)</td>
</tr>
</tbody>
</table>
Gadda G, Taibi A, Sisini F, Gambaccini M., Zamboni P., Ursino M.

A NEW HEMODYNAMIC MODEL FOR THE STUDY OF CEREBRAL VENOUS OUTFLOW

Am.J.Physiol Heart Circ.Physiol 2015 Feb1;308(3): H217-31
CCSVI POSITIVITY in definite Meniere's disease

- 250/281 patients with MD (89%)
- 12/102 healthy subjects (12%)
STEP II: THE ROLE OF MRI IN THE DIAGNOSIS OF CCSVI
MRI IN THE DIAGNOSIS OF CHANGE OF ANATOMICAL VENOUS SYSTEM

- ATRESIAS
- AGENESIS
- HYPOPLASIAS
- TWIST
- STENOSIS
- MALFORMATIONS
- ANATOMICAL VARIATIONS
MRI VASCULAR VENOUS SYSTEM OF THE NECK

The speed of the drainage of jugular system
From April 2013 to June 2016

N. 94 PROCEDURES (45 Males, 49 Females)
Age: average 47 years

Unilateral Meniere’s Disease: 61 cases
Bilateral Meniere's disease: 33 cases

Onset of the disease from 28 years to 2 years before

All patients presented two/five parameters positive for CCSVI according to Zamboni Protocol
PTA FOR CCSVI: Personal Protocol

- Local anesthesia
- Percutaneous trans-femoral venous catheterization (sn / dx)
- Cavography (Lower and Upper)
- Selective catheterization of the internal jugular veins and of the azygos vein
- Selective venography in the three projections and assessment of the empty time
- Sodium heparin 2500 IU
- PTA catheter non-compliant with Ø 10-20 mm (routine Ø 14-16 mm for IJV) (routine Ø 10-12 mm for azygos)
- Manual compression for hemostasis
- Compressive dressing (no need for percutaneous systems of hemostasis)
- Bed rest with leg extended for 12 hours
Post-operative therapy and follow up procedures

- LMWH 6000 IU x 2 x 20 days
- Mesoglycan therapy: 100 mg / day for 12-24 months
- Clinical monitoring by ENT and echocolor doppler at 1, 3, 6, 12, 15, 18, 24 months,
- Dosages: Vit. B12, Folic Acid, Vit. D, Homocysteine
Type A (4%) stenosis of both proximal segments of the Azygos vein and the IJV with a contralateral IJV size increased (> cross-sectional area)

Type B (35%) hemodynamically significant stenosis of both IJV and proximal Azygos Vein

Type C (60%) bilateral stenosis of the IJV with normal azygos

Type D (1%) multiple azygos and lumbar system lesions.

In Meniere’s Disease mainly Type C and Type B CCSVI were observed

The collateral circulations most frequently occurring are those of the condylar system, pterygoid plexus and thyroid veins
We quantify the effect of internal-jugular vein function on intracranial venous haemodynamics, with particular attention paid to venous reflux and intracranial venous hypertension. Haemodynamics in the head and neck is quantified by computing the velocity, flow and pressure fields, and vessel cross-sectional area in all major arteries and veins. For the computations we use a global, closed-loop multi-scale mathematical model for the entire human circulation, recently developed by the first two authors. Validation of the model against in vitro and in vivo Magnetic Resonance Imaging (MRI) measurements have been reported elsewhere. Here, the circulation model is equipped with a sub-model for venous valves. For the study, in addition to a healthy control, we identify two venous-valve related conditions, namely valve incompetence and valve obstruction. A parametric study for subjects in the supine position is carried out for nine cases. It is found that valve function has a visible effect on intracranial venous haemodynamics, including dural sinuses and deep cerebral veins. In particular, valve obstruction causes venous reflux, redirection of flow and intracranial venous hypertension. The clinical implications of the findings are unknown, though they may relate to recent hypotheses linking some neurological conditions to extra-cranial venous anomalies.
RESULTS

Angiographic success v / s Intention-To-Treat: 92/94 (96%)

Major complications: 0% (DVT, rupture, hemorrhage)

Minor complications: three patients 4% (Fibrosis IGV by sonography after one month and one case of inguinal hematoma)

Unchanged: 5% (Four Patients)

Secondary Clinical deterioration : Ten Patients (11%)

Restenosis: Eleven Patients (Doppler ultrasound each three months after PTA): 12%, five of which had a secondary clinical deterioration
Results on Meniere's disease symptoms

ONLY BY ENT ASSESSMENT
Percutaneous Transluminal Angioplasty is compatible with other previous invasive or mini-invasive therapy (vestibular neurotomy, endolymphatic sac surgery, intratympanic therapies, Meniette...)

PTA does not exclude a rescue therapy through them
What we expect on Meniere’s disease symptoms:

Disapperance and / or reduction of symptoms that would lead to at least one improvement:

• In hearing
• In the number and degree of episodes of vertigo.
• In reduction of tinnitus
• In reduction of the subjective auricular fullness
• In Quality of Life, measured by DHI
24 MONTH FOLLOW-UP

Tinnitus and fullness
Hearing Loss
Spells of vertigo
Quality of life (DHI)

30 patients reached this deadline

<table>
<thead>
<tr>
<th>Patients</th>
<th>Men</th>
<th>Women</th>
<th>MD mean history</th>
<th>Affected side</th>
</tr>
</thead>
<tbody>
<tr>
<td>30</td>
<td>13 (43.3%)</td>
<td>17 (56.7%)</td>
<td>58 months</td>
<td>R: 10, L: 11, Bil: 9 (70% 30%)</td>
</tr>
</tbody>
</table>
TINNITUS and FULLNESS: a «brute» subjective judgment

<table>
<thead>
<tr>
<th></th>
<th>TINNITUS</th>
<th>FULLNESS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vanished</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Improved</td>
<td>11 (36.7%)</td>
<td>20 (66.7%)</td>
</tr>
<tr>
<td>Unmodified</td>
<td>16 (53.3%)</td>
<td>10 (33.3%)</td>
</tr>
<tr>
<td>Worsened</td>
<td>3 (10%)</td>
<td>0</td>
</tr>
</tbody>
</table>
TINNITUS: A structured judgment (THI)

Pre-PTA THI: 54.4
Post-PTA THI: 47.8
P = 0.32 (N.S.)

The structured judgment confirmed the «brute» one
## Hearing loss

<table>
<thead>
<tr>
<th>Condition</th>
<th>PTA 0.5-3 kHz</th>
</tr>
</thead>
<tbody>
<tr>
<td>Improved (&gt;10dB)*</td>
<td>13 (43.3%)</td>
</tr>
<tr>
<td>Unmodified (&lt;10dB)</td>
<td>15 (50%)</td>
</tr>
<tr>
<td>Worsened (&gt; 10dB)</td>
<td>2 (6.7%)</td>
</tr>
</tbody>
</table>

* In 5/13 Patients: 25-40 dB

Pure Tone Average is considered improved / worsened if a 10 dB or more difference is noted.

*Committee on Hearing and Equilibrium AAO-HNS, 1995*

Pre-Angioplastica Pure Tone Average: 52.9 dB
Post-Angioplastica Pure Tone Average: 46.8 dB
P=0.14 N.S.

In 5/30 patients hearing loss improved between 25-40 dB.
### Spells of vertigo

#### Avg spells/month post-treatment (24 mon recommended)

\[
\text{Control Level} = \frac{\text{Avg spells/month pre-treatment (6 mon recommended)}}{\text{Avg spells/month post-treatment (24 mon recommended)}} \times 100
\]

<table>
<thead>
<tr>
<th>Control Level</th>
<th>A</th>
<th>B</th>
<th>C</th>
<th>D</th>
<th>E</th>
<th>F</th>
</tr>
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<tr>
<td>N° Pazienti 20</td>
<td>0</td>
<td>1-40</td>
<td>41-80</td>
<td>81-120</td>
<td>&gt; 120</td>
<td>Secondary treatment required due to disabling vertigo</td>
</tr>
<tr>
<td>%</td>
<td>46.7%</td>
<td>36.7%</td>
<td>6.7%</td>
<td>6.7%</td>
<td>3.3%</td>
<td>25 (83.3%)</td>
</tr>
<tr>
<td>AVG/month pre ± SD</td>
<td>7.9±6.3</td>
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<tr>
<td>AVG/month post±SD</td>
<td>1.06±1.9</td>
<td></td>
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</tbody>
</table>
QOL: Dizziness Handicap Inventory

Pre PTA DHI: 55.12
Post PTA DHI: 32.46
P < 0.0001

Physical and emotional scales showed the biggest involvement before PTA and the biggest improvement after PTA.
A first preview: a 24 month follow up comparative study on the control of MD symptoms after either PTA or medical therapy (30 vs. 30 patients)

<table>
<thead>
<tr>
<th></th>
<th>MD and PTA</th>
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<th>MD and Medical therapy</th>
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<tbody>
<tr>
<td></td>
<td>Pre-PTA</td>
<td>Post-PTA</td>
<td>P value</td>
<td>Pre-PTA</td>
<td>Post-PTA</td>
<td>P value</td>
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<tr>
<td>DHI</td>
<td>54.6</td>
<td>31</td>
<td>&lt;0.001</td>
<td>55</td>
<td>48.1</td>
<td>0.1 NS</td>
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<tr>
<td>THI</td>
<td>50.2</td>
<td>43.5</td>
<td>0.24 NS</td>
<td>52.4</td>
<td>49.6</td>
<td>0.54 NS</td>
</tr>
<tr>
<td>Pure tone Average</td>
<td>52.9 dB</td>
<td>46.8 dB</td>
<td>0.14 NS</td>
<td>49.8</td>
<td>55.8</td>
<td>0.09 NS</td>
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<tr>
<td>VERTIGO</td>
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<tr>
<td>A+B</td>
<td>25 (83.3%)</td>
<td></td>
<td></td>
<td>19 (63.3%)</td>
<td></td>
<td>0.03</td>
</tr>
<tr>
<td>C+D</td>
<td>2</td>
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<td>F</td>
<td>1</td>
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<td></td>
<td>7</td>
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<tr>
<td>Fullness</td>
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<tr>
<td>Improved</td>
<td>20 (66.7%)*</td>
<td></td>
<td></td>
<td>5 (16.7%)*</td>
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<td>0.03</td>
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<td></td>
<td>14</td>
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<tr>
<td>Worsened</td>
<td>0</td>
<td></td>
<td></td>
<td>11</td>
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<tr>
<td>Vanished</td>
<td>0</td>
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</table>

Pure tone Average post therapy (PTA vs medical therapy): p=0.009. Results are favourable in PTA.
Clinicians measure, patients feel what happened by a very simply patient oriented assessment?

Better or worse? This is the question

<table>
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<th>24/30</th>
<th>3/30</th>
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<tr>
<td>Unchanged</td>
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<tr>
<td>Worse</td>
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</table>
Where are we going?
We can affirm that

- CCSVI and MD are frequently associated conditions

- PTA procedure cures anatomic and functional CCSVI anomalies

- In a two year follow up, PTA procedure gives a good control of MD symptoms, particularly of vertigo spells and fullness. For hearing loss, our data seems to show its stabilization in a 24 month follow-up, if compared to medical conventional therapy
We cannot affirm that

- CCSVI is the major cause of MD
- PTA “cures” MD
The stasis of the venous flow in the head and neck may be considered a further etiopathogenetic mechanism which adds to many other already known and that defined MD as a multifactorial disease.
Much of the «dark side» is still to be studied. We have to be guided by the forces of our knowledge and intellectual honesty, having to give up on many of our current certainties.