Endovascular treatment of CCSVI really works: the benefits of treating venous brain congestion can be documented

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Our experience in CCSVI (February 2010-February 2018)

Up to date CCSVI endovascular treatment
1357 patients, 3257 veins (2.4 lesions per patient)

MS: 1315 patients;
Migraine: 25 patients;
LAS: 9 patients;
Parkinson dis.: 7 patients;
Left sided amaurosis: 1 patient.

<table>
<thead>
<tr>
<th>Major adverse events</th>
<th>Number of complications</th>
<th>%</th>
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<tbody>
<tr>
<td>Death</td>
<td>0</td>
<td>0%</td>
</tr>
<tr>
<td>Major bleeding</td>
<td>0</td>
<td>0%</td>
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<tr>
<td>Clinical deterioration of MS</td>
<td>0</td>
<td>0%</td>
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</tbody>
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<table>
<thead>
<tr>
<th>Minor Access Site Complications</th>
<th>Number of complications</th>
<th>%</th>
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</thead>
<tbody>
<tr>
<td>Groin hematoma</td>
<td>5</td>
<td>1.01%</td>
</tr>
<tr>
<td>AV Fistula Formation</td>
<td>0</td>
<td>0%</td>
</tr>
<tr>
<td>Puncture Site Infection</td>
<td>0</td>
<td>0%</td>
</tr>
</tbody>
</table>

Safety profile

6 months Doppler and clinical follow-up (n=376)

<table>
<thead>
<tr>
<th>Index</th>
<th>Number of cases</th>
<th>%</th>
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</thead>
<tbody>
<tr>
<td>Doppler Fup:</td>
<td></td>
<td></td>
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<tr>
<td>Restenosis</td>
<td>120</td>
<td>32%</td>
</tr>
<tr>
<td>Rethrombosis</td>
<td>82</td>
<td>22%</td>
</tr>
<tr>
<td>New thrombosis</td>
<td>18 (8 stents)</td>
<td>5%</td>
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| Clinical Fup:     |                 |   |
| Functional improve | 235             | 62.5%|
| Clinical deterioration | 156  | 41%|
| No change         | 70              | 18.5%|

Mean EDSS before: 6.7; Mean EDSS after: 5.2
Blinded flow assessment at 12 months revealed restored flow in 38 of 71 patients (54%) in the PTA group and 14 of 37 (38%) in the sham group.

Direct relationship between flow restoration and new T2 MRI lesions shown in BRAVE dreams trial

- Elevated levels of hypoxia-inducible factor-1α, as well as p53, another hypoxic stress protein, have also been observed in MS plaques.
- Evidence is evolving that cerebral hypoperfusion in MS is associated with chronic hypoxia, focal lesion formation, diffuse axonal degeneration, cognitive dysfunction, and fatigue. Restoring CBF may therefore emerge as a new therapeutic target in MS.

Zamboni et al., JAMA Neurol. 2018;75(1):35-43.
Blood gas analysis substudy

- Our research included total of 228 patients
  - 178 patients with CCSVI and MS /average age 44.86/, with different degree of jugular vein stenosis /53 patients with 50-80% stenosis, 125 patients with above 80% stenosis/
  - 50 healthy control group /average age 54.6/
- Samples were taken under standard conditions during an invasive or interventional procedure from the femoral introducer and from the distal part of jugular and azygous veins
- At ambience temperature 20°C
- 2 ml of blood in a heparinized syringe after initial aspiration of 5 ml through the same catheter in order to remove remainings of contrast media, saline or blood from other regions

Blood-gaz analysis in Jugular veins in patients with CCSVI before and after treatment. Immediate improvement:

The most probable reason for this immediate truncular veins blood gas analyzer improvement is the immediate improvement in microcirculation (both perfusion and run off) and more efficient gas exchange on microcirculatory level.

- Here is the the direct prove:
  On a group of patients[9] with evidence of CCSVI submitted to balloon angioplasty or stenting we performed SPECT- 99mTc-HMPAO dynamic brain scintigraphy before and after the endovascular procedure and showed:
- improvement of the brain perfusion in the treated hemisphere
- improvement of the wash-out timing of the involved zone
- reduced perfusion brain asymmetry after the procedure
Case presentation

- 39 y male
- Severe progressive disability (fatigue on 150m, blurriness of vision, discoordination, loss of concentration during the last several months)
- Negative for MRI demyelination lesions
- Diagnosed (EC Doppler US) with severe CCSVI

Total occlusion of the innominate vein in a patient with disabling fatigue and vertigo not covering the Kurtzke criteria for MS

Vessel recanalization using Coronary CTO technique (Asahi Miracle wires and OTW RyuJin low profile balloons)

Stepwise incremental balloon predilation

Partial recanalization after ballooning. Collaterals still persisting
Full recanalization and flow restoration after stent implantation. Collaterals disappeared. In one heart cycle the IJV is emptied.

SPECT - 99mTc-HMPAO

BECFORE
Generally underperfused brain Spots with totally missing perfusion L to R assimetria

1h AFTER
Good general perfusion No spots with missing perfusion L to R equalization

MULTIPLE SCLEROSIS LESIONS:
FLAIR and Perfusion Weighted Imaging (PWI) can be used to study the hemodynamics of the brain

Anatomic evidence of lesions from FLAR imaging
Perfusion weighted MRI shows all MS lesions have the same vascular characteristics

Courtesy Mark Hacke

Chronic demyelination plaques were more prevalent in WM regions with lower relative perfusion.

Holland CM², Guttmann CR, J Neuroimaging. 2012 Apr;22(2):129-36; 2011 Mar

Discussion
Simple PTA in CCSVI is probably not the optimal treatment. We have to establish reliable clinical and anatomical predictors for vascular and clinical success in order to answer the important questions:

Vascular responders?
MRI responders?
Clinical responders?
Conclusions

- CCSVI is a real vascular pathologic entity and is probably a trigger for more than one neurologic degenerative disorders such like MS, Migraine, isolated Vertigo, Meniere syndrome, Parkinson syndrome
- Endovascular treatment (balloon angioplasty and stenting) of CCSVI is feasible and safe
- Methods and strategies improving the early and late patency rate have to be elaborated because the good clinical result is strongly dependent on the vascular patency and flow restoration