

## **Clinical disability and venous vessel pathology in multiple sclerosis**

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**Introduction.** The new vascular hypothesis as a cause of multiple sclerosis (MS) has aroused immense interest in different groups of specialists and the lay population, respectively. The demonstration of the venous intraluminal changes in the extracranial venous pathway has provided a completely new insight in the field of demyelinating disease. Until recently, MS was considered as an inflammatory immuno-mediated disease starting usually with a relapsing-remitting course. The role of an abnormal venous drainage, described as chronic cerebrospinal venous insufficiency (CCSVI), has been considered as an important factor in the etiology of MS (Zamboni et al. 2009). CCSVI is characterised by multiple stenoses of the extracranial veins – jugular and azygous veins. By pathohistological investigation the perivenous distribution of demyelinating lesions was described. With the high resolution MR venography a central vein in the long axis of the MS lesion was highlighted. Even a genetic factor in the development of vascular malformation is discussed. Several studies are trying to elucidate the influence of CCSVI as a primary or secondary defect in the development of this very disabling disease – MS. In spite of the promising results, there is still a great opportunity for much scientific discussion. In this study we are going to demonstrate the connection between the degree of disability and the number of intraluminal venous changes in MS patients.

**Methods.** The MS patients, diagnosed by Revised McDonald criteria, who fulfilled 2 or more of the 5 proposed criteria obtained by Doppler sonography required for the CCSVI, underwent selective venography. Venography was performed by introducing the angiographic catheter into the right femoral vein. To prevent a painful sensation a mild local anaesthesia was used. Disability status was assessed by the Expanded

Disability Status Scale (EDSS). The value between 1-3 is considered as mild, more than 3 as moderate, and the value of 6 and more as severe impairment of the ambulation. According to disability, we divided the patients into groups with EDSS < 3.0, 3.1-6.0 and > 6.1.

**Results.** In our study we enrolled 65 consecutive MS patients – 18 patients with relapsing-remitting (RR) MS – mean age at procedure was  $30.3 \pm 8.0$  yrs, 29 with secondary progressive (SP) – mean age  $44.2 \pm 13.0$  yrs, and 18 with primary progressive (PP) – mean age  $49.4 \pm 8.8$  yrs, course of disease. Median disease duration of the RR group was  $5.1 \pm 1.0$  yrs, of SP  $13.6 \pm 8.1$  yrs, and PP  $10.4 \pm 5.8$  yrs. Median EDSS scores were 2.3, 6.0 and 6.5, respectively. The degree of stenosis of the jugular veins in SP patients was slightly higher than in RR and PP cases (Figure). The mean number of the endovascular dilatations in SP and PP cases was slightly higher than in RR cases. In the all three groups of patients 180 dilatations were performed. In the severe disabled patients group with EDSS > 6.1, the number of dilatations was significantly higher ( $p < 0.002$ ) than in patients with the lower EDSS. There is a strong correlation between EDSS and the number of dilatations ( $r = 0.417$ ;  $p < 0.005$ ).

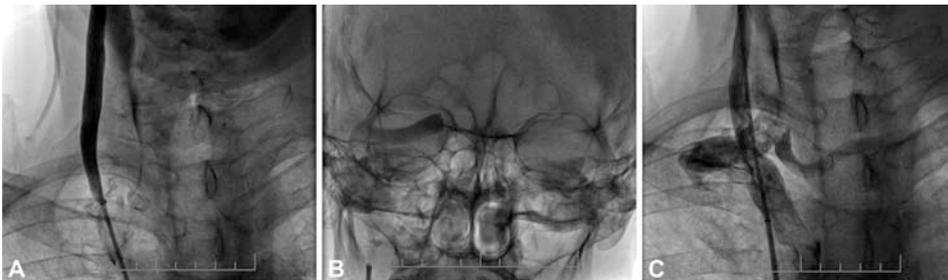


Figure. Severe ostial stenosis of right jugular vein in a 51-year old male patient with severe ataxia (A). Stasis of venous flow in transversal sinus (B). Venous flow after dilatation (C).

**Discussion.** The stenoses of the extracranial venous pathway in all stages of MS were described. In the PP group of patients, significant impairment of the azygous vein was obtained. This finding supports the careful examination of the spinal cord venous system particularly in PP patients. Even in mildly affected patients important endovascular involvement was observed.

**Conclusion.** The intraluminal narrowing of the extracranial veins was demonstrated in all MS cases. It seems that CCSVI in MS patients contributes to their clinical picture and plays an important role by developing a devastating impairment of the ambulation. Even in the beginning phase of disease - the RR course of disease - severe involvement of the venous pathway was discovered. In patients with the progressive course of the disease, more prominent endovascular changes in the azygous vein and an increased number of dilatations were described. The venous vessel abnormality found even in mildly disabled patients is a warning sign, which urges one to adopt an early vascular intervention, particularly in the patients with clinical isolated syndrome. An early vascular procedure may protect against further impairment of the nervous tissue.

**References:**

(1) Zamboni P et al. J Neurol Neurosurg Psychiatry 80:392, 2009. (2) Polman CH et al. Ann Neurol 58:840, 2005. (3) Kurtzke JF. Neurology 33:1444, 1983.