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The Hemodynamics of Blood Flow through the Internal Jugular Veins after CCSVI Endovascular Treatment and its Impact on the Quality of Life in Patients with Chronic Cerebrospinal Venous Insufficiency

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Abstract

Objectives: The aim of the study was to compare pre- and post-operative blood flow through the internal jugular veins (IJVs) in patients with multiple sclerosis and chronic cerebrospinal venous insufficiency, who were subjected to endovascular treatment. The results were correlated with respect to changes in the quality of life.

Methods: 144 MS patients underwent endovascular treatment of the IJVs. The blood flow through the IJVs was assessed by the means of the Doppler ultrasonography. The clinical neurological evaluation was based on the various diagnostic tools (scales). The assessment of the blood flow through the IJVs and an evaluation of the quality of life changes were performed before surgery, and at 1, 3 and 6 months after surgery.

Results: A statistically significant increase in the blood flow through the IJVs was identified on both sides during all three postoperative controls. The relationship between the IJV flow changes and the parameters related to the quality of life assessment, a statistically significant positive correlation between the flow improvement in the right IJV and Multiple Sclerosis Impact Scale, as well as Fatigue Severity Scale scores, were found. For the remaining evaluated scales (Expanded Disability Status Scale, Heat Intolerance Scale and Epworth Sleepiness Scale), as well for the flow in the left IJV, there were no statistically significant correlations confirmed.

Conclusion: Despite a significant improvement in the blood flow through the IJVs after endovascular interventions on the IJVs in CCSVI patients, it has not demonstrated that hemodynamic changes improve the quality of life in MS patients.

Keywords: CCSVI; Multiplex sclerosis; Vein hemodynamic; Liberation procedure

Introduction

Multiple sclerosis (MS) is generally considered to be an autoimmune inflammatory disease caused by unknown factors. This theory has been challenged in recent years, among others, by Zamboni et al., who point to disturbances in the outflow of blood from the central nervous system as one of the causes of degenerative changes in the Central Nervous System (CNS). These changes are referred to as chronic cerebrospinal venous insufficiency (CCSVI).

CCSVI is related to the morphological abnormalities of those veins that drain blood from the brain and spinal cord. These take the form of endovascular partitions, membranes, malfunctioning valves or segmental vein hypoplasia, which cause the impaired blood outflow from the CNS [1].

The consequence of the venous blood flow impairment includes venous hypertension, which can disintegrate the blood brain barrier and promote the accumulation of iron deposits, and inflammatory response [2-4].

An increased incidence of venous pathology in patients with MS suggests that these changes may be an important factor in the development and progression of this disease. In a group of 499 patients, out of whom 289 suffered from MS, Zivadinov et al. found that 56% of patients with MS demonstrated changes that met the ultrasound criteria for CCSVI proposed by Zamboni.

Similar pathology was reported in only 7% of volunteers not suffering from MS [5]. These observations were confirmed in additional studies [6]. Thus, it can be expected that an improvement of the venous outflow from the CNS should provide beneficial effects on the clinical course of MS and potentially on patients' quality of life [7].

Although the role of CCSVI in MS is still not fully understood, Beggs suggests that venous hypertension in the sinuses of the dura can affect the hemodynamics of both cerebrospinal fluid and the blood flow within the brain [8].

Although the physiological mechanisms related to the cerebral venous outflow are still poorly understood, it seems that the abnormalities in the venous system may affect a number of neurological disorders, such as MS, leukoaraiosis, dementia and normal pressure hydrocephalus [9].

Some authors question the existence of CCSVI and its effect on MS. Doepp et al. studied 56 patients with MS along with 20 cases from the control group and did not find narrowing or changes in the direction of the flow in the jugular veins [10].

The aim of the study was to compare pre- and post-operative blood flow through the internal jugular veins in patients meeting the criteria for CCSVI, who were subjected to endovascular treatment to correct the blood outflow disturbances from the CNS.

The results were correlated with respect to changes in the quality of life. The study assumed that one of the important hemodynamic evaluation parameters of the blood flow, in addition to measuring of the intravenous pressure, is to determine minute volume of the blood flow (volume flow), which can be calculated non-invasively by the means of US Duplex Doppler examination.

Material and Methods

Single-centre, prospective evaluation of 144 patients with confirmed MS aged from 23-67 years (mean, 41; male/female, 85/59) was performed. The duration of illness ranged from 1-41 years (average 13 years).

More than half of the patients in the study group suffered from the relapsing-remitting form of MS (74/144, 51%), while less than 1/3 suffered from the secondary progressive form (46/144, 32%) and fewer patients from the primary progressive form of MS (24/144, 17%).

The patients were qualified to surgery in terms of meeting the following conditions: diagnosis of MS based on the McDonald's criteria confirmed by an independent neurologist [7].

As well as concomitant CCSVI confirmed by the means of the US Doppler examination with an implementation of the Zamboni criteria [8].

A distribution of diagnosed jugular venous pathology according to the type of MS is shown in Figure 1.

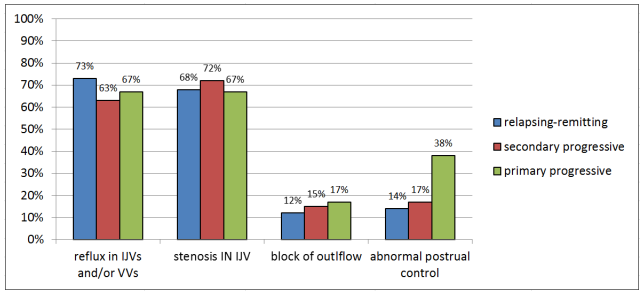

Figure 1: Jugular vein abnormalities related to the type of SM diagnosed by the means of US duplex Doppler examination.

The study excluded patients with vascular malformations of the CNS, vascular inflammatory diseases, congenital vascular anomalies and those who have had a history of venous thrombosis within the cerebral and/or extracranial veins.

All of the patients underwent endovascular treatment of the internal jugular veins-during the procedure, in all cases; bilateral phlebolography of the jugular veins was performed. According to the duplex Doppler results and phlebographic confirmation, 80 patients (56%) were subjected to bilateral and 64 (44%) to unilateral balloon angioplasty (PTA) of the internal jugular veins.

During the procedure, a PTA balloon of 10-14 mm diameter was used. In 17 cases after unsuccessful angioplasty, the self-expandable nitinol stents (Smart stent, CORDIS) were implanted with the balloon post-dilation (the average size of the stent was 12 or 14 mm in the diameter).

The blood flow through the internal jugular veins was assessed by the means of the duplex Doppler and pulsed Doppler implementation. The test was conducted using the Logiq Book Xp General Electric US machine using a linear probe with a frequency of 7.5-10 MHz.

The volume flow (V_{flow}) was calculated from the following formula:

$$V_{flow}=P_p \times V_{mean} \times 60$$

The planimetric method was used to determine the cross-sectional area (Pp) of the internal jugular vein. This was done by tracing the circumference of the vessel in the transverse projection of the B-mode presentation, with minimum probe pressure (to avoid deformation of the wall). The camera software was applied for calculation.

Measurements were performed three times and the result presented as the arithmetic mean. Mean speed (Vmean) was determined from the Doppler spectrum using the software from a recording lasting 30 sec.

A sampling gate was adjusted to cover the entire range of the vein diameter. The measurements were carried out in the middle segment of the internal jugular vein, at the same point pre- and post-operatively.

All of the measurements were taken under the same thermal conditions, after at least 5 min of rest in the supine position, under quiet regular breathing.

All of the patients were assessed by an independent neurologist pre- and post-operatively. The clinical assessment, including an evaluation of neurological deficits and the severity of disability, was based on the expanded disability status scale (EDSS).

The intensity and severity of several MS-related symptoms, as well as their influence on the quality-of-life, was evaluated by the following diagnostic tools (scales), which were based on the patient's self-assessment: Multiple sclerosis impact scale (MSIS-29), fatigue severity scale (FSS), heat intolerance scale (HIS) and epworth sleepiness scale (ESS) [11].

The quality of life assessment was performed in the same time intervals as the internal jugular vein flow evaluation. The assessment of the blood flow through the internal jugular vein and an evaluation of the quality of life changes were performed four times in each test group: before surgery, during qualification to the treatment, and at 1, 3 and 6 months after surgery.

The study was approved by the Local Ethics Committee; an informed consent was obtained from all of the participants.

Statistical analysis

The U Mann-Whitney test was used in statistical analysis to compare the blood flow through the internal jugular veins. The correlation of changes in the flow rate was examined after surgery in relation to changes in the quality of life scales (MSIS, FSS, HI and EDSS).

Results

A 6-month follow-up in 45 patients (31.2%) revealed restenosis in control UDP Colour Doppler studies. These patients were excluded from further statistical analysis. Before endovascular surgery, the median value of the blood flow through the internal jugular vein was 156.7 ml/min (max. 844, min. 0 ml/min) on the left side, and 209.8 ml/min (max. 959, min. 2.4 ml/min) on the right side. A statistically significant increase in the blood flow through the internal jugular veins was identified on both sides during all three postoperative controls. After 1 month of treatment the median of the blood flow through the internal jugular vein increased to 246 ml/min on the left side (max. 878.8, min. 6.5 ml/min), and to 303 ml/min (max. 1062 ml/min, min. 25.2 ml/min) on the right side. The control carried out after 3 months showed that the median blood flow through the internal jugular vein was 245 ml/min on the left (max. 1126; min. 7.9 ml/min) and 282 ml/min (max. 1330; min. 14.6 ml/min) on the right side, respectively. After 6 months of treatment, the median value was 274 ml/min (max. 1169; min. 20 ml/min) on the left side and 299 ml/min (max. 779; min. 23 ml/min) on the right side. In the quality of life assessment, statistically non-significant changes in the MSIS, FSS, HI and ESS scales were observed within 6 months of follow-up. Looking for the relationship between the internal jugular vein flow changes and the parameters related to the quality of life assessment, a statistically significant positive correlation between the flow improvement in the right IJV and MSIS, as well as FSS scores, were found.

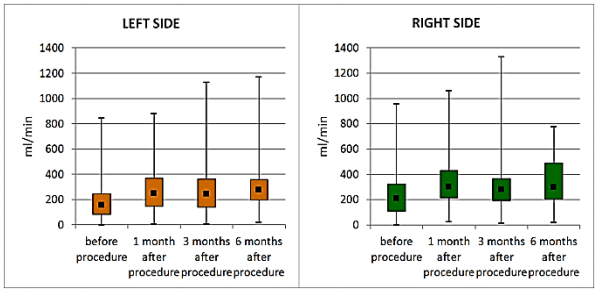

Figure 2: The comparison of the blood flow through the left and right internal jugular vein before and 1, 3 and 6 months after endovascular treatment.

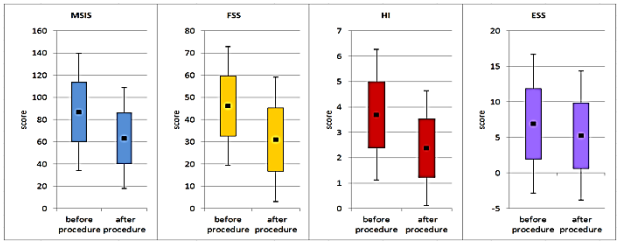

Figure 3: Results of the quality of life assessment based on MSIS, FSS, HI and ESS scales (pre-operative assessment and 6 month follow-up evaluation).

For the remaining evaluated scales (EDSS, HI and Sleepiness scale), as well for the flow in the left IJV, there were no statistically significant correlations confirmed. The reported observations were noticed in all postoperative evaluations (i.e.1, 3 and 6 months after procedure) (Figures 2-5).

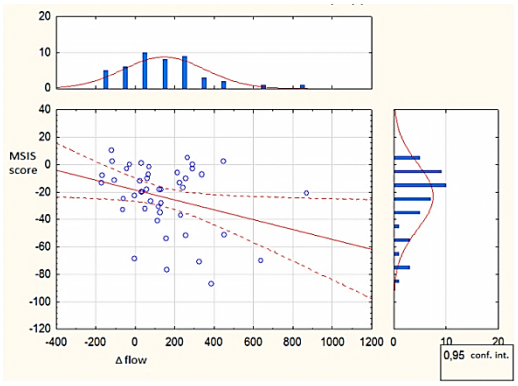

Figure 4: The correlation between MSIS scales score and right IJV flow changes within the right internal jugular vein (6 month follow-up results).

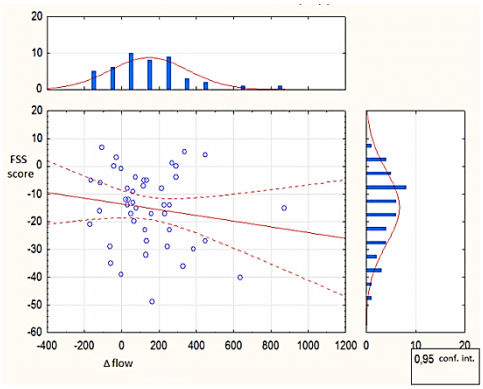

Figure 5: The correlation between FSS scales score and right IJV flow changes within the right internal jugular vein (6 month follow-up results).

Discussion

It has been over six years since Paolo Zamboni cited the similarity between the pathophysiology of chronic venous insufficiency of the lower limbs and the development of demyelinating lesions in MS [12]. At that time it seemed that the "new light" had been shed on the so far unresolved mechanism of MS development, in the form of CCSVI [1]. CCSVI aroused widespread interest both among doctors and patients with MS. However, Zamboni's theory is currently a source of much controversy and is disputed by many authors [13-18].

In a group of 100 patients with MS, Rodger did not observe the ultrasonographic features of reflux strictures or other changes attributed to CCSVI in the jugular veins. In his study group, only one patient met Zamboni's ultrasonographic CCSVI criteria. Also, no differences in the venous flow velocity between MS patients and healthy controls were identified in MRI studies [19].

Despite the controversy surrounding the CCSVI theory, endovascular procedures were recently started in order to correct pathologies in the veins draining the central nervous system. In some publications dealing with the effects of surgical treatment, authors show a significant improvement, which is particularly evident in the case of chronic fatigue syndrome [13,14,20-24]. Previous studies have focused on the analysis of beneficial effects on neurological aspects and safety assessment of the procedures [14,24]. Although disturbances in the hemodynamics of the cerebral flow are central to the Zamboni theory, there has been little data published on the effects of jugular venous endovascular procedures on the values of the cerebral flow.

Under physiological conditions, the blood from the brain and spinal cord in a supine position outflows mainly through the internal jugular veins. In healthy subjects, the minute volume on each side is at an average of about 700 ml/min [15]. Our group of patients at baseline showed significantly lower flow values, which averaged 156.7 ml/min on the left, and 209.8 ml/min on the right side. Already during the first control after surgery, a significant increase in the blood flow was reported in both internal jugular veins, which persisted at 3 and 6 months after the procedure, with the exception of patients with restenosis, where it involved nearly 30% of cases (Figure 6).

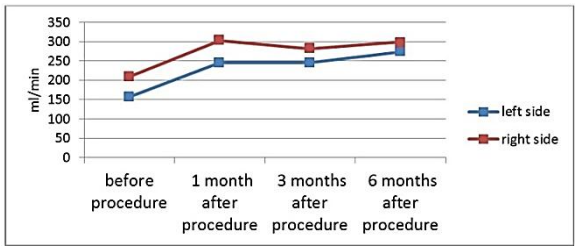

Figure 6: Comparison of the blood flow through the internal jugular veins before and after endovascular treatment.

Macgowan et al. compared the jugular venous flow in patients with MS and healthy volunteers using MRI. The right and left vein flow values were IJV=342 ± 180 and 190 ± 131 ml/min respectively and did not differ significantly from the corresponding flow values recorded in healthy volunteers. Similar results were reported in the study by Rodger, as discussed above [19,25].

Scalise et al. showed in a group of 45 MS patients, who underwent jugular veins venoplasty, a statistically significant improvement in the venous hemodynamics and venous hemodynamic severity score (VHISS) [26], which, as in our study, demonstrated the impact of angioplasty procedures on the changes in hemodynamics within the cerebral flow. The result of the work carried out by Sternberg et al. may be an indirect evidence of the impact of treatments on the jugular venous hemodynamics. They showed that jugular vein angioplasty in patients with MS normalized the blood pressure. An increase in pressure was obtained in patients with low pressure (systolic ≤105 mmHg, diastolic ≤70 mmHg), while a decrease in this value was recorded in patients with pressure values above norm (systolic ≥130 mmHg, diastolic ≥80 mmHg) [27]. As might be expected, the beneficial hemodynamic effects of a vascular intervention should be translated into an improvement in the neurological condition of surgical patients. Although in our study higher minute volumes persisted during subsequent check-ups, an improvement of the blood flow through the internal jugular veins has not been translated into a significant improvement in the clinical condition of patients. Our observations suggest that, firstly, jugular vein angioplasty, and in some cases stents, did not improve the flow to the values obtained in healthy subjects. Secondly, the endovascular intervention, although statistically significantly improved the outflow from the CNS, did not significantly affect the quality of life of the treated patients.

Perhaps this mediocre clinical effect is due to the fact that the treatment was carried out only on the internal jugular vein and the impaired outflow from the CNS can be caused by changes in the vertebral and azygos veins. The presence of pathology within these vessels or the intracerebral veins cannot be reflected by corresponding hemodynamic effects, especially when the patient is in a sitting or standing position, when the outflow from the CNS occurs primarily through the vertebral and azygos veins [28].

Siddiqui et al. demonstrated that clinical and MRI outcomes are no better or worse in patients with MS who receive venous angioplasty compared to control group. No significant between-group changes in EDSS, MSFC, cognitive or QoL outcomes were detected. 4 relapses occurred in the treated group and 1 in the sham group in 6-months follow-up but there was no statistical evidence that a more relapses in the treated patients were related to angioplasty vs sham treatment status [29].

Several published studies, as well as our own observations, reveal the disappearance of a positive clinical effect of the treatment over time [30,31]. The explanation of the reasons for such changes requires further observation and cohort studies.

Conclusion

Despite a significant improvement in the blood flow through the internal jugular veins after endovascular interventions on the internal jugular veins in CCSVI patients, it has not demonstrated that hemodynamic changes improve the quality of life in MS patients. The authors suggest the cessation of jugular venous angioplasty procedures on a large scale until the publication of randomized clinical trials, which would confirm or challenge the usefulness of angioplasty in MS patients.

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