

Venous Imaging and Venous Angioplasty in Multiple Sclerosis (MS)

Two recent studies by an Italian vascular surgeon, Dr. Paolo Zamboni, describing a potential new approach to treating Multiple Sclerosis (MS), have generated significant interest. The studies by Dr. Zamboni suggest that there *may* be an association between chronic cerebrospinal venous abnormalities and MS. However, this possible association requires confirmation by independent investigators conducting larger, “controlled” research trials. In fact, preliminary results from the University of Buffalo suggest the association is much weaker than that reported by Dr. Zamboni. Funding for further studies is currently being expedited by MS Societies in several countries including Canada.

On the basis of Dr. Zamboni’s studies, many MS patients have sought diagnostic imaging services, neurological and vascular surgery consultations, and venous angioplasty.

Synopsis of Dr. Zamboni’s Studies:

Dr. Zamboni’s first study reported the coexistence of MS and venous abnormalities which have been called “chronic cerebrospinal venous insufficiency” or CCSVI.

In his second study, Dr. Zamboni performed venous angioplasty on MS patients with coexistent CCSVI (as defined in his first study). Although the percentage of patients who were symptom-free was reported to have increased after venous angioplasty, the actual annualized relapse rate for the entire group remained unchanged. These findings, which appear somewhat contradictory, are likely explained by a small number of people having more relapses after intervention and / or by differences in the period of observation before and after the procedure. Nonetheless, the relapse outcomes do not clearly support a clinical benefit of venous angioplasty.

Dr. Zamboni also described improved neurological status and reduced inflammatory activity, as detected by Magnetic Resonance Imaging (MRI), in patients with the “Relapsing – Remitting” form of MS. However, this study did not have an untreated comparison (“control”) group of patients, and outcomes were not measured according to accepted research standards (below).

Why must there be further research to determine if Dr. Zamboni's results are truly related to venous angioplasty?

Neurological Function

Improvement in the main study measure of neurological function, the "Multiple Sclerosis Functional Composite" (MSFC), is often seen due to "practice effects." Performance on the walking, hand function, and cognitive tasks that make up this scale improves initially because of practice and increasing familiarity with the tasks by the patients being tested. Therefore, in research studies, the scale must be repeated by study participants at least three or four times before a baseline (pre-treatment) assessment is recorded. No such practice trials were undertaken in Dr. Zamboni's study. Thus, improvement may have been due to "practice."

Quality of Life Measurement

Quality of life typically improves after many research-related interventions and it is well recognized that results after interventions cannot be interpreted without a randomly determined "control" group; i.e. a group of similar patients who are tested and followed in the same fashion but who did not receive the intervention being studied.

MRI

As reported by the study authors, the MRI scans in Dr. Zamboni's trials were undertaken at different intervals before and after the intervention, on different MRI scanners, and using different MRI protocols. Therefore, the results of the scans cannot be reliably compared or interpreted.

Relapse Frequency

In other MS treatment trials, relapse frequency decreases even in untreated (control or placebo-treated) patients. The reported increase in the number of people who were relapse-free after treatment in Dr. Zamboni's study is therefore expected. However, without an untreated comparison group, this possible benefit cannot be interpreted as being due to venous angioplasty itself. In addition, the occurrence and number of relapses in Dr. Zamboni's study were determined only by recall of the patients, rather than through assessment by their healthcare providers. Thus, the relapse numbers can only be considered estimates that require confirmation in well designed clinical trials.

Cerebrospinal venous occlusion

Jugular venous occlusions occur in other situations and do not cause MS or brain injury

Results from subsequent studies:

Dr. Zivadinov (University of Buffalo) has reported results of venous ultrasounds completed on 500 people. In his study CCSVI was found in 56.4% of people with MS, 22.4% of people without MS and 42% of patients with other neurological diseases. Doepp et al (Annals of Neurology) using color doppler technique, reported no CCSVI in 56 MS patients and 21 controls in Germany. Groups from Sweden and United Kingdom have also reported similar preliminary results. While the final answer is not clear, the above studies do not confirm Dr. Zamboni's findings.

MS in Nova Scotia:

Nova Scotia has a high prevalence of MS and has had a world class MS research program for 30 years. These physicians are interested in participating in a formal multicentre clinical trial if and when there is validation of Dr Zamboni's hypothesis. These experts keep the Department of Health, MS patients and the public informed of potential new therapies as they evolve.

Nova Scotia Department of Health and Wellness's Position:

- **At this time, it is only a hypothesis that CCSVI contributes to, or causes, Multiple Sclerosis, and that venous angioplasty is clinically beneficial.**
- **Further, independent and controlled studies are required to prove, discount, or better understand Dr. Zamboni's study results.**
- **At present, there is no proven indication for venous imaging or venous angioplasty in patients with Multiple Sclerosis. Therefore, unless they are part of an approved research protocol, these procedures will *not* be provided in NS to persons with MS.**
- **If, and when, there is independent scientific validation of Dr Zamboni's results, the Department of Health will consider introducing the new procedure into Nova Scotia.**

Follow up for patients who have had venous angioplasty performed for MS:

- **There is no proven indication for venous imaging or venous angioplasty in patients with Multiple Sclerosis and this procedure is not available in Nova Scotia for these patients at present. This means that patients cannot obtain these tests within the District Health Authorities in NS to check on the status of their veins after a venous angioplasty has been performed.**
- **Routine follow up by the family doctor or neurologist is available to patients in the same manner as it would have been had they never received a venous angioplasty.**
- **Urgent medical complications occurring in a patient who has had a venous angioplasty will be seen, assessed and treated in the same way as any patient presenting with a medical complication to a physician. Appropriate treatment would not include further angioplasty.**