

CCSVI Science – The Latest Results and their Relevance

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The recently held ECTRIMS conference contained the results of 14 studies which have relevance for CCSVI and MS. Of the 14 studies presented, 10 supported the concept that CCSVI is highly associated with MS and that it likely contributes to the disease process. Three were negative and one curiously contained both positive and negative information. Seven of the positive reports came from the extensive work being done on CCSVI and MS at the University of Buffalo. I have reported some of the initial results of this work in a previous column and it is worth repeating that their results involved 499 subjects including those with MS (243), CIS (21), other neurological diseases (15) and healthy controls (73).

The detection of CCSVI was done mainly by Doppler ultrasound technology and it was found that CCSVI was almost 3 times as common in persons with MS compared with healthy controls. This strongly supports the concept that CCSVI is highly associated with MS. Some new results which are relevant include persons with MS and CCSVI had significantly higher lesion volume, lower gray matter volume and lower brain volume than those with MS and no CCSVI. As stated by the authors, “Presence of CCSVI is significantly related to more severe lesion and brain atrophy MRI measures” and this is solid evidence that CCSVI plays an important role in the MS disease process.

The Buffalo workers also found that “Subjects with CCSVI were significantly older than subjects without CCSVI” and that “The presence of CCSVI in MS patients was associated with more advanced MS disease subtypes and more severe motor, cerebellar and brainstem involvement”. These findings may mean that the presence of CCSVI results in more severe MS. Alternatively, they may mean that the MS disease process makes CCSVI worse and thus, the longer and more severe MS is, the greater the venous impairment.

Other notable research findings presented by University of Buffalo researchers include:

- 1) Greater disability and longer disease duration in MS were correlated to higher iron content in the brain. This finding relates to CCSVI in that CCSVI provides one of the best explanations for increased deposition of iron in the brain.
- 2) The venous vasculature of the brain in persons with MS is significantly less than that of healthy controls. This was found to be due to decreased cerebral blood flow (hypoperfusion). This finding has relevance to CCSVI because it has been postulated that CCSVI would result in hypoperfusion which in turn could cause weakening of the BBB and the loss of myelin.
- 3) "MRV has limited value to assess CCSVI for both diagnostic and follow-up purposes". This finding is important because it helps to evaluate studies which test the association of CCSVI and MS solely through the use of MRV. Clearly such studies have "limited value", especially if they are small and are done by persons with little to no previous experience with detecting CCSVI.

Finally, the University of Buffalo researchers treated 15 patients with CCSVI with venous angioplasty to correct any venous blockages. The findings from this work include, venous angioplasty is a very safe procedure, rates of restenosis were moderate for jugular veins (29%) and absent for the azygos vein, and that there was a significant decrease in lesion number six months following treatment. This study demonstrates the undoubted existence of CCSVI in persons with MS and that CCSVI treatment may well be of value for slowing the MS disease process.

Dr Simka and his team from Poland presented the results of two important studies. Their findings are based on their clinical treatment of 330 patients with MS and CCSVI and this represented over 95% of the patients they had evaluated. The finding that over 95% of 350 persons with MS had CCSVI as determined by venography leaves no doubt as to the high association of CCSVI with MS. Another important finding was that there were no serious adverse effects of 414 venous angioplasties and 173 stent implantations. These data demonstrate that venous angioplasty is a very safe procedure. They also provide

some confidence that stent implantation may also be very safe although more and longer term data are needed.

The Polish clinicians found, in contrast to the Buffalo results, that “Severity of venous obstacles neither correlated with patients' age, nor did it with duration of the disease”. They also found that parameters of CCSVI correlated with various clinical characteristics of MS (e.g. disability level, eye problems). This led to the reasonable conclusions that “CCSVI may play a role in the pathogenesis and progression of MS” and that the venous malformations are congenital in origin.

There were 4 negative studies presented but notably all involved a small number of subjects compared with the Buffalo and Poland work. One study from Germany involved 59 patients and used only Doppler ultrasound to detect CCSVI. They found no CCSVI, a basically absurd result given the results of the Polish and Buffalo work. A very small study from Holland tested 20 patients with MS for CCSVI using MRV and found only 4 with CCSVI. The established unreliability of MRV, the low number of subjects, and the researchers' lack of experience, readily account for such a result. A study from Italy tested 50 patients with CIS for CCSVI using Doppler ultrasound. They found only eight (16%) had CCSVI. This result is likely due to testing only CIS patients and the use of Doppler ultrasound which is very operator dependent and thus sometimes unreliable.

The final study was done in Lebanon and included some positive results as well as negative ones. Importantly, the researchers used venography for detecting CCSVI so their results have to be taken seriously. They found that 12 of 13 (92%) of persons with MS for over 10 years had venous anomalies and such a result is consistent with those from Poland (i.e. a high association). In persons with MS for less than 5 years, they found only 6 of 18 (33%) had venous problems. This suggests that CCSVI may well worsen and become obvious as MS progresses as the Buffalo results indicated. Finally, only one of eleven persons with CIS had venous anomalies (9%). Again this may indicate that CCSVI either is harder to detect at the start of MS or that it develops due to the MS disease process. In contrast, the more experienced Buffalo workers found about 40% of CIS subjects had CCSVI and that 75% had at least one venous anomaly.

So what does all this new information tell us? The studies with hundreds of subjects and the use of venography by experienced clinicians produce by far the most reliable results. Such work tells us that CCSVI is very highly associated with MS (>90%) and that it very likely contributes to the MS disease process. However, it is still unsure if CCSVI is mainly a cause or an effect of MS. It is also apparent that small studies which use only non-invasive techniques for determining CCSVI are extremely unreliable and the results cannot be taken seriously.

In summary, the new results strongly support the involvement of CCSVI in MS and thus it is important for all persons with MS to be tested and treated for CCSVI as soon as possible.