Reviewer's report

**Title:** Chronic cerebrospinal venous insufficiency in Multiple Sclerosis: an highly prevalent age-dependent phenomenon without clinical correlations

**Version:** 2  **Date:** 18 September 2012

**Reviewer:** Marian Simka

**Reviewer's report:**

**Major Compulsory Revisions**

1. **Abstract.** Unexplained terms, like criterion 4, should not be used in abstract. Please remember that majority of potential readers will read abstract only. Thus, abstract should present the paper in a microcosm and should be self-sufficient.

2. **Abstract.** The authors have concluded that CCSVI was not correlated with MS. It is quite contrary to the results (statistically significant higher prevalence of CCSVI among MS patients compared to healthy controls).

3. **Abstract.** The authors concluded that CCSVI seemed to be age-dependent phenomenon. Still, this statement is poorly evidenced (alternative explanations are possible, which I will further discuss). Similarly, no data are backing the idea of an accelerated aging of the veins or their chronic inflammation (published evidenced has revealed quite the contrary phenomena). Consequently, these statements should be removed and the abstract should be rewritten.

4. **Results.** Sensitivity and specificity are improper statistical variables used. It is possible to calculate sensitivity or specificity while comparing one diagnostic test to "gold standard" test or a test with established diagnostic accuracy. Here the authors are comparing sonographic diagnosis of CCSVI with clinical diagnosis of MS, which is highly inappropriate. Consequently, the chapters “Results” and “Discussion” should be rewritten.

5. **Discussion.** A higher prevalence of CCSVI in older MS patients could be simply the result of selection bias, but it is also possible that CCSVI is linked to MS in such a way that it favors disease development in relatively low-predisposed (older) subjects. Such a potential relationship has been discussed in:

   
Consequently, the authors cannot state that they have excluded a congenital nature of CCSVI lesions. Moreover, there is another paper (original research) that favors the idea of CCSVI being a congenital pathology:

6. Discussion. Actually there is no anatomical conflict between sternocleidomastoid muscle and jugular vein in the lower part of the neck, still such a conflict may be present in the middle part of the neck, which has been described in the literature. However, the authors were examining the patients and controls with their necks not rotated (am I right?) - thus excluding this potential source of bias. The idea of undesired contraction of neck muscles resulting in compression of jugular vein is not supported by the anatomy of this area (contrary to compression of the vein during rotation).

7. Discussion. If CCSVI were simply age-dependent, then a higher prevalence of CCSVI should also be found in control group.

8. Discussion. The idea of chronic inflammation resulting in CCSVI is not backed by published evidence. Please look at:


9. Discussion, last paragraph. Conclusions are neither backed by the results of this study nor by published evidence. This part should be rewritten.

10. Table 2. The terms “sensitivity” and “specificity” are not correct. The table should be removed.

11. Minor Essential Revisions

12. Abstract. In general, abbreviations should not be used in an abstract (only if absolutely needed to follow the word limit).

13. Background. In addition to sonographic studies (with rather inconsistent results) research that has used catheter venography should be cited.


14. Patients and methods. “genetically related” and “genetically unrelated” – these terms should be explained (most likely they are incorrect).
15. Results. “one or more positive criteria”. It should be explained which criteria were regarded (Zamboni’s criteria for CCSVI?)

16. Results. “CCSVI status” What does it mean?

17. Results. “mostly impaired functional system” What does it mean?

18. Results. “increased prevalence” What does it mean; a “higher prevalence”?

19. Discussion. “a recent study [20]”. Actually the cited paper is a review and not an original paper, thus the term “study” seems inappropriate.

20. Discussion. Paper [21] deals with jugular reflux and not with CCSVI. These are very different pathologies.

21. Discussion. “detectable flux” What does it mean?

22. Discussion. “controls 21” – should be “controls [19]”

23. References. Some papers should be included, as previously suggested.

24. Figure 1. It is very difficult to follow the bars. Perhaps the bars should not be grouped: “CIS”, “PPMS”, “SPMS” etc. but: “CCSVI”, “negative CSA”, etc. In addition, the bars should rather be presented vertically and not horizontally.

25. Figure 1 legend. “B-mode anomalies were the more” What does it mean?

26. The paper is written in poor English, sometimes it is very difficult to understand the text. English proofreading would be appreciated.

**Level of interest:** An article of importance in its field

**Quality of written English:** Not suitable for publication unless extensively edited

**Statistical review:** No, the manuscript does not need to be seen by a statistician.

**Declaration of competing interests:**

received publication fees from Servier International;
received speaker fees from American Access Care;
received congress costs reimbursement from Esaote International;
employed in the hospital, where the treatments for CCSVI are patient-paid