Reviewer's report

Title: Clinical Correlates of Chronic Cerebrospinal Venous Insufficiency in Multiple Sclerosis

Version: 2 Date: 12 September 2011

Reviewer: Robert Fox

Reviewer’s report:

Weinstock-Guttman and colleagues report a post-hoc analysis of a large CCSVI study. In this report, they correlate CCSVI status and severity (using VHISS) and disability as measured by EDSS and MSSS. As observed in a previous report of this study, they observed an increased prevalence of CCSVI in progressive MS patients compared to relapsing MS patients. Similarly, VHISS was higher in SPMS patients, although no formal comparison was performed except for a 4-group Kruskal-Wallis test. Surprisingly, EDSS >4 was not associated with the presence of CCSVI, and MSSS showed only a trend in an uncorrected analysis, and no association after correcting for sex and age.

VHISS was associated only with brainstem EDSS, with trends in pyramidal, cerebellar, and sensory subscores. No correlation between VHISS and overall EDSS was provided.

However, the discussion includes the statement, “VHISS was shown to correlate significantly with the clinical disability EDSS and MSSS as well as with most of the EDSS subscale scores (pyramidal, cerebellar, brainstem and sensory.” No statistics were provided in the Results section regarding correlation between the presence/absence of CCSVI and EDSS subscores – only table 3, which shows the comparison, but provides no analysis. In general, there is a significant disconnect between the Results shown and the conclusions drawn in the Discussion.

A deeper discussion is needed regarding the disconnect between disease stage and disability as they relate to CCSVI. Disease stage correlates well with CCSVI, but disability much less so (if at all).

Additional comments:

1. The adjustment for multiple comparisons at p=0.01 needs more formal justification. The 60 comparisons in table 3 suggest that 0.01 is not sufficient adjustment.
2. There are many typographical errors throughout the manuscript.
3. Much of the Table 2 legend has no relevance to the content of Table 2.
4. The correlations between VHISS and EDSS subscores should be shown, not just cited as a p-value.
5. The relevance of ANM to CCSVI needs to be more clearly stated, or removed
6. The disclosures are incomplete: the authors currently perform CCSVI testing as a clinical service, with direct charges to MS patients. This is a relevant disclosure that should be included.

**Level of interest:** An article of limited interest

**Quality of written English:** Acceptable

**Statistical review:** Yes, and I have assessed the statistics in my report.

**Declaration of competing interests:**

I have no competing interests.