Author's response to reviews

Title: Chronic cerebrospinal venous insufficiency in Multiple Sclerosis: an highly prevalent age-dependent phenomenon

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Author's response to reviews: see over
To the Editor-
Dr. Robert Zivadinov
BioMed Central

Dear Dr. Robert Zivadinov,

I send you the final copy of our manuscript, n 3697861107767469, entitled “Chronic cerebrospinal venous insufficiency in Multiple Sclerosis: an highly prevalent age-dependent phenomenon”.

The paper has been professional edited by Edanz Group, and the minor criticism suggested by the reviewer 1 have been solved.

I have upload a file were we answer point-to-point to the reviewer comments.

As you requested I have included in this letter the two versions of the abstract (original version and Edited version by the Reviewer).

Thank you again for considering the final paper for publication.

Best regards

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Reviewer's report:
Major Compulsory Revisions
1. Since the English is very poor, the paper needs extensive reediting.
   The paper was extensive reedited

2. Since I am afraid that the abstract cannot be much improved unless the job is done by very professional company, a proposal of reedited abstract is attached.
   The abstract was changed.

Minor Essential Revisions
1. Keywords should ideally come from the MeSH list. CCSVI and Echo-color Doppler are not in this list. Should be substituted by: Venous insufficiency and Ultrasonography.
   The changes were made

2. The term "Colour Doppler sonography" instead of "Echo colour Doppler" should be used.
   The changes were made

Abstract

Original version

Background
The aim of our research was to investigate the prevalence of chronic cerebrospinal venous insufficiency (CCSVI) by intra and extra cranial Echo-Colour-Doppler (ECD) in Multiple Sclerosis (MS) patients and in healthy controls (HC) and its clinical and demographic correlations.

Methods
We included 171 consecutive MS patients belonging to Relapsing Remitting (RR), Secondary Progressive (SP), Primary Progressive (PP) forms of disease and Clinically Isolated Syndromes (CIS), and 41 matched HC. We performed neck and transcranial ECD, according to Zamboni procedure, to define CCSVI condition. Clinical and demographic data were collected, EDSS was evaluated and MSSS measured. Prevalence, sensitivity and specificity and Odds ratios were calculated for CCSVI and single venous hemodynamic criteria. ECD results were correlated with demographic and clinical data.

Results
We achieved concordant CCSVI diagnosis among operators in 146 MS patients and 38 HC. Prevalence of CCSVI was 76% in MS patients and 16% in HC (p<0.001). B-mode abnormalities of IJV as stenosis, malformed valves, annulus and septa were the more frequently detected anomalies, both in MS patients (80.8%) and controls (47.4%). CCSVI was positively related with age in the MS group (p=0.003) but not in HC group (p=0.635). There were no correlations between CCSVI presence and clinical features, while the isolated absence of flow in the jugular veins was significantly more frequent in primary and secondary progressive patients respect to non progressive ones (p<0.005 and p<0.05 respectively), but it was also strongly related to age (p<0.0001).

Conclusions
CCSVI is a highly prevalent phenomenon in MS, but it seems to be age dependent and without clinical correlations.
Background. The aim of our research was to investigate prevalence and clinical relevance of chronic cerebrospinal venous insufficiency (CCSVI) in multiple sclerosis (MS) patients and health controls using extra- and intracranial colour Doppler sonography.

Methods. We examined 171 consecutive MS patients, presenting with clinically isolated syndrome, relapsing remitting, secondary progressive or primary progressive MS and 41 healthy controls. Sonographic examination was performed according to Zamboni’s protocol and was done by three independent sonographers. Results of sonographic examination were compared with clinical and demographic characteristics of the patients.

Results. CCSVI, defined as the presence of at least 2 positive Zamboni’s criteria, was found in 76% of MS patients and 16% of control subjects (p<0.001). Sonographic diagnosis of CCSVI given by all three examiners was concordant in 146 MS patients (85.4%) and 38 controls (92.7%). B-mode anomalies of internal jugular veins, such as: stenoses, malformed valves, annuli and septa were the most common lesions detected, both in MS patients (80.8%) and in controls (47.4%). We revealed a positive correlation between sonographic diagnosis of CCSVI and patients’ age (p=0.003). However, such a correlation was not found in healthy controls (p=635). Of note, no significant correlations were found between sonographic signs of CCSVI and clinical characteristics of MS, with the exception for absent flow in jugular veins, which anomaly more often found in primary (p<0.005) and secondary (p<0.05) progressive patients if compared with non-progressive patients. Still, an absent flow in jugular veins was also significantly (p<0.0001) correlated with patients’ age.

Conclusion. Sonographically defined CCSVI is very common in MS patients. However, it seems to be primarily associated with patients’ age, and poorly correlated with clinical course of the disease.