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Andreas Laupacis MD, MSc, FRCPC
Executive Director, Li Ka Shing Knowledge Institute
Canada Research Chair in Health Policy and
Citizen Engagement
Professor, Faculty of Medicine
University of Toronto

June 4, 2012

Dr. Alain Beaudet, Chair
Scientific Expert Panel on CCSVI and Multiple Sclerosis
Canadian Institutes of Health Research
160 Elgin Street, 9th floor
Ottawa, ON
K1A 0W9

Dear Alain:

On behalf of the co-authors, I am pleased to send you and the CIHR Expert Panel for Chronic Cerebrospinal Venous Insufficiency (CCSVI) and Multiple Sclerosis (MS) a review of the evidence that has been published since our second report in November 2011.

Four new studies have been published that assessed the frequency of CCSVI in patients with MS and controls. They ranged in size from 40 to 181 patients with MS. When these studies were added to the meta-analysis, there continues to be a strong, statistically significant odds ratio for the association of CCSVI with MS, although the odds ratio has decreased from 12.8 in our November 2011 report to 8.4 in this report. Heterogeneity in the results continues to be so great that definitive conclusions still cannot be made. We explored whether study blinding explained the heterogeneity. Although blinding of the interpretation of diagnostic tests is clearly important, especially for a test as subjective as ultrasonography, study blinding did not explain much of the heterogeneity in the results.

We note that an international group of individuals representing various international groups with an interest in venous abnormalities met in Bologna, Italy and published a detailed protocol for the evaluation of CCSVI with ultrasonography. This may help standardize the technique – as you know, there has been concern that the variability in results mentioned in the previous paragraph may at least be partially explained by differences in ultrasound technique. Perhaps the most important recommendation made by the group was to omit the evaluation of reflux in the deep cerebral veins from the assessment of CCSVI.

One new study assessed the harms of peri-procedure venoplasty, and like the studies published previously, found the frequency of serious harms to be low.

We are now aware of six randomized trials of venoplasty for MS that are underway, or about to get underway. The main design features of five of the trials are described in the report. We suggest that those conducting the trials consider prospectively planning an individual-patient meta-analysis, since this will be very helpful in exploring the efficacy and harms of venoplasty in subgroups of patients.

The report also summarizes the results of three new studies that compare different modalities for the assessment of cerebral veins, as well as seven other studies that did not meet our inclusion criteria for the systematic review, but are briefly described for completeness.

We hope that you and the members of the Expert Panel find this report helpful. Please let us know if you have any questions or concerns.

Yours sincerely,

A handwritten signature in black ink, appearing to read "Andreas Laupacis". The signature is written in a cursive style with a long horizontal stroke at the end.

Andreas Laupacis MD, MSc, FRCPC
Executive Director, Li Ka Shing Knowledge Institute

on behalf of the Canadian CCSVI Systematic Review Group

AL:cac