Some link between CCSVI and MS but quality of evidence prevents definitive conclusion

October 3 2011

Chronic cerebrospinal venous insufficiency (CCSVI) appears to be more common in people with multiple sclerosis than in people without the condition, states a review of published studies in *CMAJ* (*Canadian Medical Association Journal*). However, there are not enough high-quality studies to allow definitive conclusions.

CCSVI was defined by Zamboni and colleagues in 2009 as ultrasound-detectable abnormalities in the anatomy and blood flow in the veins draining blood from the brain and back. Dr. Zamboni found that CCSVI was much more common in people with multiple sclerosis than in people without multiple sclerosis and proposed that multiple sclerosis is caused by CCSVI.

The role of CCSVI in multiple sclerosis, a degenerative disease of the central nervous system, is controversial, and some researchers have not been able to replicate Zamboni's findings. Researchers from St. Michael's Hospital, University of Toronto, and Sunnybrook Health Sciences Centre in Toronto, and the University of Calgary in Alberta, conducted a meta-analysis of studies comparing the frequency of CCSVI in patients with and without multiple sclerosis. A meta-analysis combines the results of published studies in as objective and unbiased a manner as possible.

Eight studies, conducted in Italy, Germany, Jordan and the United States,

were included in the meta-analysis. The quality of the studies varied. Many of the studies were small and had incomplete descriptions of the training of those conducting the ultrasound studies. None of them reported the degree to which those conducting the ultrasounds knew whether or not the patient had multiple sclerosis.

The researchers found a large variation in the frequency of CCSVI in multiple sclerosis patients, from 0% in some studies to 100% in Zamboni's study. There was also a large variation in the degree to which CCSVI was associated with multiple sclerosis. Some studies found that CCSVI was much more frequent in patients with multiple sclerosis than those without multiple sclerosis, while other studies found a similar frequency of CCSVI in the two groups. However, when the results of all the studies were combined statistically, CCSVI was found more frequently in those with multiple sclerosis than in those who did not have multiple sclerosis.

"We found a strong and statistically significant association between chronic cerebrospinal venous insufficiency and multiple sclerosis. However, the large amount of heterogeneity among the study results prevents a definitive conclusion," writes Dr. Andreas Laupacis, Li Ka Shing Knowledge Institute of St. Michael's Hospital, Toronto, with coauthors. "The source of the heterogeneity is not clear. It is not obviously caused by differences in the definition of chronic cerebrospinal venous insufficiency, patient characteristics or the methodologic quality of the studies."

"We also could not identify any factor that accounted for the large and problematic difference between the studies in the frequency of chronic cerebrospinal venous insufficiency among patients with multiple sclerosis," state the authors.

They suggest that the difference could be due to small sample sizes of

the studies included in the analysis, as well as to differences in ultrasound techniques and quality control. Ultrasonography is dependent on the training and competence of the operator.

It is important to recognize that even if there is an association between chronic cerebrospinal venous insufficiency and multiple sclerosis, this ".... does not mean that the condition causes multiple sclerosis," caution the authors. If future studies find that CCSVI truly is more frequent in people with multiple sclerosis, it could be that multiple sclerosis causes CCSVI, or that CCSVI happens to occur more frequently in people with multiple sclerosis without causing the disease.

The authors conclude that "further high-quality studies, using identical ultrasound protocols, are needed to definitively determine whether chronic cerebrospinal venous insufficiency is more frequent among patients with multiple sclerosis than among those without it."

In a related commentary, Dr. Robert Fox from the Mellen Center for Multiple Sclerosis Treatment and Research at the Cleveland Clinic, Cleveland, Ohio, writes "The meta-analysis by Laupacis and colleagues is a good starting point; however, much work remains to be done before we can be certain whether chronic cerebrospinal venous insufficiency is a paradigm shift in the classic sense … or just another fad."

More information: DOI:10.1503/cmaj.111074

Provided by Canadian Medical Association Journal