New studies question vascular multiple sclerosis hypothesis and treatment

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Two important new studies challenge the controversial hypothesis that venous congestion?chronic cerebrospinal venous insufficiency (CCSVI)?contributes to the development of multiple sclerosis (MS). This theory has resulted in many MS patients receiving experimental endovascular angioplasty, a treatment for MS unproven by clinical trials. The studies refuting the CCSVI theory with the first negative medical evidence on the subject, are available today in *Annals of Neurology*, a journal published by Wiley-Blackwell on behalf of the American Neurological Association.

For nearly 150 years it has been known that focal MS lesions tend to develop around cerebral veins that are thought to the portal by which inflammatory cells targeting myelin enter the brain. However, a 2009 study by Zamboni et al. offered an alternative theory suggesting that chronically impaired venous drainage (blood flow) from the central nervous system?a term that he labeled Chronic Cerebrospinal Venous Insufficiency or CCSVI?leads to MS development.1 Zamboni et al. also claimed that endovascular angioplasty was markedly effective in MS patients.2 Zamboni's work gained much attention in the press, especially their report that ultrasound diagnosis of CCSVI perfectly matched an MS diagnosis with 100% sensitivity and 100% specificity.

"These two papers should add a note of caution for MS patients and physicians who are contemplating interventions for possible venous abnormalities based on the findings of Zamboni. At this time, the theory must be considered unconfirmed and unproven. Such interventions carry risk, and several people have already been harmed by the inappropriate application of venous angioplasty and stenting for MS," says Stephen L. Hauser, M.D., the Robert A. Fishman Distinguished Professor and Chair of the Department of Neurology at the University of California, San Francisco, and editor-in-chief of the Annals of Neurology. A previously published review of the evidence in the Annals by Khan et al. noted that treatment procedures, based upon these findings, have included placing stents in the jugular veins of MS patients which led to serious injury in some cases.

In the current issue of the *Annals*, Florian Doepp, M.D., and colleagues in Germany performed an extended extra- and trans-cranial color-coded sonography study on 56 MS patients (36 female; 20 male) and 20 control subjects (12 female; 8 male). The analysis included extra-cranial venous blood volume flow (BVF), internal jugular vein (IJV) flow analysis during Valsalva maneuver (VM), as well as tests included in the CCSVI criteria.

Results showed that blood flow direction was normal in all participants, excluding one subject with relapsing-remitting MS. Furthermore, the research team noted that

blood volume flow (BVF) in both groups were equal in the supine body position. In summary, the researchers determined that none of the study participants fulfilled more than one criterion for CCSVI.

"Our results call into question the existence of CCSVI in a large proportion of patients with MS," said Dr. Doepp. "We did not find supporting evidence that cerebral venous congestion plays a significant role in the development of MS. Further studies are needed to clarify the difference between MS patients and healthy subjects in blood volume flow regulation," concluded Dr. Doepp.

A second study by researchers at Umeå University in Sweden also concluded that CCSVI does not contribute to the development of MS. The Swedish research team led by Peter Sundström, M.D., Ph.D., tested the vital component of the CCSVI theory?the obstructed IJV flow?in 21 MS patients and 20 healthy controls using magnetic resonance imaging with phase contrast (PC-MRI).

"Using PC-MRI, we were not able to reproduce the findings by Zamboni et al. which suggest CCSVI contributes to the development of MS," said Dr. Sundström. The researchers found no significant differences between the MS group and control group relating to total IJV blood flow. "Our study found no support for using endovascular procedures such as angioplasty or stenting to treat MS patients," Dr. Sundström affirmed.

MS is an inflammatory disease of the central nervous system in which lesions (plaques) form in the white matter of the brain and destroy the myelin sheath around nerve fibers. Initial symptoms of MS?typically blurred or double vision, muscle weakness, sensory changes, or difficulty with balance?usually appear between the ages of 20 and 40. The course can be relapsing-remitting or relentlessly progressive, and if untreated results in permanent neurologic disability in most affected individuals. MS affects 2.5 million individuals worldwide, making it one of the most common neurological disorders and causes of disability in young adults.

SOURCE [1]

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