Recommendations for Multimodal Noninvasive and Invasive Screening for Detection of Extracranial Venous Abnormalities Indicative of Chronic Cerebrospinal Venous Insufficiency: A Position Statement of the International Society for Neurovascular Disease

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Appendices A–D, **Figures E1–E12**, and **Tables E1–E3** are available online at *www.jvir.org*.

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Under the auspices of the International Society for Neurovascular Disease (ISNVD), four expert panel committees were created from the ISNVD membership between 2011 and 2012 to determine and standardize noninvasive and invasive imaging protocols for detection of extracranial venous abnormalities indicative of chronic cerebrospinal venous insufficiency (CCSVI). The committees created working groups on color Doppler ultrasound (US), magnetic resonance (MR) imaging, catheter venography (CV), and intravascular US. Each group organized a workshop focused on its assigned imaging modality. Non–ISNVD members from other societies were invited to contribute to the various workshops. More than 60 neurology, radiology, vascular surgery, and interventional radiology experts participated in these workshops and contributed to the development of standardized noninvasive and invasive imaging protocols for the detection of extracranial venous abnormalities indicative of CCSVI. This ISNVD position statement presents the MR imaging and intravascular US protocols for the first time and describes refined color Doppler US and CV protocols. It also emphasizes the need for the use of for noninvasive and invasive multimodal imaging to diagnose adequately and monitor extracranial venous abnormalities indicative of CCSVI for open-label or double-blinded, randomized, controlled studies.

ABBREVIATIONS

CCSVI = chronic cerebrospinal venous insufficiency, CNS = central nervous system, CSA = cross-sectional area, CV = catheter venography, IJV = internal jugular vein, ISNVD = International Society for Neurovascular Disease, MS = multiple sclerosis, PREMiSe = Prospective Randomized Endovascular Treatment in Multiple Sclerosis, VH = venous hemodynamic, VV = vertebral vein

The extracranial venous drainage of the cerebrospinal nervous system is complex, not widely examined, and only partially understood (1,2). It is often asymmetric and presents significantly more variability than the extracranial arterial anatomy that supplies the central nervous system (CNS). Contrary to other venous territories, relatively little is known about anatomic variations and the hemodynamics of the internal jugular veins (IJVs) (2,3), and even less is known about the azygos vein (4). Currently, disagreement remains about the physiologic range of hemodynamic measurements in these veins, including determination of normal or abnormal function. The walls of the IJVs and azygos vein are typically very compliant, with lumen diameters that are variable and influenced by postural change, respiration, cardiac function, hydration status, and even by the pulsation of nearby arteries (5,6). When imaging the extracranial venous drainage of the CNS, it is difficult to confidently account for all these factors, and this can influence the diagnostic value of the assessment, regardless of the imaging modality used.

Chronic cerebrospinal venous insufficiency (CCSVI) is a condition characterized by impaired venous drainage of the brain and spinal cord as a result of outflow obstruction in the extracranial venous system caused by stenoses or obstructions of the IJVs and/or azygos vein. Currently, its noninvasive diagnosis is based on the color Doppler ultrasound (US) evaluation of five venous hemodynamic (VH) criteria in the extracranial (ie, neck) and intracranial veins (4). The initial study found that two or more of the five proposed criteria were met in a high proportion of patients with multiple sclerosis (MS) (4). However, subsequent studies demonstrated that the condition is not unique to patients with MS and that healthy individuals and patients with other CNS disorders can also fulfill multiple VH criteria (7–13). Conversely, several recent color Doppler US studies reported extremely low rates of CCSVI, diagnosed based on two or more positive color Doppler US criteria, in patients with MS and healthy individuals (14–20).

Because the reproducibility of the categoric CCSVI color Doppler US-based diagnosis depends on the training level and skills of the operator and blinding and reading criteria (7,8,20–23), the usefulness and applicability of the CCSVI color Doppler US-based diagnosis in clinical research and practice is limited. Moreover, because healthy individuals do not have CNS disorders, its clinical relevance as a nosologic entity was immediately questioned (24). CCSVI implies a pathologic condition or disorder characterized by extracranial venous structural/morphologic, hemodynamic/functional abnormalities. Whether this condition is primarily characterized by clinical symptoms, such as headache, fatigue, sleep disturbances, and autonomic dysfunctions that can be improved by using endovascular treatment is unclear at this time (25).

A variety of other noninvasive and invasive imaging modalities have been proposed for the screening and diagnosis of CCSVI (5). In addition to color Doppler US, magnetic resonance (MR) imaging, specifically MR venography, has been proposed as a screening examination for CCSVI (8,16,26–31). MR venography allows noninvasive visualization of the entire venous system of the neck, central chest veins, brachiocephalic veins, and dural sinuses, but it cannot satisfactorily evaluate the azygos and hemiazygous veins (5). Catheter venography (CV) is considered the invasive gold-standard method for visualization of the IJVs and