multiple sclerosis
international federation

MSIF CCSVI Research Bulletin, 01 December 2011

Research papers:

Kantarci F, Albayram S, Demirci NO, Esenkaya A, Uluduz D, Uysal O, Saip S, Siva A. **"Chronic cerebrospinal venous insufficiency: does ultrasound really distinguish multiple sclerosis subjects from healthy controls?"** *Eur Radiol.* 2011 Nov 29. [Epub ahead of print]

PMID: 22124776

Abstract

OBJECTIVES:

To investigate the differences between multiple sclerosis (MS) and control subjects by using extracranial venous grey-scale, colour and spectral Doppler ultrasound.

METHODS:

The study included 62 subjects with a definitive diagnosis of MS and 54 control subjects. The cross sectional area (CSA), reflux during Valsalva manoeuvre, presence or absence of flow in the internal jugular vein (IJV) were assessed in upright and supine positions. The IJV and vertebral vein (VV) flow volumes (BFV) were also studied.

RESULTS:

Reflux in the IJV, an upright CSA greater than a supine CSA, and the presence or absence of flow in the IJV were not different between MS and control subjects. A CSA ≤ 0.3 cm(2) was observed to be significantly higher in MS subjects. The IJV BFV was not significantly different between the groups; however, the VV BFV was significantly higher on the right side and lower on the left side in MS subjects.

CONCLUSIONS:

Our use of ultrasound criteria reported in the literature for MS reveals differences between healthy controls and MS subjects that also overlap. Our experience suggests that Doppler ultrasound may not be clinically reliable and more studies are needed to clarify its role, if any. Key Points • Chronic cerebrospinal venous insufficiency is a controversial topic in multiple sclerosis. • Ultrasound assessment of extracranial veins has yielded different results in the literature. • These differences may be due to dependence on Doppler and selection bias. • We found variations in vertebral vein flow in patients with multiple sclerosis.

Dolic K, Weinstock-Guttman B, Marr K, Valnarov V, Carl E, Hagemeier J, Brooks C, Kilanowski C, Hojnacki D, Ramanathan M, Zivadinov R**. "Risk Factors for Chronic Cerebrospinal Venous Insufficiency (CCSVI) in a Large Cohort of Volunteers."** *PLoS One.* 2011;6(11):e28062. Epub 2011 Nov 30.

PMID: 22140507 Free PubMed Central article PMCID: PMC3227626

Abstract

BACKGROUND:

The role of intra- and extra-cranial venous system impairment in the pathogenesis of various vascular, inflammatory and neurodegenerative neurological disorders, as well as in aging, has not been studied in detail. Nor have risk factors been determined for increased susceptibility of venous pathology in the intra-cranial and extra-cranial veins. The aim of this study was to investigate the association between presence of a newly proposed vascular condition called chronic cerebrospinal venous insufficiency (CCSVI) and environmental factors in a large volunteer control group without known central nervous system pathology.

METHODS AND FINDINGS:

The data were collected in a prospective study from 252 subjects who were screened for medical history as part of the entry criteria and participated in the case-control study of CCSVI prevalence in multiple sclerosis (MS) patients, and then were analyzed post-hoc. All participants underwent physical and Doppler sonography examinations, and were assessed with a structured environmental questionnaire. Fullfilment of ≥2 positive venous hemodynamic (VH) criteria on Doppler sonography was considered indicative of CCSVI diagnosis. Risk and protective factors associated with CCSVI were analyzed using logistic regression analysis. Seventy (27.8%) subjects presented with CCSVI diagnosis and 153 (60.7%) presented with one or more VH criteria. The presence of heart disease (p=.001), especially heart murmurs (p=.007), a history of infectious mononucleosis (p=.002), and irritable bowel syndrome (p=.005) were associated with more frequent CCSVI diagnosis. Current or previous smoking (p=.029) showed a trend for association with more frequent CCSVI diagnosis, while use of dietary supplements (p=.018) showed a trend for association with less frequent CCSVI diagnosis.

CONCLUSIONS:

Risk factors for CCSVI differ from established risk factors for peripheral venous diseases. Vascular, infectious and inflammatory factors were associated with higher CCSVI frequency.

Dolic K, Marr K, Valnarov V, Dwyer MG, Carl E, Karmon Y, Kennedy C, Brooks C, Kilanowski C, Hunt K, Siddiqui AH, Hojnacki D, Weinstock-Guttman B, Zivadinov R. **"Intra- and Extraluminal Structural and Functional Venous Anomalies in Multiple Sclerosis, as Evidenced by 2 Noninvasive Imaging Techniques."** AJNR Am J Neuroradiol. 2011 Dec 22. [Epub ahead of print]

PMID: 22194367

Abstract

BACKGROUND AND PURPOSE:

Chronic cerebrospinal venous insufficiency (CCSVI) is a vascular condition characterized by anomalies of the main extracranial cerebrospinal venous routes that interfere with normal venous outflow. Research into CCSVI will determine its sensitivity and specificity for a diagnosis of MS, its prevalence in MS patients, and its clinical, MRI, and genetic correlates. Our aim was to investigate the prevalence and number of intra- and extraluminal structural and functional extracranial venous abnormalities by using DS and MRV, in patients with MS and HCs.

MATERIALS AND METHODS:

One hundred fifty patients with MS, 104 (69.3%) with RR and 46 (30.7%) with a progressive MS course, and 63 age- and sex-matched HCs were scanned with 3T MR imaging by using TOF and TRICKS sequences (only patients with MS). All subjects underwent DS examination for intra- and extraluminal structural and functional abnormalities of the IJVs. Absent/pinpoint IJV flow morphology on MRV was considered an abnormal finding. Prominence of collateral extracranial veins was assessed with MRV.

RESULTS:

Patients with MS had a significantly higher number of functional ($P < .0001$), total ($P = .001$), and intraluminal ($P = .005$) structural IJV DS abnormalities than HCs. There was a trend for more patients with MS with extraluminal IJV DS abnormalities ($P = .023$). No significant differences were found on the MRV IJV flow morphology scale between patients with MS and HCs. Patients with progressive MS showed more extraluminal IJV DS abnormalities ($P = .01$) and more MRV flow abnormalities on TOF ($P = .006$) and TRICKS ($P = .01$) than patients with nonprogressive MS. There was a trend for a higher number of collateral veins in patients with MS than in HCs ($P = .016$).

CONCLUSIONS:

DS is more sensitive than MRV in detecting intraluminal structural and functional venous abnormalities in patients with MS compared with HCs, whereas MRV is more sensitive in showing collaterals.

Floris R, Centonze D, Fabiano S, Stefanini M, Marziali S, Del Giudice C, Reale CA, Castelli M, Garaci F, Melis M, Gandini R, Simonetti G. **"Prevalence study of chronic cerebrospinal venous insufficiency in patients with multiple sclerosis: preliminary data."** *Radiol Med.* 2012 Jan 7. [Epub ahead of print]

PMID:22228125

Abstract

PURPOSE:

This study aimed to evaluate the prevalence of chronic cerebrospinal venous insufficiency (CCSVI) in patients with multiple sclerosis (MS).

MATERIAL AND METHODS:

From November 2009 to February 2010, 74 participants (40 MS patients and 34 healthy controls) were enrolled in a randomised singleblind prospective study. All participants underwent ultrasonography (US) to detect signs of CCSVI.

RESULTS:

CCSVI was detected in 55% of patients in the MS group and 35% in the control group; the difference was not statistically significant (p=0.089).

CONCLUSIONS:

In our experience, a slight difference exists in the prevalence of CCSVI between MS and healthy controls, but it is not as yet clear which parameters may be most significant. This preliminary study failed to show a statistically significant difference in the prevalence of CCSVI among patients affected by MS. It did, however, reveal a tendency that requires a larger number of patients to achieve statistically significant results.

Ertl-Wagner B, Koerte I, Kuempfel T, Blaschek A, Laubender RP, Schick M, Steffinger D, Kaufmann D, Heinen F, Reiser M, Alperin N, Hohlfeld R. **"Non-specific alterations of craniocervical venous drainage in multiple sclerosis revealed by cardiac-gated phase-contrast MRI."** *Mult Scler.* 2011 Dec 22. [Epub ahead of print]

PMID: 22194216

Abstract

Objective: There is an on-going controversy about venous drainage abnormalities in multiple sclerosis (MS). We applied cardiac-gated phase-contrast and venographic magnetic resonance (MR) techniques to compare venous drainage patterns in patients with MS, healthy controls, and subjects with migraine.Methods: A total of 27 patients with MS (21 female, age 12-59 years, mean disease duration 8.4 ± 8.5 years) and 27 age- and gender-matched healthy controls (21 female, age 12-60 years) were investigated with velocity-encoded cine-phase contrast MR sequences and a 2D time-of-flight MR venography of the cervicocranial region on a 3-T MRI. The data were compared with 26 patients with chronic migraine headaches (19 female, age 17-62 years), previously investigated with the same

protocol. The degree of primary and secondary venous outflow in relation to the total cerebral blood flow (tCBF) was compared both quantitatively and qualitatively. Statistical analyses were performed using linear regression models.Results: Secondary venous outflow was significantly increased in patients with MS compared with healthy controls, both qualitatively ($p < 0.001$) and quantitatively ($p < 0.013$). The observed changes were independent of age and disease duration. Very similar alterations of venous drainage were detectable with the same approach in patients with migraine, without significant differences between MS and migraine patients ($p = 0.65$).Conclusion: Our MRI-based study suggests that patients with MS have alterations of cerebral venous drainage similar to subjects with chronic migraine. These non-disease-specific changes seem to a secondary phenomenon rather than being of primary pathogenic importance.

Haacke EM, Feng W, Utriainen D, Trifan G, Wu Z, Latif Z, Katkuri Y, Hewett J, Hubbard D. **"Patients with Multiple Sclerosis with Structural Venous Abnormalities on MR Imaging Exhibit an Abnormal Flow Distribution of the Internal Jugular Veins."** *J Vasc Interv Radiol.* 2012 Jan;23(1):60-68.e3.

PMID:22221473

Abstract

PURPOSE:

To evaluate extracranial venous structural and flow characteristics in patients with multiple sclerosis (MS).

MATERIALS AND METHODS:

Two hundred subjects with MS from two sites (n = 100 each) were evaluated with magnetic resonance (MR) imaging at 3 T. Contrast-enhanced time-resolved MR angiography and time-of-flight MR venography were used to assess vascular anatomy. Two-dimensional phase-contrast MR imaging was used to quantify blood flow. The MS population was divided into two groups: those with evident internal jugular vein (IJV) stenoses (stenotic group) and those without (nonstenotic group).

RESULTS:

Of the 200 patients, 136 (68%) showed IJV structural abnormalities, including unilateral or bilateral stenoses at different levels in the neck (n = 101; 50.5%) and atresia (n = 35; 17.5%). The total IJV flow normalized to the total arterial flow of the stenotic group (56% ± 22) was significantly lower than that of the nonstenotic group (77% ± 14; P < .001). The arterial/venous flow mismatch in the stenotic group (12% ± 15) was significantly greater than that in the nonstenotic group (6% ± 12; P < .001). The ratio of subdominant venous flow rate (Fsd) to dominant venous flow rate (Fd) for the stenotic group (0.38 ± 0.27) was significantly lower than for the nonstenotic group (0.59 ± 0.23; P < .001). The majority of the stenotic group (67%) also had an Fsd of less than 3 mL/s, a Fd/Fsd ratio greater than 3:1, and/or a total IJV flow rate of less than 8 mL/s.

CONCLUSIONS:

MR imaging provides a noninvasive means to separate stenotic from nonstenotic MS cases. The former group was more prevalent in the present MS population and carried significantly less flow in the IJVs than the latter.

Clinical case report:

Kipshidze N, Rukhadze I, Archvadze A, Kipiani V, Kipshidze N, Lapiashvili E, Kaloiani V. **"Endovascular treatment of patients with chronic cerebrospinal venous insufficiency and multiple sclerosis."** *Georgian Med News.* 2011 Oct;(199):29-34.

PMID:22155803

Abstract

Multiple sclerosis (MS) is an inflammatory demyelinating disease of the central nervous system (CNS) by an unknown pathogenesis. MR venography and postmortem studies have demonstrated a topographic correspondence between multiple sclerosis (MS) plaques and the cerebral venous system pathology. In recent observational studies performed on patients from distinctive gene pools, the prevalence of chronic cerebrospinal venous insufficiency (CCSVI) in MS ranged from 56% to 100%. Endovascular treatment (percutaneous transluminal angioplasty (PTA) with or without stenting) of CCSVI was reported to be feasible with a minor complication rate. In 4 patients with different forms of multiple sclerosis venography was performed that revealed stenosis of the proximal region of the jugular vein (right or left). Percutaneous transluminal balloon angioplasty (PTA) was performed in all patients. There were no complications and mean stenosis was reduced after PTA from 59,75% to 36,75%. Follow-up included clinical observations and magnetic resonance imaging (MRI). In all the cases we observed positive remission of the disease, the first ever documented case of MRI index improvement. PTA seems to be an effective treatment for patients with CCVI and multiple sclerosis, However, randomized studies are warranted to establish the efficacy of this new treatment for MS.

Reviews:

Bergqvist D, Wanhainen A**.[Cerebrospinal venous insufficiency as a cause of MS weakly supported. Unreasonable to offer balloon dilatation therapy now].**

[Article in Swedish] *Lakartidningen.* 2011 Sep 28-Oct 4;108(39):1899-901.

PMID: 22111226

Mehta M. **"Review of CCSVI and MS for EJVES."** *Eur J Vasc Endovasc Surg.* 2012 Jan;43(1):131.

PMID:22177012