Patients with Multiple Sclerosis with Structural Venous Abnormalities on MR Imaging Exhibit an Abnormal Flow Distribution of the Internal Jugular Veins

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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.

ABBREVIATIONS

CCA = common carotid artery, CCSVI = chronic cerebrospinal venous insufficiency, CE = contrast-enhanced, EJV = external jugular vein, Fd = dominant venous flow rate, Fsd = subdominant venous flow rate, FIJV = IJV flow, Fta = total arterial flow, LIJV = left internal jugular vein, IJV = internal jugular vein, MIP = maximum-intensity projection, MS = multiple sclerosis, PC = phase-contrast, RIJV = right internal jugular vein, 3D = three-dimensional, TOF = time of flight, 2D = two-dimensional, Venc = encoding velocity

Recent advances in multiple sclerosis (MS) suggest that there may be an association between impaired venous flow and the disease (1–5). Ultrasound (US) imaging (1,6–8) and magnetic resonance (MR) imaging (9–12) have been used to study these venous abnormalities. Each method has its strengths and weaknesses, but the three-dimensional (3D) information available to MR imaging might provide a more complete, or at least complementary, picture versus

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Appendices I–VII are available online at *www.jvir.org.*

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that presented with US, and it could also serve as an excellent means to judge anatomy and flow simultaneously. In the present study, data are presented for 200 patients with MS recruited from two sites (100 subjects from each site) who underwent conventional MR imaging as well as what is referred to as the chronic cerebrospinal venous insufficiency (CCSVI) protocol. This protocol collects data for vascular anatomy and flow in the major veins in different parts of the neck and brain. Combining these two pieces of information provides a powerful means to study vascular anomalies in MS. The goal of this study is to highlight the major venous anomalies as seen with MR imaging and report the flow characteristics, especially flow through the internal jugular veins (IJVs), in this population. This information might prove useful in better stratifying patients with abnormal venous flow and perhaps prove useful in treatment studies.

MATERIALS AND METHODS

A conventional clinical protocol for MS was combined with a specially designed CCSVI protocol. The conventional protocol included a T1-weighted scan before and after contrast agent administration, a two-dimensional (2D) fluid-attenuated inversion recovery scan, and a T2 scan when cerebrospinal fluid had to be visualized. The CCSVI protocol consisted of the following vascular sequences: a coronal 3D time-resolved contrast-enhanced (CE) MR arteriovenography scan, a transverse 2D time-of-flight (TOF) MR venography scan, and a 2D phase-contrast (PC) MR scan for flow quantification (sequence parameters detailed in Appendix I [available online at *www.jvir.org*]). Deidentified data from 200 patients with MS (100 from each of two sites) who underwent the CCSVI MR imaging protocol were evaluated. Of the 200 patients, the MS type was available for 133 patients: primary progressive MS (n = 34), secondary progressive MS (n = 31), and relapsing/remitting MS (n = 68). Institutional review board approval was obtained to perform the quantitative evaluation presented in this article.

Scanning Procedure

Data were collected at site 1 on a 3-T Tim Trio scanner (Siemens, Erlangen, Germany) with a 12-channel head/neck coil arrangement and at site 2 on a 3-T Signa HDxt scanner (GE Healthcare, Milwaukee, Wisconsin) with an eight-channel head/neck coil arrangement. The subject was centered at the orbital ridge for the brain scans. T1, fluid-attenuated inversion recovery, and, when needed, T2 data were acquired. After these scans, the subject was moved to the center at the chin in preparation for contrast medium injection. Just before injection, 2D TOF MR venographic data were collected. Contrast medium was then injected (OptiMARK [Covidien, Hazelwood, Missouri] at site 1 and Magnevist [Bayer, Wayne, New Jersey] at site 2, both with 0.2 mL/kg [0.1 mmol/kg]), and time-resolved MR angiographic data were collected for 20 time points. Then, 2D PC MR scans were obtained at three different levels in the neck (C2/C3, C5/C6, and T1/T2). Finally, the subject was recentered at the orbital ridge and a postcontrast T1 image matching the precontrast image was collected. Parallel imaging was used to speed up data acquisition by a factor of two when possible.

Data Processing

Data were processed by using Signal Processing in Nuclear MR software (SPIN, Detroit, Michigan) to evaluate vessel morphology. The time-resolved 3D CE MR arteriovenography data were viewed as original and subtracted data (ie, venous phase minus arterial phase) in 3D. Poor flow indicated by persistent contrast enhancement was cross-examined with 2D TOF MR venography and PC MR imaging. Anatomic assessment of data involved the identification of stenosis, aplasia, and atresia of the IJVs.

The 2D TOF MR venographic images were used to quantify any narrowings perceived in the coronal views of the 3D CE MR arteriovenography images because it provided higher in-plane resolution for cross-sectional measurements. IJVs that showed a cross-sectional area of less than 25 mm^2 (ie, one third of the cross-sectional area for an average IJV diameter of 1 cm [13,14] assuming a circular shape) in the lower-level C5/C6 or T1/T2 levels were considered stenotic. For upper-level narrowing (C2/C3), a cross section of less than 12.5 mm^2 was considered to represent a stenotic IJV. Observed stenoses were then categorized into groups according to their location: upper and lower neck levels, unilateral on the right IJV (RIJV) or left IJV (LIJV), or bilateral stenosis. At either neck level, any measured cross-sectional area greater than the stenosis threshold was considered to represent a nonstenotic result.

Atresia of an IJV was identified when the vessel came to a clear and abrupt ending at some point in the IJV body between the sigmoid sinus and its confluence with the subclavian vein. Time-resolved 3D CE MR arteriovenography data and 2D TOF MR venography were used to confirm the lack of structural patency of a vessel. This could appear in the form of a terminating sigmoid sinus with the IJV being reconstituted from the vertebral system or as a lower-level truncation with a thin string down one side. Aplasia, a congenital condition in which an IJV fails to develop entirely, could potentially be identified by the complete lack of ability to image a complete IJV in any of the data collected.

The vessel lumen for veins and arteries seen in PC MR images were delineated by using the magnitude and phase images as input. A baseline correction was applied to remove any phase shift caused by eddy currents and gradient imperfections (Appendix II, available online at *www.jvir.org*). In the case that phase aliasing was present, phase unwrapping was performed (Appendix III, available online at *www.jvir.org*). The corrected and unwrapped phase values in the vessels were then mapped to velocity measurements by using the encoding velocity (Venc) value. Subse-