Intraluminal and extraluminal extra-cranial structural and functional venous abnormalities in multiple sclerosis patients and healthy controls

Robert Zivadinov[1,2], Kresimir Dolic[1], Karen Marr[1], Vesela Valnarov[1], Michael G. Dwyer,[1] Ellen Carl[1], Yuval Karmon[2], Cheryl Kennedy[1], Christina Brooks[1], Colleen Kilanowski[1], Kristin Hunt[1], David Hojnacki[2], Bianca Weinstock-Guttman[2]

[1]Buffalo Neuroimaging Analysis Center, State University of New York, Buffalo, NY, USA; [2]The Jacobs Neurological Institute, Department of Neurology, University at Buffalo, State University of New York, Buffalo, NY, USA;

Introduction: Chronic cerebrospinal venous insufficiency (CCSVI), a recently proposed hemodynamic condition in multiple sclerosis (MS) patients, is based on Doppler Sonography (DS) criteria. However, at this time the comparative value of DS vs. magnetic resonance venography (MRV) is unknown and the frequency of structural and functional abnormalities is not well defined.

Objective: To identify frequency of structural and functional extra-cranial vein abnormalities by using DS and MRV in a large cohort of patients with MS and healthy controls (HC).

Methods: 150 MS patients (104 relapsing-remitting, 38 secondary-progressive, 8 primary progressive), and 63 age- and sexmatched HC were scanned on a 3T MRI using 2D-Time of Flight (TOF) and 3D-Time Resolved Imaging of Contrast Kinetics (TRICKS) sequences (only MS patients). All patients and controls underwent DS examination. The DS abnormal findings for internal jugular veins (IJVs) were presence of intra- and/or extra-luminal abnormalities, and absence of detectable flow for vertebral veins (VVs). Intraluminal DS IJV structural abnormalities consisted of web, flap, septum membrane and malformed valve. Extraluminal DS IJV structural abnormalities consisted of stenosis and annulus. Functional DS IJV abnormalities

consisted of reflux, paradox and no flow. The abnormal flow/morphology on MRV was defined as absent and/or pinpoint flow of the IJVs and as absent flow of VVs. Prominence of collateral extra-cranial veins was assessed with MRV.

Results: 98 (67.12%) MS patients and 18 (28.57%) of HC presented >=2 venous hemodynamic criteria and were classified, as having CCSVI (p<.0001). 111 (74%) of MS patients and 34 (54%) of HC presented with at least one structural abnormality in IJVs (p=0.004) on DS. The mean number of intraluminal (1.53 vs. 0.9, p=0.005), extraluminal (0.31 vs. 0.13, p= 0.023) and functional (1.13 vs. 0.51, p<0.001) IJV abnormalities was higher in MS patients compared to HC. Progressive MS patients showed significantly more extraluminal IJV DS abnormalities (0.43 vs. 0.25, p=0.01) then non-progressive MS patients, but not of intraluminal or functional. No DS flow differences were observed for VVs between MS patients and HC or according to disease course. MRV showed abnormal IJVs flow morphology in 30.7% of MS patients and 27% of HC (p=NS). Significantly more venous abnormalities were observed on flow morphological scale in progressive compared to non-progressive MS patients on TOF (p=0.006) and there was a trend for more abnormalities in progressive MS patients on TRICKS (p=0.016). No VV flow differences were detected on MRV between the groups. There was a trend for higher mean number of collateral veins in MS patients compared to HC on TOF (2.56 vs. 2.1, p=.016). MS patients with higher number of functional IJV DS abnormalities showed significantly higher number of collateral veins on TRICKS (r=0.27, p=0.009) and on TOF (r=0.27, p=0.006).

Conclusion: This study examined frequency and number of intraluminal, extraluminal and functional structural IJV abnormalities in MS patients and HC and in progressive vs. non-progressive MS patients by using 2 different non-invasive techniques. The study findings suggest that intraluminal abnormalities may precede appearance of extraluminal abnormalities in MS patients by several years. This calls in question pathology model in which intraluminal abnormalities cause functional abnormalities and the latter contribute to creation of extraluminal abnormalities.