The Central Vein Sign in Multiple Sclerosis: a real-life multi-centre MAGNIMS study

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Introduction

There is no single test for multiple sclerosis (MS) and a variety of demyelinating conditions can mimic its appearance[1]. The central vein (CV) sign is a hallmark of MS lesions, as demyelinating plaques form perivascularly[2], and has the potential to become a diagnostic biomarker in MS. Up to date, most of the studies of CVs in MS have been single centre and included small sample sizes[3]. Here we present preliminary results of the first multi-centre study to test the usefulness of the CV sign as an MS specific biomarker.

Methods

479 patients with a variety of conditions including MS and its mimics were included in this preliminary analysis (see *Table 1*).

Table 1 The number of patients per disease type

Disease	CIS/MS	NMOSD	SVD	Vasculitis	Migraine	Diabetes
No of subjects	312	18	64	34	24	20
Total		160				

CIS- clinically isolated syndrome; NMOSD- neuromyelitis optica spectrum disorder; SVD- small vessel disease

Each patient had 3T MRI including FLAIR and SWI/T2* which were co-registered using 3D Slicer (see *Fig 1*). The scans were contributed from 8 MAGNIMS centres and had variable protocols. Each co-registered scan was divided into eight equally-sized blocks to avoid rater bias based on lesion distribution patterns. The blocks were randomised across subjects.

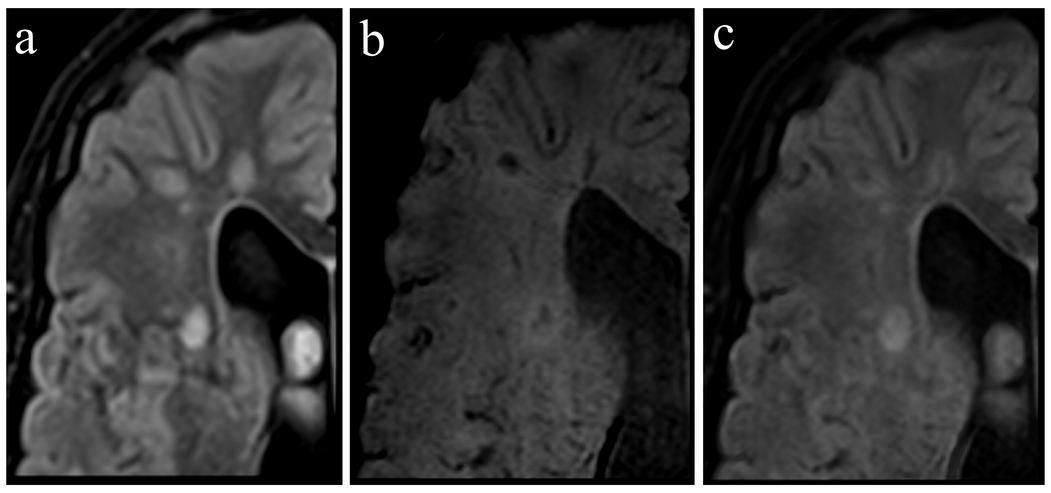

Figure 1 (A) An example block from a FLAIR image showing multiple WM lesions. (B) The corresponding SWI image showing veins. (C) An overlay of FLAIR and SWI images which allows the visualisation of both lesions and veins.

3D Slicer was used to examine an overlay of FLAIR and SWI/T2* to detect the presence of lesions and veins (see *Table 2* for lesion and vein criteria). Each lesion was measured (long and short axes measurements), and classified based on location (juxtacortical, periventricular, other) and presence or absence of a (central) vein.

Table 2 The criteria used for lesion and central vein selection.

Lesion	Vein
• WM lesions only • At least 3mm or 5 voxels in its short axis • Clearly identifiable from surrounding WM • Confluent lesions split into 'fingers' or excluded if not possible	• Equidistance from lesion edges • Passes through at least one lesion edge & visible outside the lesion • Detectable in at least 2 planes (3D data only) • Runs along the long lesion axis (ovoid lesions only)

Results

In this first interim analysis 3784 lesions were included.

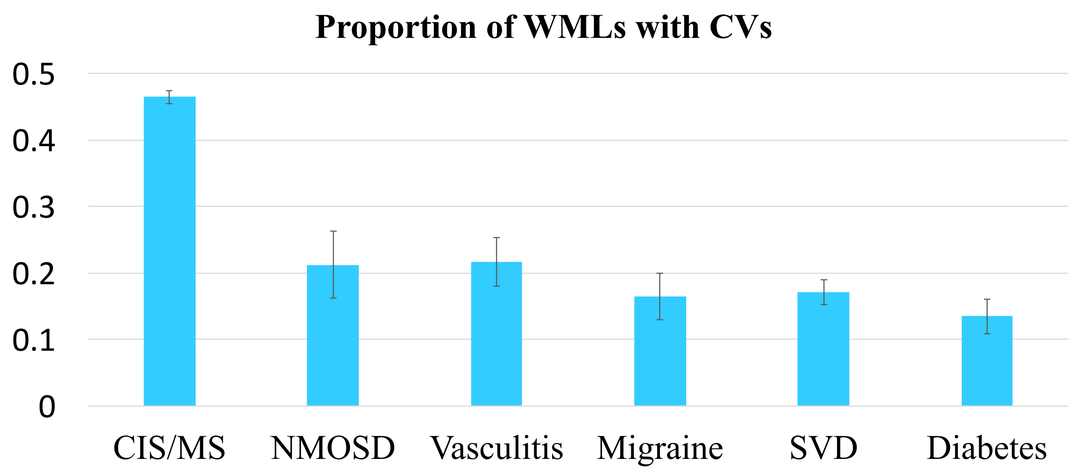

Figure 2 The proportion of WM lesions with central veins (including SE) in each disease.

Sensitivity and specificity values based on 35% threshold of WMLs with CVs for patients with >2 lesions were equal to 0.63 and 0.84, respectively.
Positive and negative predictive values were 0.90 and 0.51, respectively.
Initial findings suggest WMLs in the centrum semiovale may best distinguish MS from non-MS (see *Fig3*).

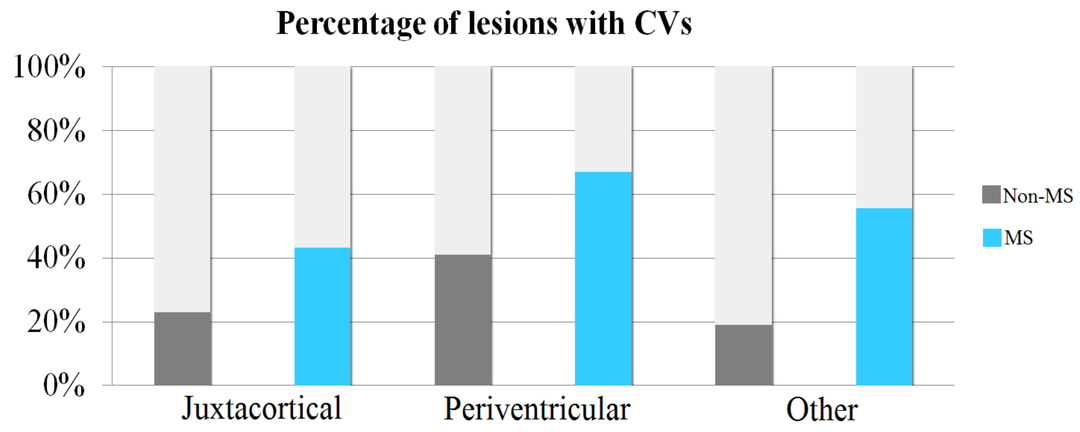

Figure 3 The distribution of WM lesions with CVs based on location in MS and non-MS patients.

Discussion

This is the first multi-centre study involving large numbers of participants to test the CV sign in distinguishing MS from mimicking disorders using real-life data.
Our preliminary findings are encouraging and further analyses will focus on simplifying the diagnostic criteria using the CV sign. We will also also assess the effects of lesion size, lesion localization and specific MR scanning parameters in detecting CVs in more detail.

References

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