Are Dilated Virchow Robin Spaces a Generalized Marker of Disease in Multiple Sclerosis?

Jacob Miles, Ariana Simps* and Simon Keller

Department of Neuroscience, Central Clinical School, Monash University, Australia

*Corresponding Author**
Ariana Simps
Department of Neuroscience, Central Clinical School, Monash University, Australia
E-mail: simpsariana1297@gmail.com

Received date: 13-February-2024, Manuscript No: JMSO-24-136009; **Editor assigned:** 15-February-2024, Pre-QC No. JMSO-24-136009(PQ); **Reviewed:** 23-February-2024, QC No. JMSO-24-136009(Q); **Revised date**: 25-February-2024, Manuscript No: JMSO-24-136009(R); **Published date:** 28-February-2024, DOI: 10.35248/2376-0389.24.11.02.537

Abstract

Virchow Robin Spaces (VRS), perivascular spaces surrounding cerebral blood vessels, facilitate fluid exchange between blood, cerebrospinal fluid, and interstitium. Enlarged VRS are common in both health and disease, with evidence suggesting associations with cardiovascular risk factors. However, their contribution to disease pathogenesis remains unclear. Limited evidence links enlarged VRS to clinical measures of disease severity across various neurological conditions.

In Multiple Sclerosis (MS), while some studies suggest associations with lesion volume and disease severity, a meta-analysis failed to replicate these findings, indicating limited utility of VRS as diagnostic or prognostic markers. Methodological limitations in VRS identification and quantification challenge the strength of these associations. Future research should focus on refined quantification methods to better understand the role of VRS in neurological diseases.

Keywords: Virchow Robin Spaces (VRS) • Neurological diseases • Multiple Sclerosis

Introduction

Virchow Robin Spaces (VRS), also referred to as perivascular spaces, encompass cerebral blood vessels and facilitate fluid exchange among blood, cerebrospinal fluid, and the interstitial. Enlarged VRS are frequently observed in brain tissue, irrespective of health or disease status. While evidence indicates a correlation between increased VRS burden and cardiovascular risk factors like hypertension and higher BMI, their precise contribution to disease pathogenesis remains uncertain. Moreover, scant evidence exists linking enlarged VRS with clinical measures of disease severity across various neurological and neurodegenerative conditions where VRS are present. In Multiple Sclerosis (MS), numerous studies have suggested associations between enlarged VRS, lesion volume, and disease severity. However, a meta-analysis involving over 450 patients across nine studies failed to reproduce these associations. It revealed elevated VRS count and volume in MS patients compared to controls, yet no significant links with disease severity or progression were observed, thus questioning the utility of VRS as diagnostic or prognostic indicators in MS [1-4]. The reliability of these findings is subject to scrutiny due to methodological limitations in identifying and quantifying VRS, with many previous studies employing crude assessments of VRS burden instead of precise quantification of their number or volume. Recent studies utilizing higher-resolution imaging techniques and larger patient cohorts have begun to address these limitations, revealing associations between VRS and various aspects of disease severity, lesion volume, cortical atrophy, and diffusion metrics [5].

Improvements in MRI resolution and detection methods are enhancing the identification of Virchow Robin Spaces (VRS) on clinical scans, yet their clinical significance remains uncertain. There's a hypothesis suggesting that it's not merely the presence of VRS but the dilation of these spaces that may indicate disease, although evidence supporting this notion is limited [6].

In a comprehensive study by Ineichen *et al.*, VRS in MS patients were extensively investigated, with a particular focus on distinguishing dilated VRS (measuring >2 mm) from undilated ones. The spatial distribution of these VRS in relation to MS lesions, brain atrophy, and clinical severity was assessed. While increased numbers of both dilated and undilated VRS were noted, they did not correlate with disease stage or cognitive function. Moreover, in a subgroup with repeated MRIs, changes in clinical stage or lesion load did not correspond with alterations in the number of dilated VRS. Post-mortem histology revealed that dilated VRS did not co-localize with demyelination, axonal damage, or microglial/macrophage activation, but rather with arteries and signs of arterial disease. These findings suggest that dilated VRS may be associated more with cardiovascular disease than with MS pathology.

Overall, the study highlights the considerable variability in the number of dilated VRS among both patients and healthy controls, even after accounting for cardiovascular risk factors.

Despite a broad definition, the occurrence of dilated VRS across all participants studied remained relatively low [7-9].

The current study lacks control for variables such as time of day and sleep, both of which are believed to influence the presence of dilated Virchow Robin Spaces (VRS) [1-3]. Diurnal variation of VRS is well recognized, with dilation often occurring during sleep. The timing of MRI scans relative to wakefulness and sleep deprivation can affect the size and visibility of VRS. Additionally, a major limitation of the study is the absence of data on the use of Disease-Modifying Treatments (DMTs) by patients and the timing of DMT intervention in relation to MRI scans. Given the widespread use of DMTs in MS cohorts, the lack of association with lesion load or other markers of active neuro-inflammation is not unexpected. While the study reveals heightened levels of dilated VRS in MS patients, the limited correlation with other indicators of disease severity suggests that dilated VRS may serve as a nonspecific marker of disease, whether neurological, cardiovascular, or a combination of both. Comprehensive studies that account for these various factors are necessary, not only in MS but also across neurological and neurodegenerative diseases, to gain a better understanding of the role of VRS in disease pathogenesis and presentation.

References

1. Barisano, Giuseppe, et al. "Body mass index, time of day and genetics affect perivascular spaces in the white matter." *J Cereb Blood Flow Metab* 41.7 (2021): 1563-1578.
2. Moses, Jasmine, et al. "Perivascular spaces as a marker of disease severity and neurodegeneration in patients with behavioral variant frontotemporal dementia." *Front Neurosci* 16 (2022): 1003522.
3. Zhang, Chao, et al. "Recovery of glymphatic system function in patients with temporal lobe epilepsy after surgery." *Eur Radiol* 33.9 (2023): 6116-6123.
4. Granberg, Tobias, et al. "Enlarged perivascular spaces in multiple sclerosis on magnetic resonance imaging: a systematic review and meta-analysis." *J Neurol* 267 (2020): 3199-3212.
5. Kolbe, S. C., et al. "Lesion volume in relapsing multiple sclerosis is associated with perivascular space enlargement at the level of the basal ganglia." *Am J Neuroradiol* 43.2 (2022): 238-244.
6. Carotenuto, Antonio, et al. "Glymphatic system impairment in multiple sclerosis: relation with brain damage and disability." *Brain* 145.8 (2022): 2785-2795.
7. Liu, Xue-Yu, et al. "Perivascular space is associated with brain atrophy in patients with multiple sclerosis." *Quant Imaging Med Surg* 12.2 (2022): 1004.
8. Ineichen, Benjamin V., et al. "Dilated Virchow-Robin spaces are a marker for arterial disease in multiple sclerosis." *EBioMedicine* 92 (2023).
9. Aribisala, Benjamin S., et al. "Sleep quality, perivascular spaces and brain health markers in ageing-A longitudinal study in the Lothian Birth Cohort 1936." *Sleep Med* 106 (2023): 123-131.

Cite this article: Miles J. Simps A. and Keller S. Are Dilated Virchow Robin spaces a generalized marker of disease in Multiple Sclerosis? J Mult Scler. 2024,11,(2),537