Virchow Robin space dilatation is a sensitive indicator of cerebral microvascular angiopathy: A study in elderly patients with dementia

A. Jackson[1], T. Patankar[1], A. Varma[2], J. S. Snowden[3], D. Neary[2]

[1]Imaging Science, University of Manchester, Manchester, Greater Manchester, United Kingdom, [2]Neurosciences, Hope Hospital, Salford, Lancashire, United Kingdom, [3]Neurosciences, Hope Hospital, Manchester, Greater Manchester, United Kingdom

Introduction:

Microvascular disease has the major etiological and pathogenetic role in vascular dementia. Histologically, microvascular disease is associated with a spectrum of changes accompanying atheromatous disease in small arteries and arterioles [1] which are classified under the term Microvascular angiopathy (MVA). Abnormal dilatation of Virchow Robin spaces (VRS) and the formation of small cystic lacunes are cardinal features of moderate to severe MVA. These changes are easily identified on MRI and provide a potential biomarker of MVA. This study test the hypothesis that the presence of abnormal dilation of VRS provides a provides information concerning the presence of MVA with dementia

Material and Methods:

75 patients with dementia (Vascular dementia (IVD; n=24), Alzheimer's disease (AD; n=35) and Frontotemporal dementia (FTD; n=16)) and 35 normal volunteers (Norm) were recruited. Patients with clinical diagnosis of IVD and Alzheimer's disease fulfilled the NINDS-AIREN criteria and those with FTD fulfilled the FTD criteria. The imaging protocol on a Philips 1.5T ACS-NT scanner included Axial FLAIR (TR 11000, TE 140, TI 2600, matrix 256^2, field of view (FOV) $230mm^2$, slice thickness 3.0mm, Axial T1W Inversion recovery (IR TR 6850, TE 18, TI 300, slice thickness 3.0 mm, matrix 256^2, FOV $230mm^2$, reconstructed as real images) and axial high-resolution 3D T1 weighted Fast Field Echo[FFE] sequences (TR 24,TE 18, matrix 256^2, FOV $230mm^2$,slice thickness 0.89 mm, Flip angle 30°). Deep White Matter and Periventricular Hyperintensities assessment was performed on matched T1WIR and T2W FLAIR images using a scoring system based on the Scheltens' scale [2]. VRS visibility was greatest on IR images (Contrast to noise ratio for VRS vs normal white matter was: IR = 64.1, FFE = 24.8) scoring was therefore performed using IR images . VRS were scored separately in centrum semiovale (0 = none; 1= less than 5 per side; 2 = more than 5 on one or both sides), mesencephalon (0 = none, 1 = VRS present), and sub-insular region lateral to the lentiform nucleus (0 = none, 1 = less than 5 on either side, 2 = more than 5 on one or both sides). VRS in the basal ganglia were scored using two separate scoring schemes, the first of these (BG1: 0= VRS only in the substantia innominata and <5 VRS on either side/side; 1= >5 VRS in the substantia innominata on either side or any VRS in the lentiform nucleus; 2= VRS in caudate nucleus on either side) reflects the anatomical distribution of basal ganglia VRS and the second (BG2: 0= VRS only in the substantia innominata and <5 VRS on either side/side, 1= VRS only in the substantia innominata, >5 dilated VRS on either side; 2= <5 in lentiform nucleus on either side, 3=5-10 VRS in lentiform or <5 in caudate nucleus on either side, 4=> 10 in lentiform nucleus and <5 in caudate nucleus on either side, 5=>10 in lentiform nucleus and >5 in caudate nucleus on either side) reflects the distribution and number. Statistical group comparisons used ANOVA with *a posteriori* Tukey test and Kruskal Wallis test with *a posteriori* Mann-Whitney U test for non-parametric data. Multiple regression analysis was performed to quantify the relationship between imaging features and diagnosis.

Results:

Inter and intraobserver variation in the VRS scoring systems was minimal with no significant differences between scores. Cohen's kappa demonstrated excellent agreement between scoring sessions for each observer (0.85-0.96). White matter lesion scores showed a trend to higher scores in the IVD group. Significant group-to-group differences were observed on a posteriori tests with scores of periventricular hyperintensity, basal ganglia hyperintensity and overall score significantly greater in patients with vascular dementia than in normals. Scores for the white matter hyperintensities, periventricular hyperintensities and total score were significantly higher in patients with vascular dementia than in those with AD. BG1 and BG2 were significantly higher in vascular dementia than in normal volunteers ($p<0.005$ and $p<0.001$ respectively), patients with AD ($p<0.001$) or patients with FTD ($p<0.01$). Multiple regression analysis in the dementia group showed that the BG2 VRS score acted as an independent predictive factor accounting for 29% of the variance in the regression model, and the Scheltens PVH score accounted for another 2%. The BG2VRS score was the most sensitive independent indicator of a diagnosis of vascular dementia and a score >2 has a sensitivity of 67% and specificity of 70% in differentiating IVD from AD or FTD whereas BG2VRS score of >4 will decrease the sensitivity to 25% but improve the specificity to 100%.

Conclusion:

VRS can be used as a surrogate marker of cerebral microvascular disease. Our study suggests that MRI evidence of VRS dilatation can be used as a diagnostic tool to aid in the differentiation of vascular from degenerative dementias.

References

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