Vascular Cognitive Impairment Neuropathology Guidelines (VCING) – a UK multi-centre consensus study

O. A. Skrobot¹, J. Attems², M. Esiri³, T. Hortobágyi⁴, J. Ironside⁵, R. N. Kalaria², A. King⁶, G. A. Lammie⁷, D. Mann⁸, J. Neal⁹, Y. Ben-Shlomo¹⁰, P. G. Kehoe¹, S. Love¹

¹Dementia Research Group, School of Clinical Sciences, Faculty of Health Sciences, University of Bristol, Level 1, Learning & Research, Southmead Hospital, Bristol, BS10 5NB, UK; ²Institute for Ageing and Health, Newcastle University, Wolfson Research Centre, Campus for Ageing and Vitality, Newcastle upon Tyne, NE4 5PL, UK; ³Nuffield Department of Clinical Neurosciences, Oxford University, Oxford, OX3 9DU, UK; ⁴Department of Neuropathology, Institute of Pathology, Faculty of Medicine, University of Debrecen, Nagyerdei krt. 98, Debrecen, 4032, Hungary & Department of Basic and Clinical Neuroscience, Institute of Psychiatry, Psychology and Neuroscience, King’s College London, De Crespigny Park, London, SE5 8AF, UK; ⁵Centre for Clinical Brain Sciences, University of Edinburgh, Western General Hospital, Crewe Road, Edinburgh, Midlothian, EH4 2XU UK; ⁶Department of Clinical Neuropathology, First floor, Academic Neuroscience Building, King’s College Hospital, Denmark Hill, London, SE5 9RS, UK; ⁷Institute of Cancer & Genetics, Cardiff University School of Medicine, Institute of Medical Genetics Building, Heath Park, Cardiff, CF14 4XN, UK; ⁸Institute of Brain, Behaviour and Mental Health, University of Manchester, A304 Clinical Sciences Building, Salford Royal Hospital, Stott Lane, Salford M6 8HD; ⁹Institute of Infection & Immunity, Cardiff University School of Medicine, Henry Wellcome Building, Heath Park, Cardiff CF14 4N, UK; ¹⁰School of Social and Community Medicine, Canynge Hall, 39 Whatley Road, Bristol, BS8 2PS, UK.

There are no generally accepted protocols for the post-mortem assessment of vascular cognitive impairment (VCI) or vascular dementia. The Brains for Dementia Research (BDR) Neuropathology group initiated a collaborative study aimed at formulating Vascular Cognitive Impairment Neuropathology Guidelines (VCING) for the post-mortem assessment and scoring of cerebral vascular disease of relevance to VCI. The study encompassed (i) an iterative series of questionnaires in which 9 UK neuropathologists used the Delphi method to agree a sampling protocol and establish consensus criteria for scoring the severity of several types of structural abnormalities of cerebral blood vessels, and of ischaemic and haemorrhagic abnormalities affecting the brain parenchyma, (ii) the blinded assessment by nine neuropathologists of 118 brains from people who had had formal cognitive assessments within 12 months of death, to assess the application of the neuropathology criteria and the inter-observer reliability of the scoring, and to use the information to inform the selection of variables for (iii) multiple regression analysis of the relationship between the cognitive assessments and those VCING standardised scores of vascular pathology that were determined reproducibly and had a frequency >10%.

Fourteen different vessel and parenchymal pathologies were assessed in 13 brain regions. Inter-rater reliability was tested by calculating Gwet’s AC2 coefficient, accounting for unbalanced marginal totals, for each pathology in each region. The benchmark proposed by Landis and Koch³ was employed to evaluate the extent of agreement: AC2 coefficient >0.4 moderate, >0.6 substantial, and
Almost perfect agreement was found when the agreed criteria were used for assessment of leptomeningeal cerebral amyloid angiopathy (CAA), cortical CAA, capillary CAA, large infarcts, lacunar infarcts, microhaemorrhage, larger haemorrhage, microaneurysms, perivascular space dilation, and perivascular haemosiderin leakage (except in frontal white matter, where the agreement was substantial). Almost perfect agreement was reached for assessment of fibrinoid necrosis in all regions apart from thalamus and putamen, where there was still substantial agreement. Almost perfect agreement was achieved for assessment of myelin loss in internal capsule and occipital white matter, with substantial agreement for frontal white matter. There was variability in assessment of the severity of arteriosclerosis: agreement was high in most regions (almost perfect in 6, substantial in 3) but only moderate in 4 regions. Similarly, reliability in assessing microinfarcts varied: almost perfect in the middle and superior frontal gyrus, occipital cortex including calcarine cortex, and internal capsule, substantial in 7 regions and moderate in 3. In general, analysis showed the VCING criteria to be reproducible. Multiple regression analysis incorporating the VCING scores will now be used to analyse the relationship of the different vascular pathologies to cognitive impairment. Our aim is to develop a practical standardised scheme for estimating the possible contribution of cerebrovascular pathology to cognitive decline.

1Landis, J. R. & Koch, G. G. The measurement of observer agreement for categorical data. Biometrics 33, 159-174 (1977)