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Stroke Literature Synopses: Clinical Science

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Historically the cognitive consequences of stroke have received less research attention than the physical aspects. Yet, neuropsychological issues are incredibly common following stroke and people affected by stroke consistently state that post stroke cognitive decline is their biggest concern. For this Clinical Synopsis I have selected three important papers themed around vascular cognitive impairment (VCI). The papers chosen are not trials of interventions to prevent or reverse VCI, as there have been depressingly few positive trials in this field. Rather, I have chosen papers with a methodological flavour. I believe, if we can get the methods correct in VCI trials then the positive results will follow.

One of the fundamental barriers to progressing VCI interventional research, is that we have no agreed definition of VCI. Many operationalised definitions of various VCI presentations are available but the content of each classification system differs and the resulting diagnoses can be contradictory. To try and bring some consistency to VCI assessment, the VICCS group propose a novel classification system. (Skrobot OA The Vascular Impairment of Cognition Classification Consensus Study. Alzheimer’s and Dementia. 2017; 13:624-633.)

Rather than create a VCI classification from scratch, the VICCS group collated and appraised all the published guidance on VCI classification. Based on this they developed new guidance for application through an iterative and circular process of anonymous review, feedback and amendment (a Delphi process). After many rounds of review, the VICCS group settled on a conceptualisation of VCI that recognises distinct entities of Post Stroke Dementia, subcortical or cortical ischaemic dementia and mixed dementia.

The VICCS process provides a template for future studies looking at clinical classification. The group followed best practice in the conduct of the study; they involved a diverse, international group of experts and they tried to harmonise the outputs with existing, high profile guidance. It remains to be seen whether the VICCS system will gain traction in the research or clinical arenas. I hope that a consensus can be reached. I will be disappointed if in a few years the Clinical Synopsis section reports on another attempt to standardise VCI.

Dementia is a progressive condition. In Alzheimer’s disease and undifferentiated dementia, we often think of a pathway that begins with clinically occult pathological process and then progresses through a mild cognitive impairment (MCI) to frank dementia. Whether this paradigm is valid or useful for the syndrome of vascular dementias is less clear. An early stage of disease is described, vascular cognitive impairment, no dementia (VCI-ND) but unlike MCI there is no consensus on how this condition should be defined.
In a UK study, the authors used a prospective, cognitive cohort of over 13,000 participants to try and operationalise an approach to VCI-ND. (Stephan et al Neuropsychological profiles of vascular disease and risk of dementia: implications for defining vascular cognitive impairment no dementia(VCI-ND) Age Ageing 2017; 46:755-60.). The population had a mix of differing vascular comorbidity and after excluding all participants with prevalent dementia, they were followed with cognitive and dementia assessment over two years.

By the authors own admission, this study does not provide the last word on VCI-ND but provides interesting results that could inform future studies. At baseline, cognitive impairment was not uniform across vascular diseases, diabetes mellitus and previous stroke seemed to be particularly associated with multi-domain cognitive issues. Over time, all vascular diseases increased risk of dementia. However, the neuropsychological profiles of cognitive problems differed between conditions. This finding has biological plausibility. The potential pathophysiology and expression of cognitive decline in cardiac disease is likely to differ from the patterns seen in diabetes mellitus and hypertension. Perhaps using the umbrella term vascular dementia is unhelpful and future studies should try and characterise the cognitive characteristics expected from vascular disease. This is easier said than done.

A condition that is frequently associated with dementia is cerebral amyloid angiopathy (CAA). A diagnosis of CAA has important prognostic and treatment implications but making an in-vivo diagnosis of CAA is not straightforward. MRI based criteria are available, but access to MRI is not always feasible or possible. As CT imaging remains the work-horse of international stroke services, a CT based diagnostic algorithm for CAA could have substantial clinical utility.

The team from Edinburgh, UK offer such an algorithm. (Rodrigues MA et al. The Edinburgh CT and genetic diagnostic criteria for lobar intracerebral haemorrhage associated with cerebral amyloid angiopathy. Lancet Neurol 2018; 17: 232–40.) In this study of 110 patients with intracerebral haemorrhage who had post mortem assessment for CAA, the authors developed a multi-item prediction tool. The authors assessed the discriminative ability of various CT features and combined those most strongly associated with CAA into a three item model. The final model included a) presence of subarachnoid blood; b) finger like projections of the bleed and c) presence of ApoE4 genotype. The tool had impressive accuracy offering near perfect CAA ‘rule out’ and ‘rule in’.

I suspect we will all start using the Edinburgh criteria in our day to day clinical work. Diagnostic and prediction rules don’t always work so well when applied in populations beyond the parent study and so the authors plan to externally validate their rule in other datasets. The other important, but difficult to answer, question is whether using the rule will make any difference to patient outcomes.

For those of you, like me, who aren’t sure if they could distinguish ‘finger like projections’, the authors even offer an on-line training resource. (https://radiopaedia.org/articles/edinburgh-criteria-for-lobar-intracerebral-haemorrhage-associated-with-cerebral-amyloid-angiopathy)