Stroke Literature Synopses:Clinical Science

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(vascular cognitive impairment)

Historically the cognitive consequences of stroke have received limited research attention. Yet, neuropsychological issues are common following stroke and stroke-survivors consistently state that cognitive decline is their biggest concern. For this Clinical Synopsis I have selected papers themed around vascular cognitive impairment (VCI). These papers are not trials - there have been depressingly few intervention trials in this field. Rather, I have chosen papers with a methodological flavour. I believe, if we get the methods correct in VCI trials then positive results will follow.

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

Rather than create a classification from scratch, the VICCS group collated and appraised all the published materials on VCI classification. They then developed their new guidance through an iterative process of anonymous review, feedback and amendment (Delphi process). After several 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 robust VICCS process provides a template for future studies looking at clinical classification. The group followed best practice in study conduct; they involved a diverse, international group of experts and they tried to harmonise the outputs with existing guidance. It remains to be seen whether the VICCS system will gain traction in the research or clinical arenas. Hopefully it can, 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 we often think of a pathway that begins with clinically occult pathology and then progresses through mild cognitive impairment (MCI) to frank dementia. Whether this paradigm is valid or useful for VCI is less clear. An early stage is described as 'vascular cognitive impairment no dementia' (VCI-ND) but unlike MCI there is no consensus definition of VCI-ND. Sound familiar?

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 VCI is unhelpful and future studies should try and characterise the cognitive characteristics expected from vascular disease.

A condition that is frequently associated with dementia is cerebral amyloid angiopathy (CAA). A diagnosis of CAA has prognostic and treatment implications but making an in-vivo diagnosis of CAA is challenging. 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: 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’.

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

I suspect we will all start using the Edinburgh criteria in our 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 (or any of the classifications discussed in this Synopsis) will make any difference to patient outcomes.