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Adding Insight to Injury!

A. R. Naylor
Glenfield Hospital

J. D. Spence
Robarts Research Institute, jdspence@uwo.ca

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EDITORIAL

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The 2017 European Society for Vascular Surgery (ESVS) guidelines on the management of carotid disease concluded there was no evidence that new 'silent brain infarction' (SBI) after carotid interventions was associated with cognitive decline[1]. However, two recent publications have reopened this debate and question whether this interpretation of the literature holds true.

Lei et al undertook a systematic review and meta-analysis of 19 case controlled studies ($n = 6712$) and three prospective cohort studies ($n = 4433$), in order to evaluate the relationship between SBI and cognitive function[2]. A meta-analysis of 9 studies showed that SBI was an important factor in cognitive decline using the Mini-mental State (MMSE) score, while a meta-analysis of four studies reported that SBI was an independent factor in cognitive dysfunction using the Montreal Cognitive Assessment (MOCA) Scale. Ten studies also reported that SBI was associated with decreases in specific areas of cognitive function[2].

There are many reasons why cognitive function studies have failed to influence clinical practice, including; a 'learning effect', through repeated patient testing, the (in) sensitivity of the neuropsychological test employed (important executive functions are poorly assessed by MMSE[3]), rare involvement of neuropsychologists, the hemisphere being tested (MMSE mainly tests dominant hemisphere function), heterogeneous patient populations (symptomatic/asymptomatic, healthy volunteers, population based cohorts), lack of controls, short duration of follow up with most studies focussing on the peri-operative period, small sample size and (therefore) underpowered studies and a lack of standardised timing of post-operative assessments[1]. Other limitations include a well recognised placebo effect on cognitive function, the placebo effect of surgical interventions on cognitive function and the fact that scores improve to a greater extent in people with better baseline scores; i.e. milder cognitive impairment.

While this meta-analysis minimised the risks of bias through careful inclusion criteria (excluding smaller series and only including controlled studies with cohorts divided into SBI and non-SBI cohorts), it is likely that many observers will still interpret their conclusions with a healthy dose of caution and scepticism.

However, another recently published study suggests that Lei's findings may be correct and that SBI after surgical interventions may be more harmful than was previously believed. The NeuroVISION study evaluated the prevalence of acute SBI after non-cardiac surgery in 1114 patients and correlated the presence (absence) of SBI with cognitive decline at one year, measured using the MOCA scale, the Digit-Symbol Substitution Test and the Trail-Making Test part B[4]. Interestingly, carotid endarterectomy (CEA) patients were specifically excluded. This very large observational study found that 7% suffered an acute SBI post-operatively, of whom 42% developed cognitive impairment at one year. The prevalence of cognitive impairment in non-SBI patients at one year was 29% (adjusted Odds Ratio 1.98 (95%CI 1.22–3.2)), giving an absolute risk increase (ARI) of 13% ($p = .0055$)). Patients developing post-operative SBI also incurred a significantly higher risk of overt stroke/TIA at one year (4% *vs.* 1%; Hazard Ratio 4.13 (95%CI 1.14–14.99)), with an ARI of 3% ($p = .019$))[4]. NeuroVISION found no evidence that the prevalence of SBI was influenced by anaesthesia type, surgical specialty, history of stroke/vascular disease, sex, or baseline physical impairment.

In a systematic review and meta-analysis of 20 RCTs comparing CEA with carotid artery stenting (CAS), the authors once again found no evidence that SBIs were associated with cognitive decline[5]. Given the findings of the NeuroVISION study, the most likely explanation for this discordance is that the RCT cohorts were simply too small to identify a real treatment effect, while the cognitive testing in these studies was suboptimal. Moreover, the fact that 29% of non-SBI NeuroVISION patients developed cognitive decline indicates that there are more causes (than SBI alone) in the pathophysiology of post-operative cognitive decline. Notwithstanding this, these data reinforce the importance of trying even harder to prevent SBI after CEA/CAS, as SBIs may be about to shed their otherwise 'benign' veneer.

It has previously been reported that recurrent cerebrovascular events were significantly more common in CEA/CAS patients developing an SBI[5], a finding corroborated by the NeuroVISION study[4]. It is essential, therefore, that a greater emphasis is now placed on better understanding the pathophysiology and prevention of post-operative SBI, in order to minimise cognitive decline. In Rot's systematic review (46 studies; 5018 patients), the weighted prevalence of SBI after CEA was 18.1% (95%CI 14–22.7), compared with 40.5% (95%CI 35.4–45.7) after transfemoral CAS[6]. In Batchelder's overview of 20 RCTs comparing CEA with CAS, factors associated with SBI after CEA/CAS included; lower systolic BP, diabetes, hemispheric stroke at presentation, left sided stenoses, plaque echolucency, increasing age, male sex, type II/III aortic arch, $> 60^{\circ}$ angle between the

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common and internal carotid arteries, the use of filter cerebral protection devices (CPD) and intra-procedural haemodynamic depression[5]. In terms of specific carotid interventions, significant SBI predictors after CEA included symptomatic status, impeded cerebral haemodynamics and increased inflammatory markers. Significant predictors for SBI after CAS included increasing age, plaque vulnerability and complex carotid/aortic arch anatomy[6].

The prevalence of SBI after transfemoral CAS is significantly higher than after CEA. However, while this has been appreciated for some time, there has only been speculation that SBIs might be harmful. One example where CAS technology might reduce the prevalence of SBI after CAS may be the emergence of Transcarotid Artery Revascularisation (TCAR). Filter based CPDs actually increase the number of post-operative SBIs[5] and the use of flow reversal during stent deployment during TCAR may reduce SBI rates to that observed after CEA[7], although (to date) studies like this contain small CAS numbers. This is but one example of how the prevalence of SBI might be reduced after CAS, but surgeons cannot assume that this is solely a 'CAS problem'. If one extrapolates the NeuroVISION data into surgical practice, 7–8 patients (per 100 CEAs) might suffer cognitive decline due to developing post-operative SBI. It is, therefore, incumbent upon all of us to review every aspect of our surgical/interventional practice (not least better case selection) in order to reduce the risks to our patients (and maybe to ourselves in the future!) from suffering avoidable cognitive decline after carotid interventions.

CONFLICT OF INTEREST

None.

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A.R. Naylor*
The Leicester Vascular Institute, Glenfield Hospital, Leicester, UK

J.D. Spence
Stroke Prevention and Atherosclerosis Research Centre, Robarts Research Institute, Western University, London, Ontario, Canada

*Corresponding author. Professor A. Ross Naylor MD, FRCS, Vascular Surgery, The Leicester Vascular Institute, Glenfield Hospital, Leicester, LE3 9QP, United Kingdom. Telephone: +44 116 2587768; Fax: +44 116 2585029.
Email-address: ross.naylor@uhl-tr.nhs.uk (A.R. Naylor)