Debate: In CAS, Embolic Injury Is Not the Only Risk to the Brain

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There is a widespread belief that the primary cause of neurologic injury during and immediately after carotid stenting (CAS) is cerebral embolization. As a result, the focus of both clinicians and industry has been on methods to reduce this risk. Other causes of periprocedural neurologic injury have largely been overlooked perhaps because they are so poorly understood.

Serum changes in biochemical markers of neurologic damage including neuron specific enolase (neuronal injury) and S100B (glial injury) were analyzed in 30 patients undergoing CAS within a randomized trial comparing protected and unprotected stenting. Samples were taken from the ipsilateral jugular vein prestenting and at 1, 6, and 24 hours post-stenting. There was a significant and group-independent rise in S100B ($p < .0005$) that did not correlate with other markers of cerebral embolization. This is evidence of glial injury independent of embolization.

As glial elements contribute to the integrity of the blood brain barrier, the rise in S100B implies transient loss of blood brain barrier function as a result of hemodynamic injury. The hyperperfusion syndrome is a distinct clinical entity but occurs in less than 1% of patients after CAS. However, procedural (< 24 hours) hypotension defined as a reduction in systolic blood pressure of greater than 30 mm Hg below prestenting values may occur in up to 76% of patients after CAS despite routine atropine administration.

A review of over 400 endovascular carotid procedures demonstrated that patients with hemodynamic instability had an increased likelihood of procedural stroke (odds ratio [OR] 2.6, 95% CI 1.2 to 5.9), myocardial infarction (OR 4.5, CI 1.2 to 16.9), and death (OR 3.6, 95% CI 1.0 to 7.6). Hemodynamic instability is therefore common and clinically relevant.

Hypotension, if sufficiently severe may cause watershed infarction. Lesser degrees of hypotension may render an otherwise inconsequential microembolic shower very relevant owing to impaired washout. Furthermore, hypotension may limit appropriate collateral flow to an ischemic territory. Hemodynamic instability is clearly detrimental to those with severe coronary artery disease and, last but not least, hypotensive responses may be a surrogate marker of high-risk patients with generalized atherosclerosis and decreased arterial compliance.

Stroke after CAS is assumed to be embolic. If, however, we scrutinize the available level 1 evidence supporting CAS (in trials against CEA) on the basis that these are robust independently-reviewed data analyzed off site, it is evident that we do not know how many of the ischemic strokes are truly embolic and likely to be in the MCA territory and how many are watershed, implying an hemodynamic etiology. There is a lack of reporting clarity despite cross-sectional imaging of the brain. Furthermore, the procedural microembolization rate (on transcranial Doppler) and the new white lesion rate on diffusion-weighted MRI correlate poorly with cognitive and overt neurologic deficit. The embolic stroke-rate for series and registries of CAS has fallen steadily, and the cause is multifactorial. The abundant macroembolic debris collected in early reports of first-generation protection devices is not routinely encountered in current clinical practice, largely because of technical refinements.

To further refine the safety profile of CAS, causes of procedural stroke other than embolization must be considered and the practical significance of intra- and postprocedural hemodynamic instability addressed by judicious control of periprocedural he-modynamics.