



Editorial

Carotid Revascularization to Prevent Stroke

Trial after trial, carotid angioplasty with stenting (CAS) has shown inferior results compared to carotid endarterectomy (CEA) in terms of prevention of stroke and stroke-related death. The International Carotid Stenting Study (ICSS), still the largest randomized trial in recently symptomatic patients, reported a significantly lower peri-procedural risk for patients undergoing CEA than for patients randomized to CAS (30 day rate of death/stroke 7.4% after CAS vs 3.4% after CEA (per protocol analysis HR 2.16 (95% CI 1.4–3.3)).¹ At first glance, the main conclusions from the Carotid Revascularization Endarterectomy vs. Stenting Trial (CREST), which included both symptomatic and asymptomatic patients, did suggest equivalence of CAS and CEA, with no significant difference between CAS and CEA in the rates of the primary composite endpoint 30 day risk of death/stroke/myocardial infarction (MI), or any ipsilateral stroke within four years (7.2% and 6.8%, respectively (HR with CAS 1.11; 95% CI 0.81 to 1.51; $p = 0.51$)). However, CREST also showed a significantly higher peri-operative stroke rate for CAS 4.1% vs. 2.3% after CEA (HR 1.79 (95% CI 1.14–2.82)).² The similar benefit between both procedures for the primary endpoint, was mainly driven by the intensively discussed and criticized inclusion of “silent” or “biochemical” MI in the composite endpoint. Based on the primary endpoint, CREST results were wrongly interpreted even in well respected media, stating that “CAS and CEA were equally as safe and effective in terms of stroke prevention”.³ In reality, ICSS and CREST actually showed very similar results, namely twice as many strokes associated with stenting as with endarterectomy. Furthermore, a pooled analysis of EVA-3S, SPACE, and ICSS showed substantially more peri-procedural deaths (RR 1.96 CI 1.04–3.72), and more peri-procedural stroke and death (RR 1.78 CI 1.40–2.25) with CAS than with CEA.⁴ Interestingly, this meta-analysis observed heterogeneity between different age groups, with a significant difference recorded only between CAS and CEA in patients older than 70 years (12.0% vs. 5.9%, risk ratio 2.04, 95% CI 1.48–2.82). In patients younger than 70 years, no difference was noted between CAS and CEA, but the 95% confidence interval (0.68–1.47) did not exclude a difference in either direction. So, for symptomatic patients with carotid stenosis >50% CAS is factually less safe and effective in terms of stroke prevention, particularly for patients older than 70 years.⁴

How can trial results be interpreted so differently? While in European guidelines the results of these trials and meta-analyses led to the conclusion that CEA was safer than CAS recommending CEA as the treatment of choice for recently symptomatic patients,⁵ surprisingly, the American Heart Association (AHA)

released its 2011 recommendations for the treatment of patients presenting with TIA or minor stroke considering CAS as an alternative to CEA for symptomatic patients at average or low risk with >50% angiographic stenosis.⁶ Although stating to include “all data available at that time” in their analysis, the AHA omitted any reference to the ICSS trial, while including CREST data. For unknown and unreported reason ICSS data were completely ignored despite the fact that CREST results were released one year after publication of ICSS. If the United States Center for Medicare and Medicaid services (CMS) in considering a proposal to allow wider indications for reimbursement of CAS, uncritically follows AHA guidelines, it clearly might not get the complete and objective information needed for a balanced decision. In the letter by Abbott et al. a multidisciplinary collaboration of world leading stroke physicians and vascular and endovascular surgeons plea against the proposed use of CAS in asymptomatic or low risk symptomatic patients.⁷ The push for wider indications for CAS in the US guidelines is merely based on the results from CREST and Sapphire trial.^{6,8} Sapphire randomized deemed high risk patients but in fact included 70% of asymptomatic patients who can never be at high risk for stroke by definition. However, as clearly outlined by Abbott et al., irrespective of symptomatic status, CAS in CREST, was associated with about double the peri-procedural rate of stroke or death compared to CEA.^{2,7} In using Sapphire criteria, innocent readers might hail CAS as the treatment of choice in the majority of these “high risk” patients. However, treating asymptomatic patients by CAS because of clinical factors that make them high risk for other events than stroke will do little to reduce the overall risk of stroke in the general population. At the level of procedural stroke risk as reported in Sapphire, all potential benefit from any intervention ceases, and neither surgery nor angioplasty can ever prevent long-term stroke in these asymptomatic patients.⁹ Clinicians that uncritically implement CAS justified on Sapphire outcomes definitely will not do their patients any service.

In considering carotid revascularization in asymptomatic patients, it is of utmost importance to realize that the natural risk for stroke has declined with the introduction of better medication.¹⁰ Furthermore, as noted after the publication of the landmark CEA trials, procedural risks may be much higher in “routine clinical practice” than within the confines of a randomized trial. The to be expected increases in the number of stenting interventions following reimbursement in asymptomatic patients will do little to reduce the incidence of stroke in the community, but it will contribute to an ever increasing financial burden to health care systems.

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True, depending on patients characteristics, one procedure might have an advantage over the other, leaving space for application of CAS in highly selected cases. The pro CAS movement keeps indicating the possible improvements in endovascular techniques that may lead to better outcomes in the near future. Strangely, however, no structural analysis of stroke mechanism has been performed within any trial so far. In our ongoing attempts to make carotid revascularization a safer procedure, and to indicate treatment on an individualized approach, understanding the underlying pathophysiological mechanism of CAS related stroke is essential in order to prevent those very same events in the future.

In summarizing the best available evidence at the moment, CEA is clearly superior to CAS, independent of symptom status and degree of stenosis, when considering the most relevant endpoint – the occurrence of stroke or death. Hopefully, governmental institutions responsible for reimbursement regulations will take careful notice of the published evidence, and of the objectively stated and multidisciplinary supported considerations presented by Abbott et al. and will not extend reimbursement coverage for CAS to routine practice management of asymptomatic or low risk patients.

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