EDITORIAL

Is Carotid Artery Stenting a Fair Alternative to Carotid Endarterectomy for Symptomatic Carotid Artery Stenosis?

KEYWORDS
Symptomatic carotid artery stenosis; Carotid endarterectomy; Carotid artery stenting

In medicine, like politics, the ‘data’ or ‘facts’ can be interpreted in more than one way. This interpretation or ‘spin’ is often more important than anything else. According to the recent guidelines by the American Heart Association/American Stroke Association (AHA/ASA) and several other associations, "carotid artery stenting (CAS) is indicated as an alternative to carotid endarterectomy (CEA) for symptomatic patients at average or low risk of complications associated with endovascular intervention when the diameter of the lumen of the internal carotid artery is reduced by more than 70% as documented by noninvasive imaging or more than 50% as documented by catheter angiography and the anticipated rate of periprocedural stroke or mortality is less than 6% (Class I; Level of Evidence B)". The recent Carotid Revascularization Endarterectomy vs. Stenting Trial (CREST) results were used to support this recommendation. However, the facts leading to this recommendation may have more than one interpretation. This commentary addresses another possible interpretation.

Carotid artery stenting: an alternative for whom?

According to Webster’s New World Dictionary, ‘alternative’ is defined as “a choice between two things”. Thus, in the AHA/ASA recommendation, the word ‘alternative’ may easily be misinterpreted as ‘equivalent’ to justify the widespread use of carotid artery stenting (CAS). Current data, however, indicate that CAS should be viewed neither as an ‘alternative’ nor as an ‘equivalent’ treatment option to carotid endarterectomy (CEA) in the majority of symptomatic patients.

In CREST, there was no significant difference in the estimated 4-year rates of the composite primary end point between CAS and CEA (7.2% vs. 6.8%, respectively; relative risk (RR) 1.11; 95% confidence interval (CI) 0.81–1.51; p = 0.51). The composite primary end point, however, consisted of stroke, myocardial infarction (MI) or death from any cause. Although CAS was associated with considerably higher periprocedural stroke rates compared with CEA (4.1% vs. 2.3%, respectively; hazard ratio (HR) 1.79; 95% CI 1.14–2.82; p = 0.012), this was offset by a reduced risk of MI (1.1% vs. 2.3%, respectively; p = 0.032). A recent subgroup analysis of CREST showed that in symptomatic patients CAS was associated with an almost twofold increase in periprocedural stroke and death rates compared with CEA (6.0% ± 0.9% vs. 3.2% ± 0.7%, respectively; HR 1.89; 95% CI 1.11–3.21; p = 0.02). Therefore, CAS only showed equivalence of outcomes with CEA when MIs were added to strokes. Quality-of-life indices, however, show that both major and minor strokes are likely to produce long-term physical limitations (with minor stroke associated with worse mental and physical health at 1 year), whereas the effect of periprocedural MI on long-term physical and mental health is less.

In addition to CREST, several other randomised studies have demonstrated that in symptomatic patients CAS is associated with higher rates of stroke, as well as...
recurrent carotid stenosis rates\textsuperscript{8–10} (Table 1). CAS is also considerably more expensive than CEA.\textsuperscript{11} In addition, several recent meta-analyses have concluded that CAS is associated with inferior outcomes compared with CEA.\textsuperscript{12–15} According to one meta-analysis (\textit{n} = 13 trials; 7484 patients; 80% symptomatic),\textsuperscript{12} CAS is associated with an increased risk of any stroke compared with CEA (RR 1.45; 95% CI 1.06–1.99; \(I^2 = 40\%\)). The conclusion reached was that "for every 1000 patients opting for CAS rather than CEA, 19 more patients would have strokes".\textsuperscript{12} These results were verified in another independent meta-analysis.\textsuperscript{13} Both meta-analyses, however, concluded that the superiority of CEA over CAS disappeared in patients \textless 70 years. According to a recent large registry (\textit{n} = 47 752 CAS and CEA hospitalisations matched by propensity score), the most appropriate procedure in symptomatic patients with carotid artery stenosis is CEA, whereas CAS appears to be a suitable minimally invasive approach for asymptomatic patients.\textsuperscript{16}

According to the recent inter-colleague Australasian CAS guidelines, "CAS may be considered as a treatment option for patients with symptomatic severe carotid stenosis who are at high risk of stroke, but are surgically unsuitable for CEA".\textsuperscript{17} This includes specific patient subgroups and conditions, namely (1) post-radiation therapy, (2) block dissection of the neck, (3) \textit{in situ} tracheostomy, (4) recurrent stenosis following previous CEA, (5) severe cervical spine arthritis, (6) surgically inaccessible carotid stenosis (e.g., obesity and high carotid bifurcation), (7) contralateral recurrent laryngeal nerve injury and (8) contralateral internal carotid artery occlusion.\textsuperscript{17} Apart from these conditions, CAS should not be considered as an alternative to CEA for the management of symptomatic carotid stenosis except in patients \textless 70 years and those participating in randomised trials.\textsuperscript{17}

Based on the results of meta-analyses,\textsuperscript{12–15} randomised controlled trials\textsuperscript{6–10} and population-based studies,\textsuperscript{11,16} CAS may be an ‘alternative treatment’ but is clearly inferior to CEA in the majority of symptomatic patients.\textsuperscript{17} Unstable symptomatic carotid plaques are associated with an increased incidence of new ipsilateral silent embolic events after CAS compared with CEA.\textsuperscript{18–20} In the absence of data showing comparable risks of stroke and silent emboli for CAS, angioplasty and stenting should only be offered to symptomatic patients when mitigating factors suggest an unacceptable risk with CEA.

It is likely that CAS will continue to improve with (1) better patient selection, (2) better embolic protection devices, (3) better stents (membrane or mesh covered), (4) technical improvements (e.g., avoiding aortic arch manipulations) and (5) additional operator experience.\textsuperscript{19} Adoption of all these may well improve CAS outcomes and make it a fair alternative to CEA, at least in certain patient subgroups. However, the current evidence indicates that we are not there yet, and it seems unfair to spin either CREST\textsuperscript{2} or the AHA/ASA guidelines\textsuperscript{1} to conclude that we are.

### Table 1 Randomized controlled trial (RCT) results showing higher rates of stroke/death and recurrent carotid stenosis after CAS than CEA.

<table>
<thead>
<tr>
<th>Study (year)</th>
<th>Study design</th>
<th>Study outcome</th>
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<tbody>
<tr>
<td>EVA-3S\textsuperscript{7} (2008)</td>
<td>4-year data of EVA-3S</td>
<td>Incidence of 30-day stroke/death rate: 15 of the 262 vs. 29 of the 265 patients, or 6.2% vs. 11.1%, for CEA vs. CAS, respectively (HR 1.97; 95% CI 1.06–3.67; (p = 0.03) for CAS vs. CEA).</td>
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<td>SPACE\textsuperscript{9} (2008)</td>
<td>2-year data of SPACE</td>
<td>Incidence of ≥70% recurrent carotid stenosis: 10.7% vs. 4.6%, for CAS vs. CEA, respectively; (p = 0.0009); or 11.1% vs. 4.6%, for CAS vs. CEA, respectively; (p = 0.0007), in the intention-to-treat and per-protocol life-table estimates, respectively.</td>
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<td>Steinbauer et al. \textsuperscript{8} (2009)</td>
<td>Single-center RCT comparing the long-term results (66 ± 14.2 vs. 64 ± 12.1 months, respectively) of CAS ((n = 43)) with CEA ((n = 44)) 120-day data from 1710 symptomatic patients randomized to CAS vs. CEA</td>
<td>Patients undergoing CAS had higher rates of ipsilateral stroke (4 of 42 vs. 0 of 42 patients, respectively; (p &lt; 0.05)) and ≥70% recurrent carotid stenosis (6 of 32 vs. 0 of 29, respectively; (p &lt; 0.05)) compared with patients undergoing CEA.</td>
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<tr>
<td>ICSS\textsuperscript{6} (2010)</td>
<td>Single-center RCT comparing the long-term results (66 ± 14.2 vs. 64 ± 12.1 months, respectively) of CAS ((n = 43)) with CEA ((n = 44)) 120-day data from 1710 symptomatic patients randomized to CAS vs. CEA</td>
<td>Patients undergoing CAS ((n = 828)) had a higher (vs. CEA, (n = 821)) risk of any stroke (65 vs. 35 events, or 7.7% vs. 4.1%, respectively; HR 1.92; 95% CI 1.27–2.89; (p = 0.002)), any stroke or death (72 vs. 40 events, or 8.5% vs. 4.7%, respectively; HR 1.86; 95% CI 1.26–2.74; (p = 0.0001)), all-cause death (19 vs. 7 events, or 2.3% vs. 0.8%, respectively; HR 2.76; 95% CI 1.16–6.56; (p = 0.017)).</td>
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<td>CREST\textsuperscript{4} (2011)</td>
<td>RCT of 2502 (1181 asymptomatic; 1321 symptomatic) patients to CEA ((n = 1240)) or CAS ((n = 1262))</td>
<td>Symptomatic patients undergoing CAS had a higher incidence of any peri-procedural stroke (37 vs. 21 events, or 5.5% vs. 3.2% (p = 0.002)); any stroke or death (40 vs. 21 events, or 6.0% vs. 3.2% (p = 0.02)) and a higher incidence of any peri-procedural stroke or death (40 vs. 21 events, or 6.0% vs. 3.2% (p = 0.02)) compared with patients undergoing CEA.</td>
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<td>EVA-3S\textsuperscript{10} (2011)</td>
<td>2-year carotid ultrasound follow-up data for 242 CAS patients and 265 CEA patients of EVA-3S</td>
<td>The rate of carotid restenosis of ≥50% or occlusion was higher after CAS than after CEA (12.5% vs. 5.0%, respectively; time ratio 0.16; 95% CI 0.03–0.76; (p = 0.02)).</td>
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EVA-3S: Endarterectomy vs. Angioplasty in patients with Symptomatic Severe Carotid Stenosis; CEA: carotid endarterectomy; CAS: carotid artery stenting; HR: hazard ratio; CI: confidence interval; SPACE: Stent-Protected Angioplasty vs. Carotid Endarterectomy; RCT: randomized controlled trial; ICSS: International Carotid Stenting Study; CREST: Carotid Revascularization Endarterectomy vs. Stenting Trial.
Conflict of Interest

None.

Funding

None.

References


3 Webster’s New World College Dictionary. Available at: http://www.yourdictionary.com/alternative.


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