Meta-analysis of randomized trials comparing carotid endarterectomy and endovascular treatment

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CRD summary
This review suggested that carotid endarterectomy was safer than carotid angioplasty, with or without stent placement, for patients with carotid stenosis suitable for surgery. However, the poor reporting of this review make it difficult to assess its' reliability, so a cautious interpretation of the findings is advised.

Authors' objectives
To compare the effectiveness of carotid angioplasty, with or without stent placement, with carotid endarterectomy in patients with carotid stenosis suitable for surgery.

Searching
MEDLINE, EMBASE, the Cochrane Database of Systematic Reviews and DARE were searched between 1966 and December 2006. Search terms were reported.

Study selection
Randomised controlled trials (RCTs) comparing carotid angioplasty, with or without stent placement, with carotid endarterectomy in patients with symptomatic or asymptomatic carotid stenosis, who had unilateral or bilateral procedures, were eligible for inclusion. Included patients could be of any age or gender. Eligible outcome measures included the incidence of death, stroke or cranial neuropathy within 30 days of the procedure, subsequent ipsilateral carotid territory stroke, and other complications related to the procedure.

Included trials assessed participants with between 50% and over 80% stenosis. Just less than half of the trials recruited symptomatic and asymptomatic patients. The majority of included trials compared carotid angioplasty with stent placement (using the Wallstent) with the surgeons' preferred method for carotid endarterectomy. Successful deployment of the stent ranged from 89% to 100%. All included trials used an additional stent after primary angioplasty. Aspirin was usually given before carotid angioplasty with stent placement; in a number of cases, aspirin was given along with antiplatelet drug (ticlopidine or clopidogrel). A distal protection device was used in just less than half of the carotid angioplasty with stent placement interventions. Antiplatelet prophylaxis was also given in some cases before carotid endarterectomy. Follow-up usually occurred at 24 hours, one, six and/or 12 months. Outcome measures varied between trials, particularly with regard to the assessment of neurological status.

All three of the authors assessed the studies for inclusion.

Assessment of study quality
Study validity was independently assessed by two reviewers using the Jadad scale, each study been awarded a score up to a maximum of five points. Disagreements were resolved by a third reviewer. Overall quality was also assessed using a Dutch checklist.

Data extraction
Odds ratios (ORs) with 95% confidence intervals (CIs) were calculated for the main outcomes using intention-to-treat data.

The authors did not state how data were extracted for the review, or how many reviewers performed the data extraction.

Methods of synthesis
Studies were grouped according to outcome and pooled odds ratios with 95% confidence intervals were calculated using
the Peto fixed-effect method. The Yates' correction was applied to any studies with zero events. Statistical heterogeneity was assessed using the $\chi^2$ and $I^2$ statistics. Further analyses were conducted using a random-effects analysis, and excluding various groups of trials based on study size, the use of distal protection devices and the inclusion of asymptomatic patients. Relative risks (RRs) were also calculated using a fixed effect analysis. Publication bias was assessed using funnel plots.

**Results of the review**

The authors reported including seven RCTs (n=1,480 carotid endarterectomy patients and n=1,492 carotid angioplasty with stent placement patients) in the review; the results of eight trials are included in the analyses. Blinding was not possible due the nature of the intervention and study design. Of the eight trials included in the analyses, all but one scored 3 points on the Jadad scale; the remaining trial scored 1 point. Sample sizes ranged from 17 to 1183; three trials recruited fewer than 105 patients.

A significant benefit for carotid endarterectomy over carotid angioplasty with stent placement was reported for death or any stroke at 30 days post-procedure (OR 1.39, 95% CI: 1.05 to 1.84; eight trials; $I^2$=59.4%); the risk of death, any stroke, or myocardial infarction at 30 days (effect size not reported); ipsilateral ischaemic stroke at 30 days (OR 1.48, 95% CI: 1.05 to 2.07); any stroke at 30 days (OR 1.50, 95% CI: 1.05 to 2.16); death or stroke at six months follow-up (OR 1.99, 95% CI: 1.09 to 3.62); and the risk of procedural failure (OR 3.42, 95% CI: 2.03 to 5.79). $I^2$, $\chi^2$ and number of included trials were not reported for many of the outcomes.

The risk of cranial neuropathy at 30 days (OR 1.99, 95% CI: 1.09 to 3.62; six trials) was significantly reduced for carotid angioplasty with stent placement in comparison with carotid endarterectomy.

No significant differences between the two procedures were reported for the odds of death or disabling stroke at 30 days (six trials), death or stroke at one year follow-up (four trials) and ipsilateral intracerebral bleeding at 30 days.

The results of further analyses were also reported in the review, but in the majority of cases did not significantly change the original findings.

Funnel plots showed no evidence of publication bias.

**Authors' conclusions**

Evidence suggested that carotid endarterectomy was safer than carotid angioplasty with stent placement for the treatment of carotid stenosis.

**CRD commentary**

This review answered a clearly defined review question. Searches were carried out on several databases, but no specific attempts were made to locate unpublished data; it was not reported whether any language limitations were used. The risk of publication bias was assessed, but given the small number of the included trials, this assessment is unlikely to be reliable. The risk of language and publication bias is therefore unclear. Some attempts were made to reduce the risk of reviewer error and bias when assessing study validity, but it was not reported whether similar precautions were taken during the rest of the review process. Trial quality was assessed using published criteria and overall appeared to be good. The trial findings were not clearly reported. There were apparent discrepancies between the number of included trials, the number of included references and the number of trials included in the pooled analyses, which made it difficult for the reader to follow the results. Statistical heterogeneity was only reported for the sensitivity analyses and for other select results, and not for all of the results, making it difficult to assess whether it was appropriate to pool certain groups of trials. Where significant statistical heterogeneity was identified, no attempts were made to address this further. It was also difficult in some cases to assess the number of trials included in the analyses. The review abstract reported a significant difference in the risk of death, any stroke, or myocardial infarction at 30 days, but no data was reported in the analysis section or accompanying tables. However, further detailed analyses were reported for the main outcome, in order to assess its robustness. Overall, the poor reporting of this review make it difficult to assess its reliability, so a cautious interpretation of the findings is advised.

**Implications of the review for practice and research**
Practice: The authors stated that carotid angioplasty with stent placement should not be performed in practice until further research is available, and that its use should be restricted to patients enrolled in randomised controlled trials comparing stenting with surgery.

Research: The authors stated that further research from trials with long-term follow-up and subgroup analyses is required to determine the long-term durability of carotid angioplasty with stent placement for stroke prevention. The authors also highlighted two relevant ongoing trials.

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