Systematic review of the perioperative risks of stroke or death after carotid angioplasty and stenting

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CRD summary
The authors concluded that risks of carotid angioplasty and stenting were generally higher than carotid endarterectomy in symptomatic patients; carotid angioplasty and stenting should not be used in good surgical candidates. This was a well-conducted review, but the lack of direct comparison between carotid angioplasty and stenting and carotid endarterectomy should be borne in mind when interpreting the conclusions.

Authors' objectives
To assess the risk of perioperative stroke or death after carotid angioplasty and stenting.

Searching
MEDLINE, EMBASE and The Cochrane Library were searched between January 1990 and June 2008 for articles in any language. Search terms were reported. Reference lists of included studies, relevant reviews and personal files were handsearched Journal of Vascular Surgery, Journal of Endovascular Therapy and Catheter Cardiovascular Interventions were handsearched. Unpublished abstracts presented at seven conferences were searched. ClinicalTrials.gov, FDA and European Medicines Agency websites were searched.

Study selection
Studies of patients with symptomatic and/or asymptomatic stenosis of the carotid bifurcation were eligible for inclusion if they received treatment by angioplasty, irrespective of the treatment (balloon angioplasty without stenting or stenting), arterial route and use of cerebral protection.

Eligible studies were required to report 30-day risk of stroke, number of strokes or death, or number of strokes, myocardial infarctions or deaths as the primary outcome. Secondary outcomes were in-hospital and periprocedural risks (within 24 hours or where timing of assessment of complications was unclear). Studies that enrolled specific populations only (restenosis after carotid endarterectomy, post-radiotherapy stenosis, fibromuscular dysplasia, carotid dissection and patients treated in an emergency setting) were excluded.

Included studies were conducted worldwide, mostly in developed world nations. Studies were published between 1992 and 2008. Studies were mostly of men with a median age of 70 years. A small proportion of patients had contralateral carotid occlusion or post-radiation carotid stenosis; more than half had coronary artery disease. Approximately half of the patients were symptomatic. Some patients also had diabetes.

Two reviewers independently screened studies for inclusion. Discrepancies were resolved through discussion.

Assessment of study quality
Two reviewers assessed study quality using the criteria: study design (randomised trial versus cohorts/registries), setting (single- versus multi-centre), patient enrolment (prospective versus retrospective and consecutive versus non-consecutive), adequate or inadequate description of population and outcome measurement (whether systematic assessment was carried out on all patients by a neurologist 30 days after the procedure or before discharge).

Data extraction
Two reviewers independently extracted the number of events for each outcome to calculate the relative risk and 95% confidence intervals (CIs). Primary authors were contacted for further details, where necessary.

Methods of synthesis
Relative risks and 95% CIs were combined using a Mantel Haenszel fixed-effect or DerSimonian-Laird random-effects model (as appropriate) after correction for over dispersion using the Freeman-Tukey variance-stabilising
transformation. Statistical heterogeneity was assessed using Cochran’s Q and $I^2$ statistics.

Subgroup analyses were performed on clinical presentation (symptomatic versus asymptomatic; stroke versus transient ischaemic attack; cerebral versus ocular event), age (>75 to 80 versus <75 to 80 years), gender, diabetes mellitus, coronary artery disease, peripheral arterial disease, contralateral carotid occlusion, restenosis after carotid endarterectomy versus de novo lesion, plaque structure (ulcerated versus smooth, presence of calcification), timing for carotid angioplasty and stenting (<14 days versus >14 days after cerebral ischaemic event), side of the treated lesion and use of cerebral protection device. Meta-regression was conducted to assess the influence of clinical presentation and study quality items on the size of the intervention effect and influence of mid-cohort year and publication year on the findings.

Sensitivity analysis was performed by excluding abstracts or post-marketing studies, as these patients may also have been included in the published studies.

Publication bias was assessed using funnel plots and Egger's test.

**Results of the review**

Two hundred and six studies (n=54,713) were included in the review: 13 randomised controlled trials (RCTs) and 193 registries. One hundred and seventy (83%) studies were in a single-centre setting, 83 (40%) studies were reported to be prospective and 119 (58%) studies reported consecutive enrolment of patients. Patient characteristics were adequately reported in 64% of studies. Study outcomes were assessed by an independent neurologist in 39% of studies (there was a discrepancy between the figures reported in the tables and text and we have used the figures from the tables).

For 30-day stroke after carotid angioplasty and stenting the relative risk was 3.9% (95% CI 3.4 to 4.4; 118 studies). For stroke or death the relative risk was 4.7% (95% CI 4.1 to 5.2; 113 studies). For stroke, death or myocardial infarction the relative risk was 5.3% (95% CI 4.6 to 6.0; 63 studies). There was evidence of statistical heterogeneity ($I^2=67\%$ stroke, $=69\%$ stroke or death and $=64\%$ stroke, death or myocardial infarction). Respective in-hospital and periprocedural risks were slightly lower (as reported in the review) and statistical heterogeneity remained for risk of stroke and risk of stroke or death. Sensitivity analysis did not alter the results significantly.

Subgroup analysis indicated that the risk of stroke or death after carotid angioplasty and stenting was higher in patients with symptomatic stenosis, patients who experienced cerebral versus ocular event, patients aged from more than 75 to 80 years and patients with a history of coronary artery bypass graft. The authors also reported higher risk in patients with peripheral artery disease, but this risk difference was not statistically significant.

Risk of stroke or death was lower in patients treated with carotid angioplasty and stenting due to restenosis after carotid endarterectomy compared to patients treated for atherosclerotic carotid stenosis. Use of cerebral protection systems was associated with lower risk. No other factors were associated with significant risk. Similar results were reported for stroke, with the exception that hypertension was significantly associated with higher risk of complications.

Other results were reported in the review. There was no evidence of publication bias.

**Authors' conclusions**

Risks of carotid angioplasty and stenting varied considerably across studies, but were generally higher than carotid endarterectomy in symptomatic patients. Carotid angioplasty and stenting should not be used in good surgical candidates.

**CRD commentary**

The review question was clear and supported by clearly defined inclusion criteria for patients, interventions and outcomes, but broad criteria for study design. A comprehensive search of the literature was undertaken. Formal assessment showed no evidence of publication bias. The authors went some way to assess the quality of the included studies, although RCTs were not assessed for criteria such as allocation concealment and blinding. The authors performed each stage of the review process in duplicate, which reduced potential for reviewer error and bias. The authors acknowledged the limitations with observational studies and heterogeneity among studies and acknowledged...
that duplicated data may have distorted the findings. Appropriate methods were used to investigate statistical heterogeneity and the influence of various factors on the findings.

This was a generally well-conducted piece of research, but carotid angioplasty and stenting was not compared directly with carotid endarterectomy in this review and this should be borne in mind when interpreting the authors’ conclusions.

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