Endarterectomy vs stenting for carotid artery stenosis: a systematic review and meta-analysis
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CRD summary
This well-conducted review found carotid endarterectomy and carotid angioplasty plus stenting had equal risks of death and non-fatal myocardial infarction. The risk of stroke between the two procedures was inconclusive, with a trend towards increased risk with stenting. The results should be interpreted with some caution given the small numbers of included trials with low event rates and short-term follow-up.

Authors' objectives
To evaluate the safety and efficacy of carotid endarterectomy compared with carotid angioplasty and stenting for carotid artery stenosis.

Searching
MEDLINE, EMBASE, Current Contents, Science Citation Index and Cochrane Central Register of Controlled Trials (CENTRAL) were searched for publications from 2003 to April 2007; search terms were reported. The reference list of a previous rigorous Cochrane review published in October 2003 on the same topic (see Other Publications of Related Interest) was also searched to identify relevant studies. References were sought from the reference lists of all the included trials and by contacting experts. There were no restrictions on language or by publication type.

Study selection
Randomised controlled trials (RCTs) that compared carotid endarterectomy with carotid angioplasty plus stenting (with and without the use of cerebral protective devices) in patients with carotid stenosis were eligible for inclusion.

Outcomes of interest were death, stroke, and myocardial infarction at 30 days and one year post-procedure.

The patients in the included trials varied in experience of symptoms and operative risk (the latter ranged from average to high risk). In included trials, angioplasty procedures included stenting; cerebral protection devices were used in the trials published since 2004. Most of the trials reported outcomes at 30 days post-procedure. One trial exclusively selected asymptomatic patients; another trial selected patients deemed to be at high risk for carotid endarterectomy. The mean age of included patients ranged from 63 years to 72.6 years (where reported); the degree of stenosis ranged from more than 50% to more than 80%.

Two reviewers independently performed the study selection; any disagreements were resolved by consensus. The Kappa test was performed to evaluate inter-reviewer reliability.

Assessment of study quality
Two reviewers independently assessed methodological quality of the included trials by evaluating allocation concealment, blinding, number of patients lost to follow-up, and premature cessation of trials prior to reaching sample sizes.

Data extraction
Two reviewers independently extracted data to permit the calculation of relative risks (RR) and 95% confidence intervals (CI) for deaths, major and disabling stroke, any strokes and myocardial infarction (both Q-wave and non-Q wave). The reviewers attempted to contact the authors of the primary trials if there was missing information or more information was required.

Methods of synthesis
Pooled relative risks and 95% confidence intervals were calculated using a DerSimonian and Laird random-effects model. The I^2 statistic was used to evaluate statistical heterogeneity across the trials. Equivalence analyses were
conducted pooling of the risk differences (RD) and 95% confidence intervals for each of the outcomes from individual trials using random-effects meta-analyses.

Subgroup and sensitivity analyses were undertaken to examine patient-level characteristics, such as symptom presence, age, gender; diabetes status, history of renal failure, plaque morphology, severity of stenosis; trial-level characteristics were also analysed (e.g. surgical volume of operators, use of cerebral protection devices, and whether RCTs ceased prematurely).

Results of the review
Ten RCTs were included in the review (n=3,182 patients). Allocation concealment was reported in six trials. Blinding of data collectors and outcome assessors was reported in two trials. There was no blinding of patients or caregivers reported in any of the RCTs. Five RCTs were stopped prematurely for futility (two trials), harm (two trials), funding shortages (one trial), and slow enrolment (one trial). Follow-up ranged between one to 48 months post-procedure.

There were non-statistically significant reductions observed with carotid angioplasty plus stenting at 30 days post-procedure in risk of death compared with carotid endarterectomy (RR 0.61, 95% CI 0.27 to 1.37; five RCTs) and risk of non-fatal myocardial infarction (RR 0.43, 95% CI 0.17 to 1.11; three RCTs), and a non-significant increase in the risk of any stroke (RR 1.29, 95% CI 0.73 to 2.26; five RCTs). There was moderate heterogeneity found across the trials for the risk of stroke (I²=40%).

The results were not significantly altered for the analysis of major and disabling strokes, with a non-significant increase in the risk of major and disabling strokes in patients who received carotid angioplasty plus stenting (RR 1.06, 95% CI 0.32 to 3.52, four RCTs); there was moderate heterogeneity reported across the trials (I²=45%).

The 30-day equivalence analyses showed there were similar effects of carotid endarterectomy and carotid angioplasty plus stenting on death (pooled RD -0.40, 95% CI -1.02 to 0.40) and non-fatal myocardial infarction (pooled RD -0.70, 95% CI -1.90 to 0.50) using an equivalence zone of 2%. The authors noted that the effects on stroke would be only equivalent if an equivalence zone of 3% was used.

Authors' conclusions
Carotid stenting and carotid endarterectomy appeared equivalent in terms of death and non-fatal myocardial infarction. Although the difference in risk of strokes between the two procedures was inconclusive, there was a trend towards reduced stroke risk with carotid endarterectomy than with stenting.

CRD commentary
The review addressed a clear question. Criteria for the inclusion of studies were stipulated. Appropriate databases were searched with no language restrictions, and there were attempts to identify unpublished studies. Steps were taken to minimise reviewer error and bias throughout the review process.

The decision to statistically combine the results appeared to be justified, although moderate heterogeneity was observed in the results for stroke outcomes with the use of carotid angioplasty plus stenting. The authors acknowledged the limitations of the review in the low to moderate quality of the included trials, premature cessation of the trials for a variety of reasons, and inadequate statistical power of the trials.

The review was generally well conducted, but the results should be interpreted with some caution because of the small numbers of trials with low event rates and short-term follow-up.

Implications of the review for practice and research
Practice: The authors did not state any implications for practice.
Research: The authors stated that investigators in ongoing trials need to consider recruiting patients until planned sample sizes are attained and to use rigorous statistical methods for early cessation of trials. Any subgroup analyses examining differing patients groups will require the conduct of large RCTs with inclusion criteria permitting the entry
of high-risk patients.

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**Other publications of related interest**

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