Updated systematic review and meta-analysis of randomized clinical trials comparing carotid artery stenting and carotid endarterectomy in the treatment of carotid stenosis

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CRD summary
Compared with endarterectomy, carotid artery stenting was associated with significantly higher rate of stroke or death 30 days after surgery, but showed a lower incidence of myocardial infarction. There was insufficient evidence to support treatment change for patients who receive carotid endarterectomy as current standard of care. The conclusions of the review are likely to be reliable.

Authors’ objectives
To compare carotid artery stenting with carotid endarterectomy for the treatment of carotid stenosis.

Searching
PubMed, Cochrane Controlled Trials Register (CENTRAL), Web of Science and Google Scholar were searched from 1990; the Chinese Wanfang database was consulted from 1995 to 2010. Reference lists from relevant articles were consulted. Only articles in English or Chinese were included. Search terms were reported.

Study selection
Randomised controlled trials (RCTs) that compared endovascular treatment (angioplasty or stenting) with endarterectomy in patients with symptomatic or asymptomatic carotid stenosis were eligible.

Outcomes of interest were death or stroke (composite outcome), myocardial infarction in the short term (less than 30 days) and intermediate term (within one year), short-term death, disabling and non-disabling stroke, facial neuropathy, bradycardia or hypotension, restenosis and haematomas.

Follow-up ranged from 30 days to 65 months. Surgical techniques varied. Endovascular surgery was most often performed with Wallstent and/or embolic protection devices (studies published from 2004), and most studies reported using aspirin with clopidogrel before the procedure. Method for carotid endarterectomy was at the discretion of the surgeon, and aspirin with or without clopidogrel before surgery was reported in more than half of the studies. Studies were published between 1998 and 2010.

Where reported, mean age of patients ranged from 67 to 73 years old. Most were men and at least half were classed as symptomatic in each of the trials. Proportion of patients with coronary artery disease ranged from 13 to 86%. Few reported rates of congestive heart failure, which ranged from three to 47%. Where reported, history of stroke ranged from 12 to 90%, transient ischaemic attack from 10 to 81%, and rates of hypertension from 53 to 98%. Proportion of patients with diabetes was between 12 and 44%, and hyperlipidaemia ranged from 19 to 86%. Rates of stenosis ranged from 75% to 86%, where reported.

Three reviewers independently selected the studies. Disagreements were resolved via discussion.

Assessment of study quality
Study quality was assessed using the Jadad scale, which covered: randomisation, blinding, withdrawals and drop-outs. The Cochrane risk of bias tool was also used. It was not clear how many reviewers assessed study quality but the authors stated it was done independently.

Data extraction
Data on adverse events were extracted to calculate odds ratios (ORs) and risk ratios (RRs), along with their 95% confidence intervals. Two reviewers extracted the data.

Methods of synthesis
Meta-analysis was used to pool the results. A fixed-effect model was employed, unless significant heterogeneity was
found using a Χ² test and the I² statistic, in which case random-effects model was used. Subgroup analyses were used to evaluate outcomes for symptomatic and non symptomatic patients, and to assess the impact of different embolic protection devices. Sensitivity analyses were performed to assess the effect of large trials and the impact of different meta-analytical models on the pooled estimates. Publication bias was assessed through funnel plots.

Results of the review
Thirteen trials (7,501 patients allocated, of which 7,348 were treated) were included. Of those, eight were conducted in multiple centres. Two scored 1 out of 5 on the Jadad scale, 10 scored three and one scored four.

The odds of stroke or death within 30 days were significantly higher following carotid artery stenting compared with carotid endarterectomy (OR 1.57; 95% CI 1.11 to 2.22; 11 trials; I²=43.3%) but there was no difference between the two procedures at one year (number of trials not reported). Subgroup analyses showed greater incidence of stroke or death in the stenting group which was significant for symptomatic patients (OR 1.89; 95% CI 1.48 to 2.41; eight trials; I²=37.7%) and non statistically significant in asymptomatic patients (OR 1.88; 95% CI 0.79 to 4.46; one trial).

The odds of a nondisabling stroke were significantly higher in the stenting group at 30 days (OR 1.87; 95% CI 1.40 to 2.50; nine trials). There was no statistically significant difference in mortality (OR 1.43; 95% CI 0.85 to 2.40; seven trials) and disabling stroke (OR 1.28; 95% CI 0.89 to 1.83; seven trials) at 30 days. Statistical heterogeneity was low for these outcomes.

Carotid artery stenting was associated with a lower rate of myocardial infarction at 30 days (OR 0.43; 95% CI 0.26 to 0.71; five trials) and within one year (OR 0.30; 95% CI 0.10 to 0.90; two trials). There was no evidence of statistical heterogeneity. Other outcomes and sensitivity analyses were reported. Funnel plots showed no evidence of publication bias.

Authors' conclusions
Compared with carotid endarterectomy, carotid artery stenting was associated with significantly higher rate of stroke or death 30 days after surgery, but showed a lower incidence of myocardial infarction. The authors stated that there was insufficient evidence to support change from routine clinical practice in patients who have carotid endarterectomy as current standard of care.

CRD commentary
The review question and selection criteria were clear. Several bibliographic sources were checked. Attempts were made to minimise error and bias at the study selection stage of the review. It appeared that similar attempts were made during data extraction and quality assessment. Overall results of the quality assessment were reported. However, all studies were classed as RCTs, several were relatively large and most were conducted in multiple centres.

The choice of a quantitative synthesis appeared appropriate. Attempts to explore heterogeneity were made. Sensitivity analyses suggested that the overall results were robust. Results of the subgroup analyses should be interpreted with caution, notably due to the limited number of studies involved and lack of definitions for symptomatic and asymptomatic patients. The authors acknowledged that follow-up duration was limited. Due to variations between the studies in patient characteristics, surgical procedures and study designs, the authors' recommendation that conclusions should be interpreted in the context of individual studies seemed appropriate. The conclusions of the review generally reflected the evidence and are likely to be reliable.

Implications of the review for practice and research
Practice: The authors stated that carotid artery stenting and carotid endarterectomy could be seen as complementary rather than competing modes of therapy. Each could be optimised with careful patient selection. They stated that carotid endarterectomy should be the first choice for symptomatic patients requiring carotid revascularisation, and carotid artery stenting could be preferable in some patients considered at high-risk or with anatomic conditions rendering surgery technically difficult. Evaluating coronary perfusion and considering age may be needed to optimise the treatment strategy.

Research: The authors stated that trials in patients with asymptomatic carotid stenosis that compared carotid...
endarterectomy, carotid artery stenting and best medical treatment were needed.

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