Stenting versus surgery in patients with carotid stenosis after previous cervical radiation therapy: systematic review and meta-analysis

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CRD summary
Both carotid angioplasty and stenting and surgery alone for carotid stenosis after previous cervical radiation therapy had low risks of cerebrovascular adverse events. Surgery had significantly higher temporary cranial nerve injury symptoms but lower rates of late cerebrovascular adverse events and restenosis. Study quality and review process limitations imply that the authors' results should be interpreted with caution.

Authors' objectives
To compare the efficacy and safety of carotid angioplasty and stenting versus surgery (carotid endarterectomy) in patients with carotid stenosis after previous cervical radiation therapy.

Searching
MEDLINE and EMBASE were searched to 17 October 2011 with no restrictions on the search; search terms were reported. Abstracts and books of major meetings and relevant articles were handsearched.

Study selection
Studies of carotid angioplasty and stenting and/or surgery (carotid endarterectomy) in patients with carotid stenosis after previous cervical radiation therapy and reporting measurement of at least one relevant outcome were eligible for inclusion. Case reports, reviews and articles under review were excluded.

The relevant primary outcomes were: any cerebrovascular adverse event, defined as a composite of any stroke and/or transient ischaemic attack; transient or permanent cranial nerve injury; and restenosis and/or occlusion (full definitions of subtypes were given). Relevant secondary outcomes were procedural specific for both techniques. For carotid angioplasty and stenting these included: technical success rate; vascular access site complication; and cardiovascular complication (detailed definitions provided). For carotid endarterectomy these included: wound infection/delayed healing and bleeding complications needing reoperation.

Indications for cervical radiation therapy were generally head and neck squamous cell malignancies; less common indications were lymphomas, parotid tumours and thyroid tumours. Radiation characteristics were poorly documented; the mean interval between radiation and carotid revascularization ranged from 1.7 to 17 years. More than 50% patients in the carotid endarterectomy group underwent previous neck surgery but this was not clarified for the carotid angioplasty and stenting group.

Two independent reviewers performed the study selection. Disagreements were resolved by consensus with a third reviewer.

Assessment of study quality
A formal assessment of study quality was not performed.

Data extraction
For perioperative outcomes, the percentage of patients who experienced an event was calculated for each group, with 95% confidence intervals (CI). For late outcomes, the incidence rate was calculated for each group (numbers of events divided by the total number of person years), with 95% CIs.

The authors did not state how many reviewers performed the data extraction.

Methods of synthesis
Results were evaluated separately for early outcome (up to 30 days) and late outcome (>30 days). For the primary outcomes, results were pooled using a random-effects model meta-analysis as heterogeneity was expected. The $I^2$
statistic was used to evaluate heterogeneity between studies ($I^2<25\%$ indicated low heterogeneity). Meta-regression was performed with the two separate procedures as a factor.

**Results of the review**

Twenty-seven studies were identified (533 patients, range four to 135). There were 361 patients with carotid angioplasty and stenting in 14 studies and 172 patients with surgery in 14 studies. All studies had an observational study design. Only one study included both carotid angioplasty and stenting and carotid endarterectomy patient groups. Mean follow-up, where reported, ranged from one to 58 months.

**Early outcome:** The risk of a cerebrovascular adverse event was 3.9% (95% CI, 2.3 to 6.7%; $I^2=22.1\%$; 13 studies) for the carotid angioplasty and stenting group, which was not significantly different from that for the carotid endarterectomy group (3.5%, 95% CI, 1.5 to 8.0%; $I^2=0\%$; 14 studies). Reported technical success rates for carotid angioplasty and stenting ranged from 94% to 100%; six failures occurred (details were provided.). The risk of cranial nerve injury in the surgery group was 9.2% (95% CI, 3.7 to 21.1%; 12 studies) and all cases except one were resolved completely within several weeks. Other procedure-specific complications for surgery were incidental (wound infection and bleeding).

**Late outcome (clinical):** The risk of a cerebrovascular adverse event was 4.9 per 100 person years (95% CI, 3.6 to 6.6; 11 studies) for the carotid angioplasty and stenting group, which was significantly higher ($p=0.01$) than that for the carotid endarterectomy group (2.8 per 100 person years, 95% CI, 2.0 to 3.9; nine studies).

**Late outcome (mortality):** Mortality rates varied between 0% and 33.0% for the carotid angioplasty and stenting group (11 studies) and 0% and 44.4% for the surgery group (nine studies). Rates were highly influenced by nonvascular causes of death.

**Late outcome (restenosis):** The risk of restenosis and/or occlusion was 5.4 per 100 person years (95% CI, 4.3 to 6.6; 13 studies) for the carotid angioplasty and stenting group, which was significantly higher ($p=0.003$) than that for the carotid endarterectomy group, 2.8 per 100 person years (95% CI, 1.9 to 4.0; nine studies). However, most in-stent restenoses behaved in a benign fashion and remained asymptomatic.

**Authors’ conclusions**

Both carotid angioplasty and stenting and carotid endarterectomy proved to be feasible revascularisation techniques with low risk for cerebrovascular adverse events. Although patients who underwent surgery had more temporary cranial nerve injury, higher rates of late cerebrovascular adverse events and restenosis were identified after carotid angioplasty and stenting.

**CRD commentary**

The review addressed a well-defined question in terms of participants, interventions and relevant outcomes. Relevant study designs were less clear. Relevant databases were searched. It appeared that only studies published in English were included and a minimal search was made for unpublished studies so some relevant studies may have been missed. Publication bias was not assessed. The authors recognised the potential effect of publication bias which they considered to be inherent due to their meta-analysis of observational studies. There was no formal assessment of study quality but the authors summarised the weaknesses of the included observational studies. Study selection was carried out with efforts to reduce error and bias but it was not reported whether this also applied to data extraction. Some relevant study details were reported but there were no details of the age and gender of the participants.

The synthesis performed seemed appropriate but meta-regression results were not reported. The authors commented that less appropriate surgical candidates would be more likely to be treated by carotid angioplasty and stenting, which could affect the overall results. They also discussed practical considerations that could affect the different outcomes of the different treatments.

Limitations in study quality and the review process imply that the authors' results should be interpreted with caution.

**Implications of the review for practice and research**

**Practice:** In patients with previous cervical radiation, the choice for revascularization therapy should be considered on an individual basis.
Research: The authors stressed the need for randomised controlled multicentre trials to compare carotid angioplasty and stenting and carotid endarterectomy.

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