Extracranial-intracranial bypass surgery to reduce the risk of haemodynamic stroke in cerebroocclusive atherosclerotic disease of the anterior cerebral circulation: a systematic review
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CRD summary
The author concluded that extracranial-intracranial bypass surgery could reduce the risk of neurological dysfunction and stroke in haemodynamic subgroups of patients with advanced occlusive cerebrovascular disease of the anterior cerebral circulation. Limitations in the quality of the included studies and review make it difficult to comment on the reliability of the author's conclusions, but the suggestion for further research appears reasonable.

Authors' objectives
To analyse the effectiveness of extracranial-intracranial (EC-IC) bypass surgery for cerebral revascularisation in haemodynamic subgroups of patients with advanced occlusive cerebrovascular disease of the anterior cerebral circulation.

Searching
MEDLINE was searched from November 1985 to November 2001; the search terms were reported. In addition, the references of relevant papers were checked. Publications were restricted to those in English, German or French.

Study selection
Studies of occlusive cerebrovascular disease in the carotid territory, and reporting data on the following symptoms, were eligible for inclusion: radiologically documented severe carotid stenosis > 50% according to North American Symptomatic Carotid Endarterectomy Trialists criteria or 75% according to European Carotid Surgery Trial criteria, or occlusion of the EC or IC internal carotid artery (ICA), middle cerebral artery (MCA); clinical evidence of transient ischaemic attack, non-disabling hemispheric stroke (a score of <3 using the modified Rankin scale, mRS), or retinal ischaemia of any type in the arterial territory distal to the angiographic lesion. Studies were not eligible for inclusion if they reported the following symptoms: vasculopathies of non-atherosclerotic origin; cerebral ischaemic episodes affecting more than one vascular territory; disabling hemispheric stroke (a score of >3 on the mRS) caused by large or multiple areas of hypodensity. The included studies used patients with different neurological states (ischaemic stroke, ischaemic event, repeated stroke, progressive stroke, or generalised cerebral ischaemia) and different haemodynamic states, and patients with some abnormal neurological stability, ICA occlusion, internal carotid siphon stenosis, MCA stenosis or MCA occlusion. The mean age of the patients was 57 years (range: 31 to 82 years).

The included studies used surgical procedures for EC-IC that involved anastomosis of the superficial temporal artery to a small piamedullary cortical artery, with or without additional carotid endarterectomy.

The included studies reported death from vascular causes (defined as cardiac, cerebrovascular, pulmonary embolism, haemorrhagic, other vascular or unknown cause) or non-vascular causes, and dependency post surgery as the primary outcomes. Peri-operative mortality was defined as any death occurring up to 30 days post surgery. Dependency ranged from no disabilities or symptoms to severe disability, as measured using the mRS. Surrogate markers, including haemodynamic profiles (regional cerebral blood flow, oxygen extraction ratio, cerebral blood volume) and graft patency (early or late graft failure, and occlusion 30 days, 1 to 12 months, or 12 months post surgery) were reported as secondary outcomes.

Randomised clinical trials (RCTs), controlled clinical trials, and case series involving more than 4 patients were eligible for inclusion. For included studies reporting follow-up, durations ranged from 2 months to 10 years (however, there was a discrepancy between the results reported in the tables and text).

The author did not state how the papers were selected for the review, or how many reviewers performed the selection.
Assessment of study quality
It was intended that the validity of controlled trials would be assessed according to the Jadad checklist, including items on randomisation, blinding and withdrawals. Cohort studies would be assessed for the following: presence of a clear definition of the study cohort, early inception point, clear pathway of patient entry, complete follow-up, description of drop-outs, objective outcome criteria, blinded outcome assessment, and adjustment for extraneous factors.

The author did not state how many reviewers performed the validity assessment, or how any discrepancies were resolved.

Data extraction
The numbers of events for each primary and secondary outcome were extracted and percentages calculated.

The author stated that discrepancies were resolved through discussion, but not how many reviewers were involved in the data extraction process.

Methods of synthesis
The included studies were combined in a narrative, with additional information in evidence tables. The \( \chi^2 \) test was used to compare the independent proportions of patients with different haematological states suffering from some form of stroke. Subgroup analyses were conducted using actuarial analysis to compare survival times and survival free of stroke by symptom. The author reported that sensitivity analyses were carried out to investigate the effect of methodological quality (blinding; allocation concealment; presence of mortality as a study outcome; and crossover) and procedure type on outcome. Publication bias was assessed using Egger’s test.

Results of the review
Twenty-seven case series (n=623) were included in the review. The sample sizes ranged from 6 to 157 patients (median of 23 patients per trial).

Ten studies scored one on the Jadad checklist, while the remaining studies scored zero.

Mortality (26 studies).
Overall, 17 patients (3%) were reported to have died (however, there was an apparent discrepancy between the tables and text); the annual risk of overall death was 0.8% and of vascular death 0.4%.

Disability (27 studies).
Post-operative mRS values for disability were reported to be 0 to 1 for 90% of patients, 2 for 1% of patients and >2 for 9% of the population (although these figures do not appear to correlate with the table provided).

Neurological stability.
Major or minor strokes occurred in 22 patients (4%) within 30 days and in 27 patients 30 days post-operatively. This translates into an overall rate of recurrent stroke of 1.3% per year and of recurrent major stroke of approximately 0.7% per year. The expected rate of survival free of stroke was reported in the review.

Patients with a haematological profile of increased pre-operative cerebral blood flow/cerebral blood volume (grade I and II) in the affected area were at a significantly greater risk of recurrent ischaemic stroke compared with patients with normal cerebral blood flow/cerebral blood volume (grade 0): 15 out of 139 patients (11%) with grade I/II compared with one out of 20 patients (5%) with grade 0 (p<0.001). Risk factors of post-operative stroke for age, original vascular territory, gender, previous stroke, and mean time period of stroke occurrence after surgery were presented in the review.

Graft patency.
The overall rate of graft patency was reported as 94%, with long-term patency reported as a 1% failure rate per year following the first year of surgery (data were not presented in the review). Post-operatively, patients with an excellent bypass reported more favourable outcomes (8% strokes; 0.2% fatal) compared with patients with a small or non-patent anastomosis (33% strokes; 22% fatal).

Sensitivity analyses did not alter the results.

**Authors' conclusions**
The treatment of symptomatic carotid occlusion or severe stenosis with EC-IC bypass surgery, in patients with haematological insufficiency, could reduce the risk of neurological dysfunction and potential stroke.

**CRD commentary**
The review question was clear, but the inclusion criteria were somewhat limited. The literature search was limited to one electronic database and another appropriate source. Although searches were conducted in three different languages, the potential for language bias cannot be ruled out. Together with the fact that there was no apparent search for unpublished material, it is possible that relevant papers might have been missed. The study selection, validity assessment and data extraction processes were not explicit, thus reviewer error and bias cannot be ruled out. The use of Jadad criteria to assess the validity of the case series did not enable any useful interpretation of the data, and sensitivity analyses based on aspects of validity such as allocation concealment when there were no RCTs was not appropriate. In addition, heterogeneity was not assessed, which means that the reliability of the studies and their subsequent synthesis is unclear. Although some details were presented clearly, potentially important clinical information on participant characteristics were not reported. Given the limitations of the reporting and quality of the included studies and review, the small sample size, and the fact that no controls were included for comparative purposes because of the nature of the study design, it is difficult to comment on the reliability of the author's conclusions. However, the suggestion for further research in haemodynamic subgroups of patients appears reasonable.

**Implications of the review for practice and research**
Practice: The author did not state any implications for practice.

Research: The author stated that an international, multicentre, randomised prospective study is required to further investigate the relationship between improved post-operative neurology and improvements in haemodynamics, as measured using single-photon enhanced computed tomography or positron emission tomography. Such research would need to consider previous study limitations and the nature of haemodynamic insufficiency and patient selection.

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Record Status
This is a critical abstract of a systematic review that meets the criteria for inclusion on DARE. Each critical abstract contains a brief summary of the review methods, results and conclusions followed by a detailed critical assessment on the reliability of the review and the conclusions drawn.