Carotid artery stenting versus carotid endarterectomy – a prospective randomised controlled single-centre trial with long-term follow-up (BACASS)

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Summary

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Background and objective: Safety and effectiveness of carotid artery stenting (CAS) was compared with carotid endarterectomy (CEA) in a single-centre prospective randomised controlled trial in symptomatic high-grade stenosis of the ICA.

Material and methods: Twenty patients with symptomatic ICA stenosis ≥70% were prospectively randomised to either CAS or CEA. Primary outcome measures were periprocedural stroke, death or myocardial infarction. Secondary outcome measures were peri-interventional transient TIA, bleeding complications, cranial nerve paralysis, length of stay and ICA patency as well as stroke or death during long-term follow-up.

Results: CAS patients had no peri-interventional complications. In the CEA group 1/10 had an ipsilateral non-disabling stroke after 16 days. During long-term follow-up (48.1 ± 21.3 months with CAS and 43.5 ± 19.5 months with CEA) neither strokes nor myocardial infarctions occurred in both groups. Length of stay was 3.5 ± 1.8 days for CAS versus 7.3 ± 3.3 days for CEA patients. CEA and CAS groups did not differ in other secondary outcome measures.

Conclusion: CAS and CEA seem to be comparably safe in our setting. More importantly, data useful for a systematic meta-analysis are provided, which include long-term results.

Keywords: carotid stenosis; stents; angioplasty; carotid endarterectomy; randomised controlled trial

Introduction

Extracranial occlusive carotid artery disease can lead to stroke, which is a major cause for death or permanent disability. Especially endangered are untreated patients with a symptomatic carotid stenosis of more than 70%. For these patients carotid endarterectomy (CEA) is the gold standard to reduce the incidence of stroke [1, 2]. As a possible alternative to CEA, carotid angioplasty and stenting (CAS) has been increasingly performed. In this study we compared the peri-interventional complications, the patency and follow-up of 20 patients with symptomatic carotid artery disease, who were prospectively randomised to CAS or CEA. As the randomisation of the large multi-centre trial Carotid and Vertebral Artery Transluminal Angioplasty Study (CAVATAS) [3] was already finished and the International Carotid Stenting Study (ICSS) [4] had not begun, we started the Basel carotid artery stenting study (BACASS) as a single-centre randomised controlled trial (RCT). Our intention was to base the treatment decision on the best evidence and generate data on safety and effectiveness of CAS and CEA in our institution, taking into account the findings of the

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recent EVA-3S [5] and SPACE [6] trials, in which CAS patients did worse (EVA-3S) or in which non-inferiority of CAS could not be shown (SPACE). Furthermore, we wanted to test the feasibility of this approach and provide data that can be used for a systematic meta-analysis.

Materials and methods

Study population

From November 1998 to February 2002, we performed a single-centre prospective randomised controlled trial at the University Hospital in Basel. Except for one, all authors were working at this hospital at the time of the study. We compared CAS with CEA for patients with symptomatic high-grade internal carotid artery (ICA) stenosis. All treated stenoses measured at least 70% (range: 70–99%). The degree of the stenosis of the ICA was preprocedurally defined on Doppler/duplex ultrasound (US), according to the CAVATAS criteria [3] and on magnetic resonance angiography (CE-MRA). A diagnostic digital subtraction angiography study was only performed in discordant findings of US and MRA, which happened in one case. MR imaging of the brain was performed in all patients to document or exclude recent territorial infarction, bleeding or mass lesion. All patients were symptomatic within the last 3 months and had a neurological examination by a stroke neurologist.

On a weekly held interdisciplinary conference about cerebrovascular interventions, we identified all consecutive patients, in whom CAS as well as CEA seemed technical feasible according to the surgeons and interventional neuroradiologists. Except for one patient with contralateral carotid occlusion (CAS group) all patients were stratified into low risk for CEA according to Gasparis et al. [7].

During the study period 82 patients had symptomatic high-grade ICA stenosis (fig. 1). Of those 62 patients had one of the following exclusion criteria: unwillingness to participate in a study (45 patients), unavailability for follow-up visits for at least 2 years, ICA occlusion, free-floating carotid thrombus, recurrent ICA stenosis, status after neck irradiation. Other exclusion criteria included history of intracranial haemorrhage within 2 months prior to the intervention, intracranial mass lesions or vascular malformations, life expectancy <2 years or allergy to contrast media. Twenty patients (mean age 70 ± 7.3, 17/20 male/female) fulfilled the study criteria and comprised our study population. Informed consent was obtained in all cases. As ran-domisation procedure sealed envelopes were used for treatment allocation. The local ethics committee approved the study.

Previous operator experience

CEA has been performed since 1970 with approximately 50 CEA per annum and CAS has been performed since 1997 with approximately 15 patients per annum during the last couple of years. In addition, our centre took part in the CAVATAS trial.

Hypothesis and outcome measures

In the current study we included patients on the basis of the hypothesis that CAS is not inferior to CEA regarding safety and effectiveness. Primary outcome measures were periprocedural stroke, death or myocardial infarction. Secondary outcome measures were peri-interventional transient ischaemic attack (TIA), haematoma, cranial nerve paralysis and length of stay. For the follow-up secondary outcome measures were patency of the treated vessel and stroke prevention related to the treated side.

Follow-up

The patients were followed up by a neurologist with duplex US and clinical neurological examinations at day one and 1, 6 und 12 months after the procedure, subsequently once a year.

All patients' clinical data were analysed and recorded on standard forms. Neurological complications were classified as TIA with a focal ischaemic neurological deficit of abrupt onset resolving completely within 24 hours. A minor stroke was defined as neurological deterioration evidenced by an increase of the National Institute of Health stroke scale (NIHSS) of <4 points without the presence of aphasia or hemianopsia and persisting longer than 24 hours; a major stroke was defined as neurological deterioration evidenced by an increase of the NIHSS of ≥4 points or the presence of aphasia or hemianopia and persisting longer than 24 hours. Reversible stroke was considered a neurological complication with a duration of >24 hours and ≤30 days. Permanent stroke was considered a neurological complication with a duration of >30 days [8].

Technique of CAS

No anaesthesia was required for CAS. The stenotic carotid artery was studied in three planes to confirm the significant stenosis and to define the working plane. A neuroprotection system was used in all cases, initially as balloon occlusion system (FilterWire™, Boston Scientific®) followed by a filter system (Angioguard RX™, Cordis®), both systems mounted on 0.014-inch micro guidewires. The stent (Carotid Easy Wallstent™, monorail, nominal diameter: 8 mm, length: 30 mm) was placed without predilatation. Stentangioplasty was routinely performed with a 5 mm/20 mm balloon, until the waist of the stent was unfolded. The inflation of the balloon was done very slowly up to a pressure of 5–8 atm and controlled by road mapping. A stent waist of ≤10% was not redilated and the neuroprotection system was withdrawn. Ipsilateral intracranial angiography was performed to exclude embolic vessel occlusion.

All patients were monitored in the intensive care unit overnight and examined by independent intensive care physicians and referring neurologists. Dual antiplatelet therapy with aspirin and clopidogrel, starting prior/immediately after CAS, was used for one month.

Technique of CEA

Carotid endarterectomies were performed half under general and half under local anaesthesia, related to surgeon preference, with continuous intra-arterial pressure monitoring. All patients treated under general anaesthesia were monitored with EEG.

After exposure of the bifurcation to beyond where the atherosclerotic plaque is thought to terminate, the plaque was removed completely. Careful arteriotomy closure or patch angioplasty followed. Arterial shunting was selectively employed in patients with prolonged clamp time or when significant EEG changes could be noticed.

Patch grafts were used routinely in the local anaesthesia patients' group. Vital signs and a neurological assessment were obtained at intervals of one hour for the first 24 hours postoperatively on intensive care unit. Antiplatelets were used as shown effective in a recent Cochrane Review [9].

Statistics

For analysing the data of this study no statistical procedure was used because of the small number of patients involved.

Figure 1   Flowchart.
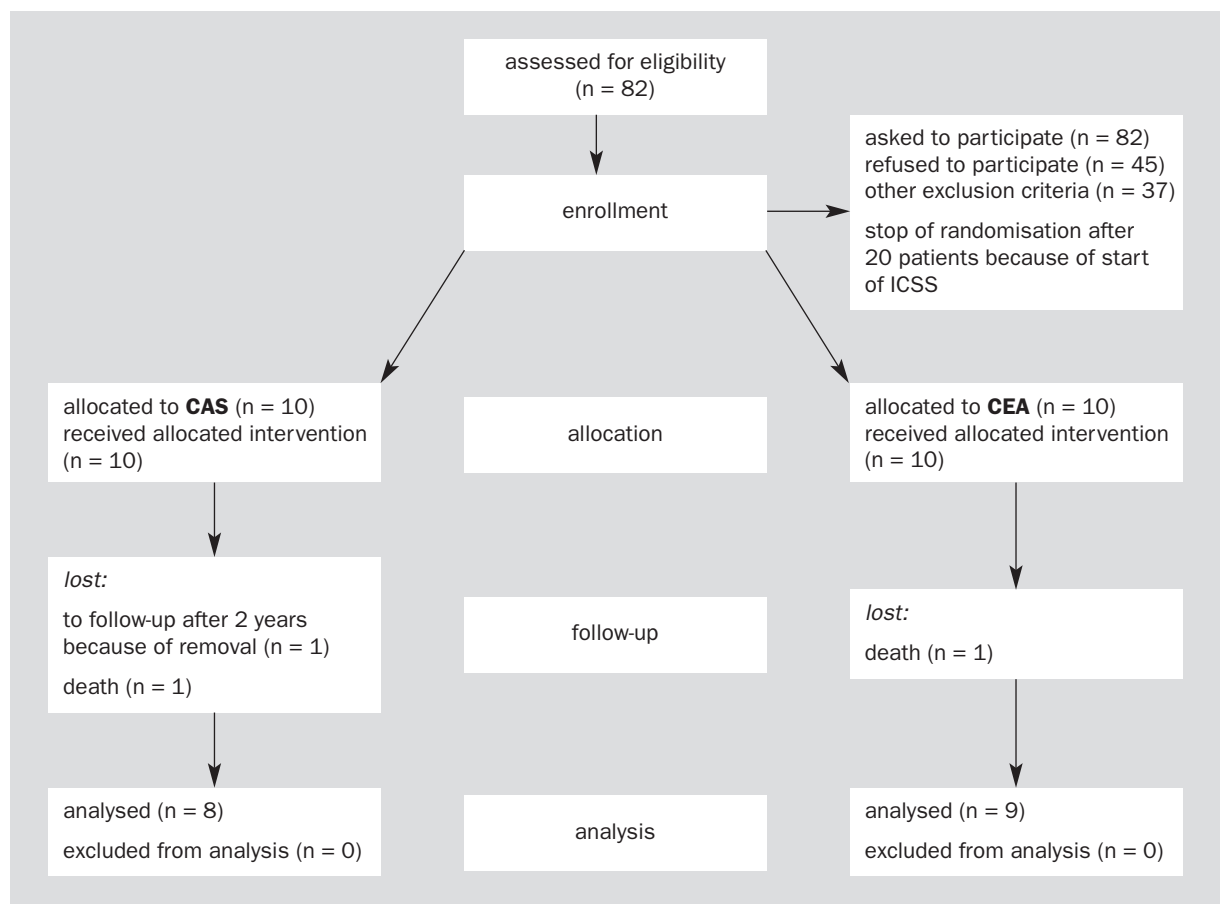
Reporting

Methods and results were presented applying recently published reporting standards for CAS [8].

Table 1   Baseline characteristics of 20 patients randomised either for CAS or CEA for symptomatic high-grade ICA stenosis.

baseline characteristics	CAS n = 10	CEA n = 10
gender (♂:♀)	8:2	9:1
mean age (SD)	69 (± 8.6) years	71 (± 5.9) years
neurologic symptoms		
amaurosis fugax	0	5
TIA	1	1
minor stroke	3	0
major stroke	6	4
risk factors		
arterial hypertension	7	8
smoking	5	6
hyperlipidaemia	7	6
diabetes mellitus	3	3
coronary heart disease	2	4
mean grade of stenosis (SD)	84.5 (± 7.8)%	82 (± 5.1)%
significant contralateral stenosis	stenosis >70%: 1 occlusion: 1	stenosis >70%: 1 occlusion: 0

Table 2   Summary of primary and secondary endpoints.

	CAS n = 10	CEA n = 10
primary endpoints*		
stroke	0	1
death	0	0
myocardial infarction	0	0
secondary endpoints		
TIA	0	0
haematoma	0	0
cranial nerve paralysis	0	0
length of stay (days)	3.5 ± 1.8	7.3 ± 3.3

* within 30 days

Table 3   Patency after two years.

	CAS (n = 8 after 2 years)**	CEA (n = 9 after 2 years)***
30–49%	1	1
50–69%	0	1
70–99%	0	0
strokes after two years	0	0

**   one patient died due to non-vascular death, another was lost to follow-up;
*** one patient died due to non-vascular death.

Results

Study population

Randomisation resulted in 10 patients each allocated for CAS and CEA, respectively. All patients received the allocated treatment without any cross-over. The 10 CAS patients consisted of 8 males and 2 females. The 10 patients treated with CEA consisted of 9 males and one female. Mean age of the CAS group was 69 ± 8.6 years, mean age of the CEA group was 71 ± 5.9 years. The mean degree of stenosis of the ICA before treatment was 84.5 ± 7.8% in the CAS and 82 ± 5.1% in the CEA group. Significant contralateral carotid stenosis or occlusion was present in two CAS patients (occlusion: 1; stenosis >70%: 1) and in one CEA patient (stenosis >70%: 1), respectively. The qualifying event was amaurosis fugax / TIA in one CAS patient and 6 CEA patients. Stroke was the qualifying event in 9 CAS patients and 4 CEA patients. Risk factors had a similar distribution among both groups (details see table 1).

In CAS as well as CEA patients postinterventional neurosonology showed no evidence of relevant residual stenosis.

Primary endpoints

Peri-interventional complications within the 30-day period did not occur in the CAS cohort. One CEA patient had an ipsilateral major stroke 16 days after the procedure. In this patient CT revealed multiple small ischaemic lesions within the territory of the middle cerebral artery, indicating an embolic stroke mechanism. Duplex US of the ICA demonstrated a wall-adherent flat thrombus at the site of surgery. Under combined treatment with heparin and antiplatelet therapy no further ischaemic events occurred. At the 30-day evaluation, hemiparesis had resolved completely. As solely very mild motoric aphasia persisted during follow-up (modified Rankin score: 1), this stroke was classified as a major (according to Higashida et al. [8]), however, non-disabling stroke (according to ICSS [4]). In both groups neither death nor myocardial infarction occurred within the 30-day period (table 2 and 3).

Secondary endpoints

None of the patients suffered from TIA, a significant cervical or inguinal haematoma or cranial nerve palsy peri-interventionally. No cardiac

arrhythmias or relevant blood-pressure changes were noticed during or after the interventions.

The time interval between admittance to hospital, treatment of stenosis and discharge was 3.5 ± 1.8 days regarding the stent and 7.3 ± 3.3 days regarding endarterectomy. After one year, follow-up was available in 10 patients of the CAS group and in 9 patients of the CEA group, where one patient had died of lung cancer. After two years, follow-up was available in 8 patients of the CAS group and in 9 patients of the CEA group. At this time, one additional patient of the CAS group was lost to follow-up and one patient of the CAS group had died because of pancreatic cancer.

After one year, one of the CAS patients developed a restenosis of 30–49% and two patients of the CEA group presented a restenosis of 30–45% and 50–69%, respectively (table 2). All stenoses did not progress in further follow-up assessments. All three patients with restenosis remained neurologically asymptomatic and were treated medically. After two years, there were no further strokes in both treatment groups.

The mean long-term follow-up period was 48.1 ± 21.3 months with CAS and 43.5 ± 19.5 months with CEA. Beyond two years, neither stroke nor death, nor restenosis occurred.

Discussion

High-grade extracranial symptomatic internal carotid artery stenosis is a modifiable stroke risk factor. Traditionally, internal carotid artery stenosis has been treated with carotid endarterectomy. CAS is an emerging potential alternative. However, whether CAS is comparable to CEA in respect of efficacy and safety is still debated and under investigation with RCTs.

Our study was done during a time period without a multi-centre RCT comparing CAS with CEA. In such a situation, a mono-centre RCT is a scientifically sound and reasonable approach to decide how to treat individual patients and gather data on safety as well as effectiveness in the own institution.

Our data proved the feasibility of this approach. Furthermore, both treatment options seem to be comparably safe in our setting.

None of the patients suffered from haematoma, cranial nerve paralysis or TIA. Regarding restenosis rates, in multi-centre surveys the rates range between 2.7 and 2.4% at one and 3 years [9, 10], comparable to our restenosis rate of 1/10 in CAS and 1/9 in CEA at one year and 1/9 in CAS and 2/8 in CEA at two years, without any severe stenosis ≥70%. In a larger study the restenosis rate in

334 prospectively randomised high-risk patients was 0.6% of the stent group and 4.3% in those, who had undergone endarterectomy at one year [11]. From the technical point of view the new self-expanding nitinol carotid stents tend to continue to expand after implantation over time and therefore stabilise the restored vessel lumen [12].

Whether our trend towards a shorter length of stay in the CAS compared to the CEA cohort is generalisable and whether such a difference translates into lower costs deserves further testing.

The major limitation of our study is the small sample size, which precludes firm conclusions concerning effectiveness. However, due to the sound randomisation procedure used and assessment of outcome variables, our data may be considered valuable for a systematic meta-analysis. Such meta-analysis seems increasingly important facing the heterogeneous results of CAVATAS, SPACE and EVA-3S. Furthermore, additional data – even from small RCTs like ours – are likely to increase the significance of such a meta-analysis as an approach to summarise the body of evidence about CAS versus CEA in symptomatic ICA stenosis. In addition, we provide RCT data on long-term outcome, which are not presented in SPACE and EVA-3S, but are nevertheless of utmost importance, taking into account that CAS/CEA are meant to prevent patients from future strokes in the long run.

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