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Overview

Carotid artery disease-treatment by endarterectomy and stenting

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Abstract

A brief outline of the relevant literature with focus on clinical outcome is given. With today´s knowledge, CEA(Carotid Endarterectomy) within 3–14 days after symptom onset remains the gold standard of treatment for symptomatic ICA stenosis >50% NASCET.

CAS (Carotid Artery Stenting) may be considered for patients <70 years of age, patients with restenosis after CEA, after neck radiation and in cases of difficult anatomy for surgery. After extensive information about the potential risks of the two methods also the patients´s choice has to be considered.

INTRODUCTION

Worldwide, stroke is the third leading cause of death after ischemic heart disease and cancer *(1)*. Approximately 20% of patients die within the first year of having stroke and another 30% remains disabled. The risk of recurrent stroke is highest within the first 30 days. Altogether, 20% of patients will experience another ischemic event in the following two years.

An important cause of transient ischemic attack (TIA) and stroke is atherosclerotic carotid artery stenosis. It accounts for about 20% of cases of brain infarction and has the highest recurrent stoke risk compared to all other subtypes of stroke *(2, 3)*. Therefore, rapid intervention in this patient group is needed and they should be managed efficiently to minimize the incidence of recurrent stroke.

SYMPTOMS

15% of stroke patients first present with classic TIA symptoms – slurred speech (dysarthia), limb weakness or numbness, transient monocular blindness (amaurosis fugax), unsteadiness (ataxia) or difficulty speaking (dysphasia) persisting for less than 24 hours *(4)*. Patients presenting with TIA and patients with minor or completed stroke should be examined and screened for carotid stenosis as soon as possible- at the latest 24–48 hours after onset of symptoms.

DIAGNOSIS

Intraarterial digital subtraction angiography (DSA) is considered as the classical gold standard for identification and quantification of carotid artery stenosis. Today, however, non-invasive methods are primarily

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used: duplex ultrasound (DUS), computed tomography angiography (CTA) and contrast enhanced magnetic resonance angiography (CEMRA).

Duplex and transcranial ultrasound examination is most frequently used in as the baseline screening method for carotid stenosis in everyday practice. It is less expensive, reliable and suitable for bedside diagnosis. The most common sites for significant plaque formation – the origin of the internal carotid artery (ICA) just above the bifurcation (around 22 %), can be examined in practically every patient *(5)*. A recent update of DUS diagnostic criteria for carotid stenosis further increases the accuracy and clinical value of the method *(6)*.

The most cost-effective diagnostic strategy is the use of DUS and CEMRA in carotid artery stenosis *(7)*. Only if the DUS is negative and the CEMRA is positive, CTA or DSA should be performed.

TREATMENT

Patients with symptomatic carotid artery stenosis should be treated in order to reduce their mostly embolic and in a lesser degree hemodynamic risk of stroke.

The standard surgical treatment, carotid endarterectomy, has been widely used and is the reference standard of treatment. Carotid artery angioplasty with stenting is an alternative method and is currently being used on selected patients.

CAROTID ENDARTERECTOMY (CEA)

In 1954 the first endarterectomy has been performed in a patient with symptomatic carotid artery stenosis. Over the years it evolved and became a routine surgical treatment for carotid stenosis although adequate clinical trials to confirm its benefits were lacking.

In 1998, two large randomized controlled trials of endarterectomy versus medical treatment published their final results. Although their design was similar, differences in inclusion and exclusion criteria, methods of determining degree of stenosis and definitions of outcome events were present.

Final results of both trials, European Carotid Surgery Trial (ECST) and North American Symptomatic Carotid Endarterectomy Trial (NASCET), have shown that CEA, when performed with low surgical morbidity and mortality, reduces the risk of stroke in patients with high-grade carotid stenosis *(8, 9)*. Both studies showed that approximately 8 patients with more then 70% stenosis would have to be treated to prevent one ipsilateral stroke in a five-year period after surgery.

For patients with moderate symptomatic stenosis (50 to 69 percent), NASCET reported greater benefit of endarterectomy compared with medically treated patients, whereas ECST showed no significant benefit. NASCET showed that 15 patients with 50 to 69% stenosis would have to be treated to prevent one stroke within five years. In both trials no significant benefit of endarterectomy could be demonstrated for patients with symptomatic carotid stenosis of less then 50 percent. These results established CEA as the gold standard treatment for the prevention of a recurrent ischemic event in symptomatic patients with ipsilateral carotid stenosis greater then 70% and without a severe neurological deficit with recent (<180 days) ischemic events and if the center's perioperative strokes and death rate is less then 6%. CEA may also be performed in symptomatic patients with stenosis of 50 to 69% free of a severe neurological deficit only if the perioperative strokes and death rate is less then 3%.

Both studies showed that the benefit of endarterectomy is greater for men then for women, for patients aged 75 and older and for patients with hemispheric symptoms. Also, the patients who have had stroke three months prior to procedure will benefit more from surgery then those with TIA. Studies suggested that a higher risk of preoperative ischemic event or death exists in patients with diabetes, elevated blood pressure, contralateral carotid occlusion and left-sided disease.

In addition, all treated patients should remain on antithrombotic therapy before, during and after surgery and followed-up by the surgeon and the neurologist (ESO Guidelines, last update 2008; http://www.eso-stroke.org/pdf/ESO08_Guidelines_English.pdf)

Patients randomized for surgical treatment within 2 weeks after their last ischemic event, benefit more from surgery *(10)*. However, surgery within 48 hours after symptom onset may carry a significantly increased mortality and stroke risk compared with surgery 3–14 days after symptom onset (11.5 vs 3.8%; *11*)

PTA WITH STENTING

Carotid angioplasty with stenting is a more recent endovascular treatment for carotid stenosis. Although it does not have a long history, it has become an alternative to CEA. It is a minimally invasive procedure requiring only a small incision in the groin and local anaesthesia.

A stent is a small tube made of nickel-titanium, a bendable metal that springs back after being bent, and is in today's practice self-expendable after placement. Emboli protection devices (EPDs) have also been designed to protect the brain from embolisation during stenting. It is used to catch the small particles that may be dislodged from the plaque into the brain circulation, which may help reduce the incidence of stroke during the procedure.

The risk of radiation exposure and allergic reaction to the dye used during the procedure is very low. Stents can be overgrown by the surrounding tissue and that can cause restenosis or even occlussion of the vessel, especially in patients noncompliant to the mandatory lifelong thrombocyte inhibition medication required. The release of multiple emboli has also been reported during CAS. Wholey *et al.* reported the stroke/death rate of 2, 23% when EPD was used. On the other hand, when the procedure was done without protection, stroke/death occurred in 5,29% of treated patients *(12)*.

Patients treated with CAS avoid surgical incision on the neck with the risk of facial nerve injuries and general anesthesia, and stay shorter in the hospital. This procedure is also feasible to treat surgically inaccessible sections of the artery and for treating restenosis after CEA.

To better define the indications for CAS versus CEA several randomized prospective trials have been designed. Carotid and Vertebral Artery Transluminal Angioplasty Study (CAVATAS) showed no difference in major outcome events between endovascular treatment and carotid endarterectomy, but 30-day death and stroke rate of carotid surgery was higher than desirable – 10,0% for CAS versus 9,9% for CEA *(13)*. This study also reported that high grade carotid restenosis was more frequent one year after CAS then after carotid surgery.

The majority of patients treated by the endovascular approach had, however, PTA alone without stent placement.

In SAPPHIRE (Stenting and Angioplasty with Protection in Patients at High Risk for Endearterectomy) study, 334 patients were included (96 symptomatic and 219 asymptomatic) *(14)*. This trial suggested that stenting with protection is not inferior and may be superior to CEA in terms of a combined end point including stroke, myocardial infarction and death.

The 3-years follow-up showed similar clinical results for CAS and CEA *(15)*.

The EVA-3S trial was stopped in November 2005 at 527 patients because of a complication rate of 9.6% for CAS versus 3.9% for CEA *(16)*.

The SPACE (Stent protected Angioplasty versus Carotid Endarterectomy; *(17)*,which has recruited 1200 patients with symptomatic, ≥70% ICA stenosis diagnosed by Duplex ultrasound in Germany, Austria and Switzerland reported for the 30 days primary endpoint (ischemic stroke and/or intracerbral bleeding with symptoms lasting >24h) results a rate of 6.84% for carotid artery stenting and 6.34% for carotid endarterectomy.This difference was not significant. However, non-inferiority of CAS was not shown. The use of EPD did not reduce complications.

In the 2-years follow up of this study *(18),* no significant differences were found for clinical endpoints. In the CAS group, however, a significantly higher (8.9% vs 3.9%) percentage of -clinically mostly silent-restenoses was observed.

Also in Europe, the ICSS (International Carotid Stenting Study, 19), showed unfavorable outcome measures (stroke, death or procedural MI) for CAS for the first 120 days after randomization- 8.5% versus 5.2% for the CEA group(p value 0.006).

A meta-analysis of all 3 European trials (EVA 3S, SPACE and ICSS; 3433 patients; *18*) concluded, that »stenting for symptomatic carotid stenosis should be avoided in older patients(age =70 years) but might be as safe as endarterectomy in younger patients«.

Another meta-analysis *(19)* including trials up to the ICSS (but excluding CREST results) concluded, that »Carotid endarterectomy was found to be superior to carotid artery stenting for short term outcomes but the difference was not significant for intermediate term outcomes; this difference was mainly driven by nondisabling stroke. Significantly fewer cranial nerve injuries and myocardial infarctions occurred with carotid artery stenting«

In North America, the CREST (Carotid Revascularisation Endarterectomy versus Stent Trial, *21*) was conducted. It's conclusion was, that-at 4 years- »among patients with symptomatic or asymptomatic carotid stenosis, the risk of the composite primary outcome of stroke, myocardial infarction or death did not differ significantly in the group undergoing carotid-artery stenting and the group undergoing endarterectomy« (CAS 7,2% vs CEA 6.8%, n.s.).

»During the periprocedural period, there was a higher risk of stroke with stenting and a higher risk of myocardial infarction with endarterectomy«

A recent analysis of the CREST data concerning restenosis at 2 years showed no significant difference- CAS 6.0% vs CEA 6.3% *(23)*.

CONCLUSION

CEA remains the gold standard of treatment for symptomatic ICA stenosis >50% NASCET.

CAS may be considered for patients <70 years of age, patients with restenosis after CEA, after neck radiation and in cases of difficult anatomy for surgery. After extensive information about the potential risks of the two methods also the patients's choice has to be considered.

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