

Carotid artery stenting versus endarterectomy for the treatment of both symptomatic and asymptomatic patients with carotid artery stenosis: 2 years' experience in a high-volume center

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Abstract

Background. Carotid endarterectomy (CEA) and carotid artery stenting (CAS) are the 2 current standard treatments for carotid artery stenosis. There is still no well-defined consensus with regard to their superiority. However, the minimally invasive nature of endovascular treatment makes CAS increasingly popular among vascular surgeons.

Objectives. The aim of the study is to compare the safety and efficacy of CEA and CAS in patients with symptomatic and asymptomatic carotid artery stenosis.

Material and methods. A single-center, retrospective analysis of patients who were treated for carotid artery stenosis using CAS or CEA between January 2014 and December 2015 was carried out. There were 471 patients (266 CEA and 205 CAS) who were eligible for inclusion. The vast majority of the patients had significant (>70%) stenosis of the internal carotid artery (92.1% of CEA and 87.8% of CAS). The occlusion of the contralateral carotid artery was observed in 9.8% of all cases (2.6% of CEA vs 17.7% of CAS).

Results. The occurrence of complications, such as stroke, myocardial infarction (MI) and death, did not vary statistically between the groups. There were 9 events of stroke in the CEA group (3.4%) and 8 in the CAS group (3.9%), 3 of which were fatal. There were no significant differences between the 2 groups ($\chi^2 = 0.76$; $p > 0.05$). There was no higher risk of mortality in any group (Fisher's exact test; $p = 0.08$). Symptomatic patients had a higher incidence of stroke than asymptomatic patients across both groups ($\chi^2 = 6.36$; $p < 0.05$; hazard ratio 3.03 (1.26–7.33)).

Conclusions. Carotid endarterectomy is equally effective as CAS in stroke prevention, but is associated with a higher incidence of cranial nerve palsy, access site hematoma and other non-stroke complications. Symptomatic patients had a higher incidence of stroke, regardless of the treatment method.

Key words: carotid artery stenting, carotid endarterectomy, carotid artery stenosis

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Introduction

Stroke is a major cause of disability in elderly patients and is the 3rd most common cause of death in developed countries. Approximately 75–80% of all strokes are of ischemic etiology, and 20% of ischemic strokes are secondary to extracranial cerebrovascular disease.¹ Atherosclerosis is responsible for carotid artery stenosis in more than 90% of patients. Endarterectomy of the carotid artery (CEA) was the gold standard for treatment of carotid artery stenosis until the introduction of carotid artery stenting (CAS) in the 1980s. Despite numerous multicenter, randomized clinical trials, it still remains unclear which of the 2 methods is superior. The aim of this study was to assess the efficacy and safety of CAS vs CEA in patients with symptomatic and asymptomatic carotid artery stenosis.

Material and methods

This is a single-center, retrospective study of patients treated for carotid artery stenosis in the Department of Vascular Surgery, 4th Military Teaching Hospital in Wrocław (Poland) between January 2014 and December 2015. Symptomatic patients were eligible for inclusion if there was 50–99% carotid artery stenosis, while asymptomatic patients were eligible if there was 70–99% carotid artery stenosis. Carotid stenosis is considered symptomatic when patients experienced a stroke, a transient ischemic attack (TIA) or amaurosis fugax in the last 6 months. Patients with a carotid artery aneurysm or carotid artery dissection were excluded from this study. For the assessment of carotid artery stenosis, each patient underwent duplex ultrasound examination prior to CAS or CEA. Patients were allocated to the study groups by the surgeon. There was no randomization since it was a case-control study. Directly before the procedure (both CAS and CEA), each patient was administered intravenously 16 mg of dexamethason, 40 mg of pantoprazol, 12 g of piracetam, and 10 mg of vinpocetine. Each patient was provided with 24-hour medical supervision after the procedure.

All patients provided written informed consent to having their data included in this study. This study was approved by the Medical University of Lodz Ethics Committee (No. 204/2015). All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

Carotid artery stenting

Every CAS procedure was performed by an experienced vascular surgeon, i.e., one who performs approx. 100 such procedures yearly. Each patient was given dual antiplatelet therapy the day before the procedure (clopidogrel and aspirin, except for patients with contraindications). Additionally,

an intravenous injection of 5,000 UI of unfractionated heparin was performed several minutes before stent implantation and low-molecular-weight heparin was administered in therapeutic doses for at least 24 h postoperatively. The common femoral artery access was used in all the procedures. Abbot Xact[®] (Abbott Laboratories, Lake Bluff, USA) and Boston Scientific Carotid Wallstent[®] (Boston Scientific, Marlborough, USA) were the stents used. Abbott Emboshield NAVA[®] (Abbott Vascular, Lake Bluff, USA) and Boston Scientific Filter Wire[®] (Boston Scientific, Marlborough, USA) were the distal neuroprotection devices used. Pre- and post-dilatation were performed when needed. In the case of bradycardia, atropine was given intravenously. Dual antiplatelet therapy was continued for 3 months unless contraindicated.

Carotid endarterectomy

The surgeries were performed under local anesthesia. The surgical technique (patch, shunt or suture) was chosen by the operating surgeon. Directly before carotid artery clamping, a 5,000 UI infusion of unfractionated heparin was administered.

Statistical analysis

Data analysis was performed using IBM SPSS v. 23.00 for Macintosh (IBM, Armonk, USA). Quantitative data, presented as mean values and standard deviations, was compared using a t-test. A χ^2 test was used to analyze nominal variables. The strength of the relationship between variables was calculated with the mean square contingency coefficient and the assessment of relative risk. Pearson's product – moment correlation coefficient was used to analyze correlations. Statistical test results were recognized as significant when the p-value was <0.05.

Endpoints

Patients were evaluated for perioperative stroke, death and myocardial infarction (MI) during 7 days of postoperative follow-up. Stroke was defined as a sudden deterioration in neurological condition, lasting for at least 24 h and confirmed by a cranial computer tomography (CT) scan. Severe stroke was defined as a stroke that led to death within 72 h of occurrence, or when the score in the modified Rankin scale was 3 points or more. Myocardial infarction diagnosis was based on clinical symptoms, the dynamic elevation of troponin levels and electrocardiography (ECG) changes.

Results

Four hundred seventy-one patients with internal carotid artery (ICA) stenosis were eligible for analysis. Two hundred sixty-six of them underwent classic CEA and 205 of them underwent CAS. Age was similar in both

groups (69.9 ± 8.8 years in the CEA group vs 68.7 ± 9.6 years in the CAS group; $p > 0.05$). There were slightly more male patients in the CAS group (52.2% males in CEA vs 61.4% males in CAS; $p < 0.05$). Elderly patients (>80 years old) constituted 16.9% of the CEA group and 17.1% of the CAS group. The vast majority of patients had significant ($>70\%$) stenosis of the internal carotid artery (92.1% of CEA and 87.8% of CAS). The occlusion of the contralateral carotid artery was observed in 9.8% of all cases (2.6% of CEA vs 17.7% of CAS). Diabetes was more prevalent in the endovascular stenting group (29.3% of CAS vs 23.3% of CEA), while dyslipidemia was more frequent in the endarterectomy group. Other risk factors for cardiovascular diseases were distributed similarly in both groups (Table 1). A distal neuroprotective device was used in 96.6% of patients in the CAS group. Table 2 shows the number of complications during 7 days of postoperative follow-up. The occurrence of complications, such as stroke, MI and death, did not vary statistically between the groups. We observed such complications in 8 patients (3.9%) after CAS and in 9 patients (3.4%) after CEA (Fisher's exact test; $p = 0.08$). Nine strokes

were observed in the CEA group, 8 of which were of ischemic etiology and 1 was caused by a intracerebral hematoma. In the CAS group, 3 out of 8 strokes that occurred were fatal. Myocardial infarction did not occur in any patient. This data did not lead to the conclusion that there was a higher risk of mortality in any group (Fisher's exact test; $p = 0.08$).

Symptomatic vs asymptomatic patients

The study showed a statistically significantly higher incidence of perioperative complications in symptomatic patients ($\chi^2 = 6.36$; $p < 0.05$). The evaluation of the relative risk (symptomatic patients vs asymptomatic ones) of stroke during the perioperative period was 3.03 (1.26–7.33). The occurrence of other complications, such as death or MI, did not differ between the 2 groups. The study did not reveal a correlation between age and the carotid artery stenosis percentage ($r = -0.79$; $p > 0.05$) or between age and the incidence of endpoint.

Table 3 shows additional adverse events. They occurred more frequently in the CEA group than in the CAS group (14.6% vs 4.39%; $p < 0.05$). In the CEA group, 12 patients (4.5%) required reoperation because of a hematoma at the site of the incision. One case of hematoma turned out to be a pseudoaneurysm due to the unsealing of the arteriotomy suture, which led to ischemic stroke. Wound infections, pulmonary edema and the inferior branch retinal artery embolism were complications observed exclusively in CEA patients.

The small number of additional complications among patients that underwent endovascular treatment is noteworthy. Only 3 (1.4%) out of 205 patients in the CAS group required surgery due to a pseudoaneurysm after puncturing the common femoral artery (AFC).

Perioperative transient central nervous system ischemia symptoms occurred in both groups with a comparable frequency during the procedure (4.1% CEA vs 5.4% CAS) and in the first 24 h after the surgery (3.0% CEA vs 2.4% CAS).

Discussion

Stroke prevention is the main purpose of the treatment of carotid artery stenosis. Despite numerous papers from recent randomized studies comparing CAS and CEA, including the International Carotid Stenting Study (ICSS), Carotid Revascularization Endarterectomy vs Stenting Trial (CREST) and Carotid and Vertebral Artery Transluminal Angioplasty Study (CAVATAS), it still remains unclear which of the 2 methods is superior.

One of the first major clinical trials comparing CAS and CEA was the Endarterectomy vs Angioplasty in Patients with Symptomatic Severe Carotid Stenosis (EVA-3S) trial. They found that the cumulative 4-year risk

Table 1. Baseline characteristics of the study population

Characteristic	CEA (n = 266)	CAS (n = 205)
Age [years]	69.9 ± 8.8	68.7 ± 9.6
Male sex [%]	52.2	61.4
Diabetes mellitus [%]	23.3	29.3
Dyslipidemia [%]	18.2	19.1
ICA stenosis		
<70%	5.6	12.2
≥70%	92.1	87.8
kinking	2.3	
Occlusion of the contralateral ICA [%]	2.6	17.7
Symptomatic patients [%]	39.5	29.3
Treatment technique [%]		
continuous stitch	86.1	–
vascular patch	13.9	–
eversion	6.0	–
shunt	3.8	–
Distal neuroprotection during procedure [%]	–	96.6

CEA – carotid endarterectomy; CAS – carotid artery stenting; ICA – internal carotid stenosis.

Table 2. Complications during 7 days of postoperative follow-up

Perioperative complications	CEA		CAS	
	total CEA (n = 266)	symptomatic patients (n = 105)	total CAS (n = 205)	symptomatic patients (n = 60)
Death	0	0	3 (1.5%)	0
Stroke	9 (3.4%)	5 (4.8%)	5 (2.4%)	2 (3.3%)
MI	0	0	0	0
Total	9 (3.4%)	5 (4.8%)	8 (3.9%)	2 (3.3%)

CEA – carotid endarterectomy; CAS – carotid artery stenting; MI – myocardial infarction.

Table 3. Additional adverse events

Perioperative complications (continued)	CAS	CEA
Laryngeal nerve palsy	0	3 (1.13%)
Pharyngeal and laryngeal hematoma	0	3 (1.13%)
Arytenoid cartilage edema	0	1 (0.38%)
Paralysis of the marginal mandibular branch of the facial nerve	0	2 (0.75%)
Reinke's edema	0	1 (0.38%)
Reoperations due to hematoma in the site of incision	0	12 (4.5%)
pseudoaneurysm	3 (1.47%)	0
ICA intravascular thrombosis	0	3 (1.13%)
Wound infection	0	1 (0.38%)
Pulmonary edema	0	1 (0.38%)
Epilepsy after local anesthetic	0	1 (0.38%)
Postoperative TIA	5 (2.44%)	8 (3%)
Postoperative psychotic symptoms requiring drug administration	1 (0.49%)	3 (1.13%)
Total	9 (4.39%)	39 (14.6%)

CAS – carotid artery stenting; CEA – carotid endarterectomy; ICA – internal carotid stenosis; TIA – transient ischemic attack.

of fatal or disabling stroke did not differ significantly between the CAS and CEA groups (6.3% vs 4%).¹ The CREST showed that the safety and efficacy of CAS and CEA were similar among patients with symptomatic and asymptomatic carotid artery stenosis. The CREST indicated that the risk of stroke, MI and death is similar in these 2 groups (5.2% CEA vs 4.5% CAS). However, it demonstrated a higher periprocedural risk of stroke and death after a CAS procedure.^{2–4} The ICSS results published in “Lancet” in February 2015 did not provide a definitive answer to the question of superiority, either. The primary endpoint was fatal or disabling stroke in any territory. According to the ICSS, stenting is as effective as endarterectomy in the prevention of fatal or disabling stroke (6.4% vs 6.5%, respectively). In the ICSS and in the CREST, carotid artery stenting was associated with a higher procedure-related and long-term risk of non-disabling stroke, but the neurological outcomes were not different.^{5,6}

Our study does not prove the superiority of CAS over CEA, either, though the number of complications is lower. We might relate this to the high number of procedures performed, the frequent application of neuroprotection devices (96.6%) and the extensive experience of the surgeons.⁶

Due to constant technological progress, the results of the trials published may not be accurate today. In these studies, some of the patients in the endovascular group were treated without stent placement, and embolic protection devices were not available.⁷ These factors might have a significant impact on the number of procedure-related complications. The availability of new, improved proximal and distal neuroprotection devices and new mesh-covered stents may reduce the number of disabling strokes.⁸

However, a substudy of the ICSS showed that patients who underwent CAS had new ischemic brain lesions about 3 times more often than patients after CEA and, surprisingly, they were more frequent when cerebral protection devices were used.⁹

The incidence of neurological complications in our department is within the target of <6% for symptomatic artery sclerosis set by the American Heart Association/American Stroke Association guidelines and <3% for asymptomatic patients set by the Therapeutics and Technology Assessment Subcommittee of the American Academy of Neurology.¹⁰

Our study failed to show a correlation between patients' age and the risk of post-procedural neurological complications. On the contrary, the ICSS, the CREST and the Stent-Protected Angioplasty vs Carotid Endarterectomy (SPACE) trial proved that CAS is associated with better outcomes when performed on younger patients, while CEA is better in older patients. The cut-off point was the age of 70 years.^{2,4,11} This is thought to be caused by increased vasa tortuosity and more calcified atherosclerotic plaques in elderly patients.^{12,13}

Limitations of the study

The patients should preferably be observed for 30 days, but in our study they were followed-up for only 7 days after surgery, so restenosis and delayed neurological events were omitted. Our study is retrospective and represents only a single institution's experience with a small number of patients. There was no randomization, so the results may be influenced by the tendency of operators to surgically treat more sick patients.

Conclusions

Our analysis showed that CEA is as effective as CAS in stroke prevention, but is associated with a higher incidence of cranial nerve palsy, access site hematoma and other non-stroke complications. Symptomatic patients had a higher incidence of stroke, regardless of the treatment method. A new multi-center, randomized trial with methodology carefully determined by advocates of both CAS and CEA should be conducted in order to provide a final conclusion for this long-lasting dispute on which method is better.

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