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Carotid angioplasty with cerebral protection

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Background. *Carotid endarterectomy (CEA) is widely used in the management of high-grade carotid stenosis. It is a surgical procedure requiring general anaesthesia and is suitable only for lesions located at or close to the carotid bifurcation. It may develop complications, such as stroke, death, cranial nerve palsies, wound haematoma and cardiac complications. The risk of complications is increased in patients with recurrent carotid artery stenosis following CEA, in subjects undergoing radiotherapy to the neck, and in patients with cardiopulmonary disease. The drawbacks of CEA have led physicians to search for alternative treatment options. Carotid angioplasty and stenting (CAS) is less invasive than CEA. The method is particularly suitable for the treatment of recurrent stenosis after previous CEA and distal internal artery stenosis, which is inaccessible for CEA. CAS does not cause cranial nerve palsies. Moreover, it does not require general anaesthesia and causes lower morbidity and mortality in patients with severe cardiopulmonary disease. The complications of CAS include stroke due to distal immobilisation of a plaque or thrombus dislodged during the procedure, abrupt vessel occlusion due to thrombosis, dissection or vasospasm, and restenosis due to intimal hyperplasia. CAS is a relatively new procedure; therefore, it is essential to establish its efficacy and safety before it is introduced widely into clinical practice.*

Patients and methods. *In Slovenia, we have also started with carotid angioplasty by the study: Slovenian Carotid Angioplasty Study (SCAS). We performed CAS in 17 patients (12 males and 5 females) aged from 69 to 82 years. All patients were symptomatic with stenosis greater than 70 %. 10 patients suffered transient ischemic attacks, 4 patients minor strokes and 3 patients amaurosis fugax.*

Results. Technical success (< 30 % residual stenosis) was achieved in all cases. In 14 patients, no residual stenosis was found, in 2 patients a 15 % residual stenosis persisted and in 1 patient, a 30 % residual stenosis was detected. In 15 patients, CAS was performed without complications, in one patient the hyperperfusion syndrome occurred and in one periprocedural stroke occurred.

Conclusions. *According to our initial experience on 17 patients CAS could gain more importance in stroke prevention with proper selection of patients with brain ischemia and improved cerebral protection during procedure.*

Key words: carotid stroke; angioplasty; stents; cerebral infraction – prevention and control

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Introduction

Stroke is an important public health problem and the third most common cause of death, after heart diseases and cancer.[1] In Slovenia, stroke incidence, measured as a first ever stroke per 100000 population, is 190.5 and mortality rate is 19.3 %.[2] The proportion of ischemic stroke increases with age (33 % before 45 and 80 % after 50). Of all cases, 20 to 30 % are supposed to be due to carotid stenosis.[3] The most common cause of carotid stenosis is atherosclerosis. The mechanism of brain ischemia was thought to be either direct hemodynamic impact on the cerebral blood circulation or indirect as a source of thromboembolic material.[4] Three possible treatment modality are available to prevent stroke caused by carotid stenos is. The first is medical treatment, second surgical treatment, and third the newest approach, endovascular treatment by carotid angioplasty and stenting (CAS).

Platelet antiaggregants such as acetilsalicil acid or ticlopidine, reduce the risk of stroke.[5,6] Recently, preventive treatment with clopidogrel in combination with acetilsalicil acid are recommended.[7] Reducing the risk factors such as smoking, obesity, dyslipidemia, hypertension, diabetes is necessary.

In surgical approach, the atheromatous plaque is extirpated, removed and the artery is sutured. The first operation on carotid artery – carotid endarterectomy (CEA) was performed by DeBakey in 1953.[8] The number of the procedures increased in the following years. In 1984, 120000 CEA operations were performed.[9] After this year the number of CEA began to decrease because of its uncertain effectivness.[10] In 1991, randomised prospective surgical trials, North American Symptomatic Carotid Endarterectomy Trial (NASCET)[11] and European Carotid Surgery Trial (ECST)[12] showed a significant stroke risk reduction by CEA compared with medical treatment in symptomatic patients with carotid stenosis greater than 70 %. The reassessment of the results by the American Heart Association (AHA) Stroke Council indicated that CEA was three times as effective as medical treatment in reducing the frequency of stroke.[13] However, CEA carried a risk of cancer complications.[1] The benefit of CEA was dependent on maintaining a low complication rate. Most important complications during the procedure were perioperative stroke and death. Combined stroke and death rates exceeding 3 % for patients with asymptomatic stenosis and 6 % for patients with symptomatic stenosis would eliminate the benefit in stroke reduction.[14] Post-CEA restenosis should also be mentioned, since they are not rare. The rate is estimated between 1.2 and 23.9 %, depending on the operative technique.[15] The risk of complications by a reoperation was high.[16] Injuries of cranial nerves was seen due to the neck incision in 7.6 to 27%.[17]

CEA is the "gold standard" so far, but it is not without risks and limits as regards high-risk patients (elderly patients, patients suffering from coronary diseases, respiratory insufficiency...), supra-aortic lesions located in the upper section, and carotid lesions associated with severe intracranial lesions. Therefore, less invasive CAS seems to have its place in the treatment of carotid stenoses.

CAS has a history more than 20 years. After experiments on animal model Mathias in 1977 proposed the treatment of carotid stenosis for the first time using angioplasty.[18] The first carotid angioplasty was performed in 1980 by Kerber.[19] Carotid angioplasty with or without stenting has been investigated during last two decades. This procedure has not received wide acceptance because of the embolic stroke risk during the procedure. Till 1997 the perioperative stroke rate following CAS without cerebral protection ranged from 5.3 % – 8.2 %.[20,21] Initial results were criticised because of high neurological complications rate.[22] The main cause of perioperative complications are thought to be embolic particles

released from the carotid plaque during angioplasty.[23] In 1990, Theron, the father of cerebral protection, developed and advocated the use of cerebral protection device during CAS.[24] The risk of embolisation and the need for cerebral protection during CAS was confirmed later.[25]

Comparing the safety and efficacy of CAS with cerebral protection versus CEA, a prospective randomised trial was being organised: Carotid Revascularization Endarterectomy versus Stent Trial (CREST), which was started in the beginning of the year 2001.[26]

In Slovenia, we have also started with CAS by setting up the study "Slovenian Carotid Angioplasty Study (SCAS)" in order to evaluate the safety and efficacy of the method.

Patients and methods

Study protocol

The study has taken the form of a prospective clinical trial conducted over a period of 2 years on 60 patients enrolled according to well-defined inclusion and exclusion criteria. The patients were evaluated independently by a neurologist prior to and during the procedure and follow-up examination performed at 1, 6, 12 and 24 months. Evaluation of cerebral protection devices was incorporated into the study.

The safety of CAS was assessed on the basis of acute procedural success and occurrence of major clinical events during or within 30 days after the procedure. The efficacy of CAS was determined with respect to minor ipsilateral neurological events, major stroke and death occurring during or within 30 days of the procedure and recurrent stenosis established within 24 months of CAS.

Oral and written information on the study was provided to all patients, and a written, witnessed informed consent was obtained from each of them. The study was been approved by the National Medical Ethics Committee.

Patients

We performed CAS in 17 patients (12 of them were males and 5 females) aged from 69 to 82 years. All patients were symptomatic with stenosis greater than 70 %. 10 patients suffered transient ischemic attacks, 4 patients minor stroke and 3 patients amaurosis fugax. Seven patients had stenosis on right internal carotid artery, 8 on left internal carotid artery and 2 on right common carotid artery. Two patients had occlusion of the contralateral carotid artery. In the first 6 patients, we did not use cerebral protection devices. In other 11 patients, cerebral protection filter devices were used.

Procedure

All patients were give aspirin, 325 mg/d and clopidogrel (75 mg/d) starting the 7th day before the procedure. Heparin, given as an intra-arterial bolus, was titrated to maintain the activated clotting time between 200 and 250 seconds. The procedures were done with local anaesthesia. Neurologic status was monitored. Atropine (0.5-1 mg) was given as required during balloon inflation. Heart rate and blood pressure were monitored throughout the intervention.

Percutaneous access was gained through the femoral artery. Selective catheterization of carotid arteries was performed with standard techniques. The diagnostic angiography visualised the origins of the brachiocephalic arteries from the aortic arch, both carotid bifurcations, both vertebral arteries, intracranial parts of both carotid arteries and the dominant vertebral artery. Once the diagnostic angiography was completed and the stenotic internal carotid artery was identified, the 5F catheter was advanced using the 0.035-inch glide wire (Terumo Radiofocus Guide Wire, Terumo, Inc.) into the ipsilateral external carotid artery. The glide wire was withdrawn and replaced with an extra stiff 0.035-inch exchange wire (Extra Stiff Amplatz Wire, 260

cm; Cook, Inc.). The 5F catheter was withdrawn, and the 8F 90-cm guiding sheath (Carotid Vista Brite Tip; Cordis, Inc.) was advanced into the common carotid artery over the exchange Amplatz wire, which was anchored in the external carotid artery. Carotid angiography was again performed to measure the vessel diameter to facilitate the sizing of balloons, stents and cerebral protection filter devices. In the patients without cerebral protection, stenoses were then crossed with flexible coronary guidewires (V-18 Control Wire; Boston Scientific Corp, Watertown, Mass). Eleven patients underwent CAS with cerebral protection filter device Angioguard (Cordis, Inc): a low-profile guidewire-based, filter-type device (4F) that was placed in the distal ICA after crossing the stenotic lesion. It captured embolic debris while maintaining distal perfusion. After that we started with intervention on stenosis. The size of the initial angioplasty balloon was dictated by the severity of the stenosis. Very severe lesions were predilated with low-profile coronary balloons (Bypass Speedy Monorail Catheter, Boston Scientific Corp); in the case of less severe lesions, the initial dilatation may be performed with a definitive balloon sized to the distal normal artery. A Carotid Wallstent Monorail (Boston Scientific Corp) was deployed across the lesion. The stent was dilated at high pressure (14 to 16 atm) to firmly embed it into the vessel wall. After that filter with trapped emboli was removed and the procedure was finished. Completion angiography was performed on the ipsilateral intracranial vessels. The patients were transferred to the intensive care unit. The sheaths were removed. The patients were discharged on either the first or second day after the procedure. Clopidogrel was continued for 3 weeks, whereas aspirin was continued permanently.

Results

Procedural results are summarised in Table 1. Technical success (<30 % residual stenosis) was achieved in all cases. In 14 patients, no residual stenosis was found, in 2 patients a 15 % residual stenosis persisted and in 1 patient, a 30 % residual stenosis was detected.

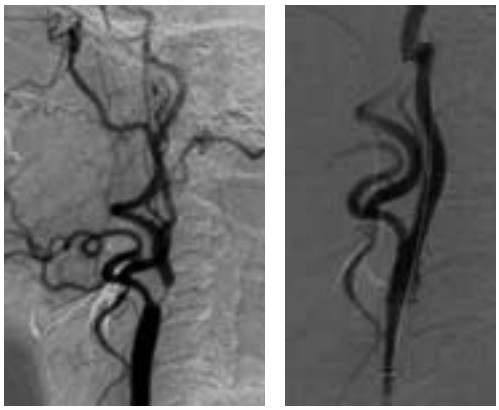

Figure 1. Digital subtraction angiography. Lateral views of the left carotid artery bifurcation. A. High grade circumferential, atherosclerotic stenosis of the internal carotid artery origin before CAS. B. No residual stenosis after CAS.

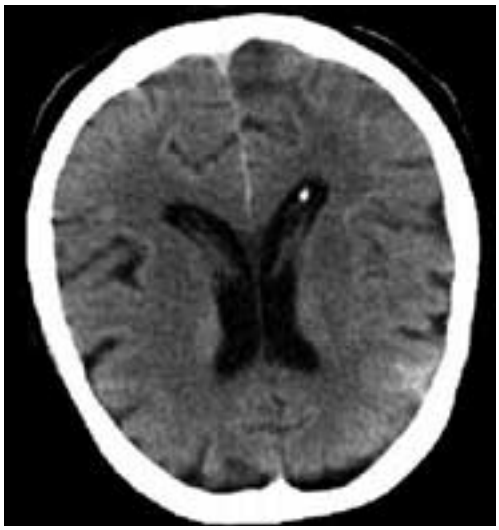

Figure 2. CT of the brain demonstrates small haemorrhage in the left frontal region.

Table 1. Procedural results in 17 patients

Pt	Vessel	Symptoms	Age in years	CLO	Stenosis % Pre	Post	Procedural Stroke	Severe CAD	Comments
1	R ICA	TIA	74		90	0	No	Yes	
2	L ICA	Stroke	72	Yes	99	0	No	No	
3	R ICA	TIA	63		70	0	No	No	
4	R CCA	TIA	68		80	0	No	Yes	
5	L ICA	Amaurosis fugax	72		95	0	No	No	After five days, an episode of seizure and transitory Tod's hemiparesis occurred. CT of the bran demonstrates small hemorrhage on the left frontal side. After a week, she recovered completely.
6	L ICA	Stroke	67	Yes	87	0	Yes	Yes	Occlusion of right ICA. Cerebral embolism occurred during the filter removal. He became aphasic and had right hemiplegy. We dissolved the embolus on the bifurcation of MCA with intraarterial thrombolysis using rTPA, but some hemiparesis persisted.
7	R CCA	TIA	66		80	0	No	No	The right iliac stenting followed same procedure.
8	L ICA	Amaurosis fugax	70	Yes	75	No	No	Yes	
9	R ICA	Stroke	64		90	15	No	No	
10	L ICA	TIA	68		76	0	No	No	
11	RICA	TIA	82		80	0	No	Yes	
12	R ICA	TIA	68		71	0	No	No	
13	L ICA	TIA	82		75	0	No	Yes	
14	R ICA	TIA	61		73	0	No	No	
15	L ICA	Stroke	76		99	30	No	Yes	
16	R ICA	Amaurosis fugax	57		85	0	No	No	
17	L ICA	TIA	53		75	15	No	No	

CAD = coronary artery disease; CCA = common carotid artery; CLO = contralateral carotid occlusion; ICA = internal carotid artery; L = left; MCA = middle cerebral artery; Pt = patient; R = right; TIA = transient ischemic attacks.

From patient 6 (Table 1), cerebral protection filter device was used.

In one patient (Patient 5, Table 1) hyperperfusion syndrome occurred. It occurred in 72-year-old female with carotid stenosis more than 90 %, who suffered from earlier amaurosis fugax. The stenting was performed successfully without residual stenosis and immediate complications (Figure 1). The 5th day after CAS, a generalized seizure with Tod's hemiparesis on the right side occurred. After admission, we performed brain CT that showed a small haemorrhage on the left front side (Figure 2). She recovered completely after a week.

Periprocedural stroke occurred in one patient (Patient 6, Table 1). This was 67 years old male with a previous minor stroke and 90 % stenosis of the left internal carotid artery due

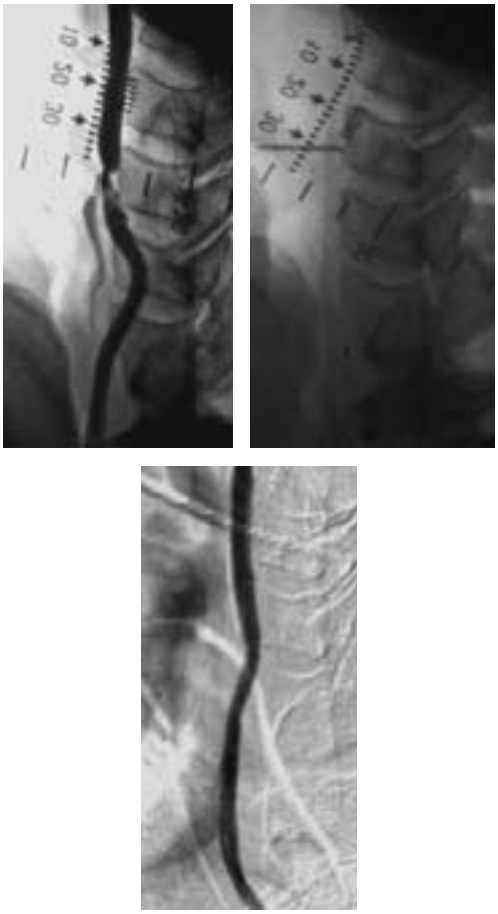

Figure 3. Digital subtraction angiography. Lateral views of the left carotid artery bifurcation. A. 90 % stenosis of left internal carotid artery before CAS. B. Cerebral protection filter device during CAS. C. No residual stenosis after CAS.

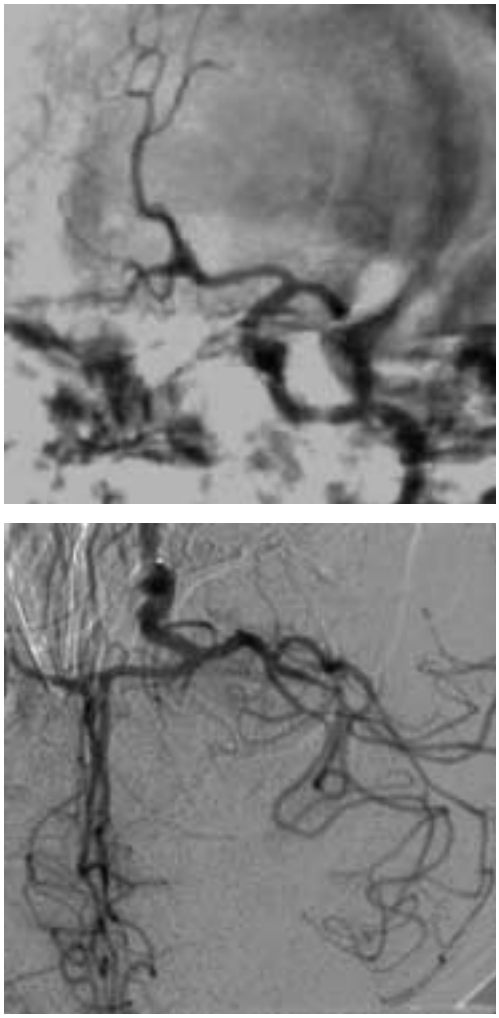

Figure 4. Digital subtraction angiography. Anteroposterior views of the left intracranial internal carotid artery with branches. A. An acute oclusion of left middle cerebral artery at the bifurcation. B. Recanalisation of the occlusion after intra-arterial thrombolysis.

to a lipid-laden plaque and the occluded right carotid artery. In this case we used a cerebral protective filter. CAS was successfully done (Figure 3). Cerebral embolism occurred during the filter removal. He became aphasic and had hemiplegy. We dissolved embolus on bifurcation of middle cerebral artery with intra-arterial thrombolisis using rTPA (Figure 4).

In 15 patients, CAS was performed without complications. The follow-up in all patients (average follow-up period of 3 months) revealed no transient ischemic attacks or new strokes. All patients remained at their neurologic baseline. Long-term clinical or imaging follow-up is not yet available.

Discussion

In the last years, angioplasty has been successfully used in coronary and peripheral disor-

ders and has been also applied at the carotid level. Throughout the world, several teams are actively engaged in research in order to determine the indications, the suitable techniques, the adjunct treatments, and the follow-up conditions. The final aim of carotid angioplasty is to prevent cerebral vascular neurological events and not to overshadow surgery. It could be an alternative or a complement to surgery if the results were comparable or better. Indications must be defined through randomised multi-centred studies and are currently much debated. Some would like them to be limited to high risk patients, restenosis, radiation-induced lesions, or lesions located in the upper internal carotid artery near the skull, while others would like them to be more extensive, including lesions of the carotid bifurcation.[27] In later time cerebral protection devices have the potential to enhance the safety of CAS.[28] First report of larger series by Wholey[29] shows that the perioperative complication rate after CAS with the cerebral protection is 1.6 % which is significantly lower than with CEA and CAS without cerebral protection.

We treat now all patients using cerebral protection filter device. In all filters we found embolic material. In two cases, filters were occluded due to a massive amount of embolic material. We suppose that, in such cases where a high risk of complications exists, it is very important to know the type of plaque, which can dislodge a large amount of embolic material. For the evaluation of plaque composition we performed ultrasound. We did not performed CAS in patients with echolucent plaques (Tip 1) due to high embolic risk.[30] Fibrous plaques seem to carry a very low risk of rupture and embolisation. We expect to learn more about plaque composition using MRI. MRI additionally shows the thickness of fibrous cap and pre-existent ruptures of the plaque.[31] By demonstrating thick or thin fibrous cap of the plaque and correlating data with the amount of emboli, trapped in the filter, we could be able to analyse the risk of periprocedural complications. This information would enable a better selection of patients for CAS. According to our initial experience on 17 patients CAS could gain more importance in stroke prevention with proper selection of patients and improved cerebral protection during procedure.

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