New possibilities in the endovascular treatment of supraaortic vessels

Ph.D. Thesis

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1 Summary

Cerebrovascular disease, including stroke, represents the third-leading cause of death in Hungary and a leading cause of disability among the elderly population. The majority of all strokes are ischemic, mostly secondary to thromboembolic disease of the supraaortic vessels. We investigated new therapeutic methods in the endovascular treatment of these diseases.

Surgical revascularization of supraaortic trunk stenosis is associated with high morbidity and mortality rates. Balloon angioplasty has become an increasingly accepted treatment of stenoocclusive supraaortic arterial disease. Natural history data and treatment guidelines do not exist for innominate and proximal common carotid artery lesions.

We have confirmed in a large series of innominate artery angioplasties that it is a safe and effective procedure with an excellent initial success rate, with a lower complication rate than the surgical option and with a similar long-term patency rate as for surgery.

In the largest published study on transfemoral angioplasty of ostial and proximal common carotid artery stenosis we have proved that endovascular treatment has high success rate with low stroke/death rate.

Carotid stenting (CAS) is an evolving alternative to surgery in the treatment of patients with carotid stenosis. Stent selection is influenced by several factors, including the carotid anatomy and lesion characteristics. We examined the wall adaptability of a new closed-cell carotid stent (NexStent), which was designed for carotid bifurcation treatment. Data obtained from angiographic and computed tomographic images indicate that the stent provides adequate expansion and adaptation to the carotid bifurcation.

There are two types of restenosis after carotid artery interventions: the early restenosis develops mainly within the first 24 months after the revascularization procedure and its pathological background is myointimal hyperplasia; on the other hand late restenosis is rather due to progression of primary atherosclerosis and occurs more than 2 years after carotid endarterectomy (CEA). We compared the early restenosis rate in a consecutive series of CAS versus CEA patients at a single cardiovascular institution. Our data suggest that the incidence of restenosis after stenting was less common than after surgery.

Aneurysms of the extracranial internal carotid artery are extremely rare; over the past decades their treatment technique has changed. Endovascular methods have become more widespread and offer an alternative to surgery, which is often difficult in this region. Stent-graft treatment represents a less invasive approach to permanent aneurysm exclusion while maintaining the patency of the carotid artery. We report two cases of internal carotid artery pseudoaneurysm that were treated using Wallgraft.

Our results may help vascular surgeons and interventional radiologists to consider risk versus benefit when deciding treatment options for supraaortic arterial stenosis.

2 Összefoglalás

A cerebrovasculáris betegség (stroke) a halálozás harmadik leggyakoribb oka Magyarországon és a tartós rokkantság vezető oka az idősebb populációban. A stroke leggyakrabban ischaemiás eredetű, főleg a supraaortikus erek thromboembóliás betegségének tulajdonítható. Dolgozatomban ezen érterület új endovasculáris kezelési lehetőségeit taglalom.

A supraaortikus nagyértörzsek sebészi rekonstrukciója magas morbiditással és mortalitással jár. A ballonos angioplasztika mára elfogadottá vált ezen erek stenoocclusiv betegségének kezelésében. Az a. anonyma és a proximális a. carotis communis obliteratív betegségének természetes lefolyása nem ismert, széles körben elfogadott kezelési ajánlások nincsenek.

Nagyszámú betegen végzett a. anonyma angioplasticán bizonyítottuk, hogy az eljárás hatásos és biztonságos, kiváló sikerességgel végezhető, szövődményrátája a műtéti megoldásnál alacsonyabb, hosszú távú eredményessége azzal megegyező.

Az irodalomban fellelhető legnagyobb esetszámú proximális carotis communis angioplasticát vizsgáló közleményben bizonyítottuk hogy az endovasculáris kezelés alacsony stroke/halál arány mellett magas eredményességel kivitelezhető.

Az irodalomban fellelhető legnagyobb esetszámú ostiális és proximális carotis communis szűkületen végzett angioplasticát közöltük le

A carotis stentelés a sebészeti beavatkozás új alternatívája a carotis szűkületes betegek kezelésében. A stent kiválasztását számos tényező befolyásolja, többek között a carotis anatómia és a plakk jellemzői. Egy a carotis bifurcatio kezelésére kifejlesztett új, zárt cellás carotis stent (NexStent) érfalhoz illeszkedését vizsgáltuk. Az angiográfiás és komputer tomográfiás képekből nyert adatok azt mutatták, hogy a stent megfelelő expanziót és adaptációt mutat a carotis bifurcatióban.

A carotis intervenciók után kétfajta restenosis alakulhat ki: a korai restenosis főleg a revascularizáció utáni első két évben alakul ki, patológiai háttere a miointimális hiperplázia. A késői restenosis inkább a primer atherosclerosis progressziója, mely a carotis beavatkozás után több mint 2 évvel történik. Összehasonlítottuk a korai restenosis gyakoriságát carotis stentelésen illetve műtéten átesett betegeken intézetünk

anyagában. Adataink azt jelzik hogy stentelés után a restenosis kevésbé gyakori mint műtét után.

Az extracranialis a. carotis interna aneurysmái igen ritkán fordulnak elő, kezelésükben az endovascularis módszerek elterjedtté váltak mivel a sebészi megoldás gyakran nehezített ebben a régióban. A stent-graft kezelés kevésbé invazív módszer az aneurysma ellátására, mellyel a carotis artéria átjárhatósága megőrizhető. Két esetben sikeresen kezeltünk carotis interna álaneurysmát Wallgraft alkalmazásával.

Eredményeink segíthetnek supraaortikus szűkületek hatékony és biztonságos kezelési stratégiájának kialakításában.

3 Abbreviations

ACAS: Asymptomatic Carotid Atherosclerosis Study

ACST: Asymptomatic Carotid Surgery Trial

AFX: Amaurosis Fugax

AMI: Acute Myocardial Infarction

CAD: Coronary Artery Disease

CAS: Carotid Stenting

CAVATAS: Carotid and Vertebral Transluminal Angioplasty Study

CCA: Common Carotid Artery

CDS: Carotid Duplex Sonography

CEA: Carotid Endarterectomy

CREST: Carotid Revascularization Endarterectomy vs Stent Trial

CT: Computed Tomography

CTA: Computed Tomography Angiography

DM: Diabetes Mellitus

DSA: Digital Subtraction Angiography

ECST: European Carotid Surgery Trial

EDV: End Diastolic Velocity

EEA: Eversion Endarterectomy

EPD: Embolic Protection Device

EVA-3S: Endarterectomy versus Angioplasty in Patients with Severe Symptomatic Carotid Stenosis

HR: High Resolution

ia.: Intraarterial

ICA: Internal Carotid Artery

MI: Myocardial Infarction

mmHg: Millimeters of Mercury

MRA: Magnetic-Resonance Angiography

MRI: Magnetic-Resonance Imaging

NASCET: North American Symptomatic Carotid Endarterectomy Trial

iv.: Intravenous

PAD: Peripheral Arterial Disease

po.: per os

pCCA: Proximal Common Carotid Artery

PSV: Peak Systolic Velocity

PTA: Percutaneous Transluminal Angioplasty

PTCA: Percutaneous Transluminal Coronary Angioplasty

PTFE: Polytetrafluoroethylene

Re-PTA: Repeat PTA

SAPPHIRE: Stenting and Angioplasty with Protection in Patients at High Risk for Endarterectomy

SAT: Supraaortic Trunk

SPACE: Stent-Protected Angioplasty Versus Carotid Endarterectomy

TIA: Transient Ischemic Attack

VBI: Vertebrobasilar Insufficiency

US: Duplex Ultrasound

4 Introduction

4.1 Cerebrovascular disease and stroke

The term cerebrovascular disease indicates abnormality of the brain resulting from a pathologic process of the blood vessels. The pathologic process may be considered not only in its mechanism - embolism, thrombosis, dissection - but also in terms of the primary disorder, i.e., atherosclerosis, arteritis, aneurysmal dilation, and malformation. Occlusive diseases of the supraaortic vessels may cause cerebral ischemia and in certain cases arterial insufficiency of the upper extremities. In about half of the cases the obstruction is located extracranially, in the cervical or thoracic segment.

Stroke is defined as sudden occurrence of a focal neurologic deficit. Ischemic stroke is caused by obstruction of an artery that supplies blood to the brain, resulting in a deficiency in blood flow; approximately 75% to 80% of all strokes are ischemic. Hemorrhagic stroke is caused by the bleeding of ruptured blood vessels in the brain, representing about 15% to 20% of strokes. Stroke mortality ranges between 12-30%, and its survivors remain at a high annual risk of recurrent ischemic events and mortality (1).

Ischemic stroke represents a major health problem and is the third leading cause of death in Hungary and important cause of long-term disability. Stroke mortality declined continuously in Western Europe since 1970. In Hungary stroke mortality increased until the early 1990s and decreased thereafter (*Figure 1*). In Hungary the average age of stroke patients is 5-10 years less than in developed countries and the stroke mortality/morbidity is significantly higher (2). The risk of stroke increases with age, and growth in the elderly population will be a source of increasing disability.

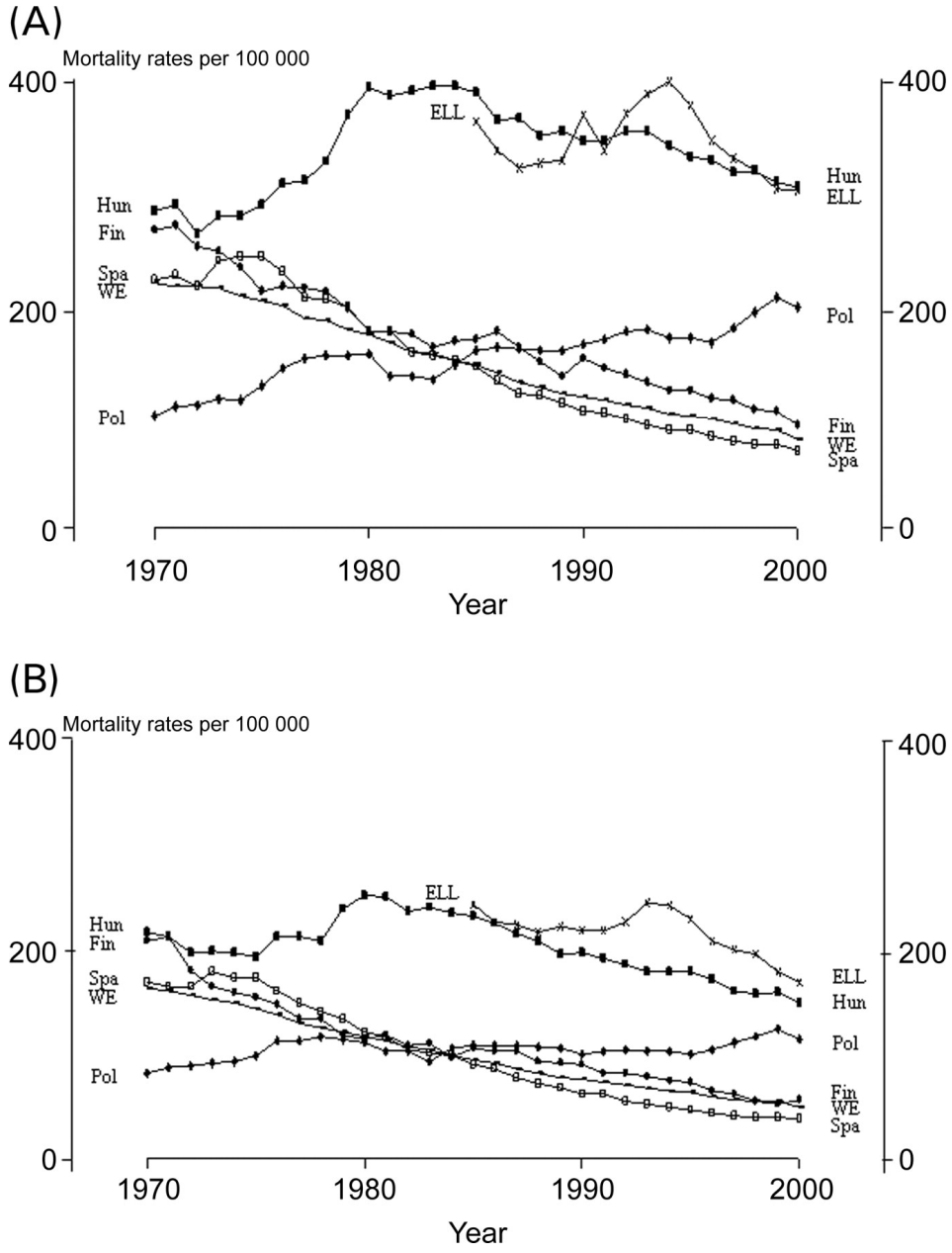


Figure 1. Trends in stroke mortality in 1970–2000 (A) for men aged 45–74 years and (B) for women aged 45–74 years. (3)
Hun: Hungary, ELL: Baltic states, Fin: Finland, Pol: Poland, Spa: Spain ,WE: Western Europe (Austria, Belgium, Denmark, England and Wales, Finland, France, Germany, Greece, Ireland, Italy, The Netherlands, Norway, Portugal, Scotland, Spain, Switzerland, Sweden)

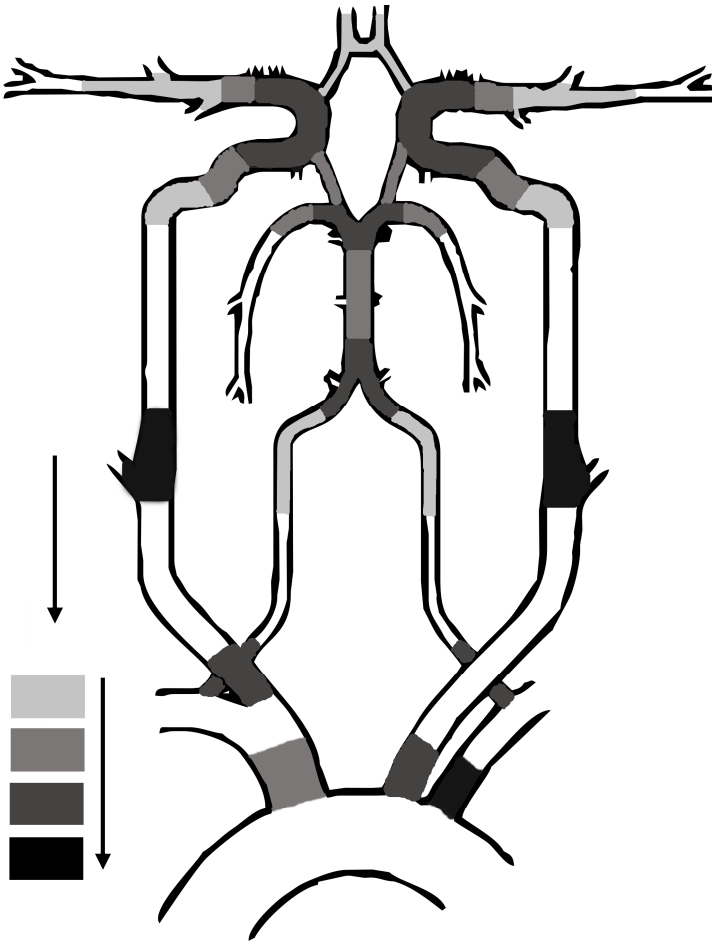


Figure 2. Frequency and severity of atherosclerotic lesions in the supraaortic arteries (4)

4.2 Atherosclerosis

Atherosclerosis of the large extracranial arteries in the neck and at the base of the brain is the underlying cause of focal cerebral ischemia in the majority of cases.

Atherosclerosis is an inflammatory disease characterized by the accumulation of white blood cells, cell debris, fatty substances (cholesterol and fatty acids), calcium, and

fibrous tissue (plaque or atheromas) on the walls of the arteries. Symptomatic plaques in the carotid artery involve primarily the carotid bulb and are characterized by increased cellular proliferation, lipids accumulation, ulceration, hemorrhage, and thrombosis. Risk factors (arterial hypertension, cigarette smoking, and high serum cholesterol levels) promote thrombus formation and continuous transendothelial seepage of plasma lipids. Atherosclerosis accounts for up to 30% of all strokes; the majority of them originate from the carotid arteries. The distribution of atherosclerosis in the cerebral arteries favors the large proximal trunks at sites of bifurcation (*Figure 2*). Atherosclerotic lesions can become symptomatic by several mechanisms: the atheromatous lesion may enlarge thus compromising the cerebral flow or they rupture and occlude the vessel lumen, or these lesions may provide a source of atheromatous or platelet emboli. Ulcerated atheromas represent especially likely sources of emboli.

4.3 Takayasu arteritis

Takayasu arteritis is an inflammatory disease of unknown origin that affects the aorta and its large branches. Progressive intimal fibrocellular thickening with elastic degeneration of tunica media can lead to stenosis, occlusion, and/or aneurysmal dilatation of the affected vessels. Supraaortic branches, such as the carotid, subclavian, and innominate arteries, are frequently involved. Takayasu arteritis most commonly affects women of reproductive age (15–45 years). The diagnosis can be confirmed by angiography, which shows the specific pattern of stenosis, occlusion, irregularity, and aneurysm involving multiple proximal branches of the aorta. During the early phase of Takayasu arteritis, mild luminal changes of the arteries may not be detectable on angiography. Cross-sectional imaging techniques are better suited for the evaluation of mural changes of the aorta during the early phase of Takayasu arteritis. Helical CT and MR imaging have the capability of revealing mural thickening of the aorta and its branches; enhancement at the inflamed segment may help in determination of disease activity (5-7).

4.4 Clinical presentation

Symptoms of cerebral ischemia depend on the type and which area of the brain is affected. Signs of ischemic stroke usually occur suddenly. Transient ischemic attack (TIA) is defined as the sudden onset of a focal neurological deficit that completely resolves within 24 hours, while stroke is conventionally defined as a new neurological deficit that persisted for a period of more than 24 hours. The duration of TIA is more often on the order of minutes than hours; 50% of TIAs resolve within 1 hour and 90% within 4 hours (8). Transient ischemic attacks in the posterior vascular territory are also referred to as vertebrobasilar insufficiency (VBI); transient ischemic episodes are slightly more common in this system than in the carotid one. Conceptually, TIA can be thought of as similar to an ischemic stroke, except that the patient returns to normal quickly. With the more widespread use of modern brain imaging, many patients with symptoms lasting <24 hours are found to have an infarction. The most recent definition of stroke for clinical trials has required either symptoms lasting >24 hours or imaging of an acute clinically relevant brain lesion in patients with rapidly vanishing symptoms. The risk of stroke within 90 days after a transient ischemic attack has been estimated to be approximately 10 percent, with half of strokes occurring within the first two days of the attack (9). The stroke risk is even higher when a transient ischemic attack results from internal carotid artery stenosis.

Depending on the lesion and the extent of collateral circulation, patients with significant stenosis of the supraaortic trunks (SAT) can present symptoms in a variety of ways. In many cases patients remain symptom free. Symptomatic occlusive disease of the subclavian artery may result in brachial artery ischemia or digital artery embolization. When occlusive lesions are proximal to the origin of the vertebral artery, vertebrobasilar insufficiency can result. Atherosclerotic disease of the carotid artery usually involves the carotid bulb, but in a small subset of patients proximal common carotid artery is involved. These patients are admitted with similar symptoms of cerebrovascular insufficiency that patients with carotid bulb disease experience. Furthermore, patients with severe innominate artery disease may develop symptoms similar to those seen in either subclavian or common carotid artery lesions.

4.5 Diagnostics

In the 1980s duplex ultrasonography became available as a reliable modality for noninvasive screening of extracranial cerebrovascular stenosis. Duplex sonography combines integrated pulse-wave Doppler spectrum analysis and B-mode sonography. The velocity changes on spectral analysis reflect changes in hemodynamics. Blood flow velocity is higher in the stenosis; distal to the stenosis reduced pulsatility, flattened systolic peak can be observed. Duplex ultrasonography is considered a valid measure of carotid artery stenosis. Doppler measures that have been correlated with angiographic stenosis include internal carotid artery (ICA) peak systolic velocity (PSV) and end-diastolic velocity, as well as ratios of ICA PSV and common carotid artery PSV.

Diseases of the supraaortic trunks are relatively uncommon and difficult to depict using duplex ultrasound. The diagnosis of innominate or subclavian artery stenosis or occlusion is based on pulse palpation of the radial arteries, comparative blood pressure measurement on both arms. Subclavian and vertebral duplex scan can identify subclavian steal phenomenon. Poststenotic Doppler spectrum in the common carotid artery is associated to significant innominate artery stenosis and it might be the only diagnostic sign of ostial common carotid artery stenosis.

Invasive tests performed to confirm duplex ultrasonography carry certain risk. Catheter-based cerebral angiography is considered as the gold standard for diagnosis of cerebrovascular disease, but its invasive nature represents a risk. Patients at the highest risk of angiography related stroke are those with atherosclerotic changes in the supraaortic vessels. Recently Computed Tomography Angiography (CTA) and Magnetic Resonance Angiography (MRA) offer noninvasive diagnostic method which could replace the conventional angiographic technique.

4.6 Surgical and endovascular treatment

4.6.1 Supraaortic trunk (SAT)

In the 1970s endarterectomy of the subclavian, innominate and proximal common carotid artery represented the most popular method of treatment. High perioperative mortality rate has been connected with the transthoracic approach that endarterectomy of the supraaortic vessels requires. Direct transthoracic reconstruction is an effective curative operation with a 5 year cumulative primary patency rate of 94% and a stroke-free survival rate of 87% (10). This procedure has been replaced by extrathoracic methods such as bypass surgery and transposition with lower complication rate (11-16). Cervical repair of atherosclerotic SAT disease has low mortality rate, but incidence of its complications remains high.

Endovascular correction of SAT stenoses has some advantages over direct surgical intervention owing to its high effectiveness, lower complication and mortality rates, and shorter hospital stay. Angioplasty offers a less invasive alternative to surgery for patients at high surgical risk and those ineligible for surgery. The first cases of supraaortic angioplasties were reported in the early 80's (17, 18). The major reason for the reluctance to perform supraaortic artery interventions was the fear of cerebral embolization and development of stroke during the procedure. During angioplasty, embolic particles may be created at almost any step of the procedure. The balloon dilation is considered to be one of the most embolic steps of the procedure due to possible dislocation of particles from the damaged plaque.

Stent implantation is a relatively new method; it is primarily used for recanalizing occlusions and as salvage therapy for suboptimal or failed result of balloon dilation. Stent treatment not only reduces recoil and prevents intimal dissection that might compromise the blood supply to the brain; it also limits the embolization of atherosclerotic particles during and after the procedure. However, there is no evidence that stenting is superior to angioplasty alone; current practice includes primary stenting in most cases for the aforementioned reasons.

4.6.2 Carotid surgery

Carotid endarterectomy is the surgical procedure during which the carotid artery is opened, and the atherosclerotic plaque and fatty material deposited on the inside of the artery wall are removed. Carotid endarterectomy (CEA) was introduced in the 1950s as a treatment option for carotid stenosis, but it was not considered as gold standard for treatment of carotid occlusive disease until two major randomized trials comparing CEA to medical therapy proved its effectiveness. These two multicenter trials were the North American Symptomatic Carotid Endarterectomy Trial (NASCET) and the European Carotid Surgery Trial (ECST) which enrolled patients with symptomatic carotid stenosis (19, 20). In the NASCET study, the absolute risk reduction of any ipsilateral stroke for patients with ≥70% stenosis at 2 years was 15.9%. There was no significant benefit for patients with less than 70 percent stenosis. In the final ECST analysis, the absolute risk reduction at 3 years was 11.6% ($p<0.001$), which is similar to the reduction in major stroke or death at 2 years reported for NASCET patients with ≥70 % stenosis.

Guidelines on surgery for asymptomatic stenosis based on the results of the Asymptomatic Carotid Atherosclerosis Study (ACAS) and Asymptomatic Carotid Surgery Trial (ACST) (21, 22). The results of ACST and ACAS were similar. Although the 5-year risk of any stroke or perioperative death in the nonsurgical group was lower in ACST (11.8%) than in ACAS (17.5%), the absolute risk reductions at 5 years with surgery were not substantially different (5.4% versus 5.9%). The benefit of surgery was proven, was not as pronounced as for the symptomatic patients.

4.6.3 Carotid stenting

Angioplasty of the carotid artery was first performed in 1980 (23). Despite the favorable results, only small series were published. As balloon angioplasty alone carries potential risk factors, including recoil, intimal dissection, and embolization, stenting helps exclude the plaque material from the circulation to prevent embolization and promote the formation of a smooth neointimal layer. The first series of carotid stenting reports appeared in the 1980s (24-26). Concern over cerebral embolization of carotid plaque material during carotid stenting (CAS) led to the introduction of embolic protection

devices (EPDs). The development of more sophisticated protection devices and their availability made the concept of cerebral protection more widely acceptable, currently there is a consensus that protection devices need to be used in each CAS procedure if a device is available. The three types of EPDs in current practice are the filter, distal balloon occlusion, and proximal balloon occlusion with or without flow reversal.

Indications for CAS initially included restenosis after CEA, radiation-induced disease and medical conditions precluding surgery (e.g., coronary artery or chronic pulmonary disease). Endovascular revascularization of carotid occlusive disease offers a less invasive treatment; several trials have compared CEA and carotid stenting.

The Carotid and Vertebral Artery Transluminal Angioplasty Study (CAVATAS) suggested that angioplasty and surgery are equally effective in preventing stroke and the death and disabling stroke rate is the same following angioplasty and surgery (27). The rates of major outcome events within 30 days of the treatment were similar. There were more cranial nerve palsies in the endarterectomy group; procedure related hematoma occurred less often after endovascular treatment than after surgery.

The Stenting and Angioplasty with Protection in Patients at High Risk for Endarterectomy (SAPPHIRE) trial enrolled patients who had at least one co-existing condition that potentially increased the risk of carotid endarterectomy (28). Carotid stenting using protection device resulted in 12.2% one-year major adverse events (stroke, death, or MI), compared to 20.1% for surgery patients. The incidence of stroke was identical for both CAS and CEA, indicating that CAS is non-inferior to CEA.

The Endarterectomy Versus Angioplasty in patients with Severe Symptomatic carotid Stenosis (EVA-3S) and the Stent-Supported Percutaneous Angioplasty of the Carotid Artery versus Endarterectomy (SPACE) are the two most recently published trials comparing CAS and CEA in symptomatic patients (29, 30). The EVA trial was stopped after the enrollment of 527 patients, because the odds ratio of stroke and death was 2.5 times higher in the CAS group. In the SPACE trial nonsignificant difference in ipsilateral stroke was observed. SPACE failed to demonstrate the periprocedural noninferiority of carotid-artery stenting to CEA; endpoint differences were small and nonsignificant. The mid-term results of the two studies indicate that if a patient has been treated successfully without any complications, the risk of stroke is very small and very comparable between CEA and CAS.

A recent metaanalysis of randomized controlled trials comparing CEA with CAS found significantly more minor strokes in stented patients; while significantly fewer cranial nerve injuries and myocardial infarctions occurred with CAS (31).

4.7 Carotid restenosis

The incidence of recurrent carotid stenosis ranges from 1 to 37%; only less than 8% of patients present with restenosis-related symptoms (32). The reported incidence of restenosis varies widely due to the differences in the definition of restenosis applied, the method for diagnosing restenosis and the duration of follow-up. When these figures were taken into account, the incidence of recurrent restenosis following CEA was found to be 6-14%, which equates to an average annual restenosis rate of 1.5-4.5% (33). A systematic review revealed a risk of recurrent stenosis of 10% in the first year, 3% in the second and 2% in the third, suggesting that the rate of restenosis is not linear throughout the follow-up period (34).

Residual disease or technical defects can be the focus of myointimal hyperplasia resulting in early restenosis (within 2 years), while progression of atherosclerosis causes later recurrences. Myointimal hyperplasia is a vascular response to injury; myointimal hyperplasia involves the migration and proliferation of vascular smooth muscle cells as well as the elaboration of extracellular matrix in the intima. Cross clamping of the carotid artery leads to ischemia/reperfusion injury; it has been shown, that an immediate complement activation could be seen after CEA and it was related to the time of clamping of the carotid artery during the surgery (35, 36). There are data indicating that reoccurrence of stenosis after carotid endarterectomy is partially genetically determined (37).

Despite the fact that CEA for recurrent stenosis can be performed with morbidity and mortality rates similar to those of primary CEA, the complication rates appear higher. These result from the fibrotic tissue reaction that obscures the normal plane of dissection, cranial nerve injuries account for the majority of complications and have been reported in up to 48% of cases.

5 Objectives

1. Although surgical revascularization of innominate artery stenosis results in long lasting patency, these procedures are associated with elevated complication rates. *We investigate the safety and long time effectivity of PTA in the treatment of innominate artery stenoses and occlusions.*

2. Surgical revascularization of proximal common carotid artery (pCCA) is an effective and durable treatment; however, the stroke/death rate associated with the transthoracic approach can be as high as 16%. The introduction of extra-anatomic repair reduced the stroke/death rate of surgical repair of pCCA to 4.3%. *Our aim is to assess primary success and safety of endovascular treatment of ostial/proximal common carotid artery lesions and to compare our results with the published data on the surgical options.*

3. Carotid stent selection is influenced by several factors, including the carotid anatomy and lesion characteristics. Stent design may affect technical success and complications in a certain subgroup of patients. *We assess the wall adaptation of a new carotid stent (NexStent) in the carotid bifurcation by means of angiography and high-resolution computed tomographic angiography (CTA).*

4. Early restenosis develops mainly within the first 24 months after the revascularization procedure and its pathological background is myointimal hyperplasia. Only a few studies have been done to compare carotid endarterectomy and stenting, with regard to the early restenosis rate after both procedures. *We compare the early restenosis rate between patients undergoing carotid artery stenting (CAS) and carotid endarterectomy (CEA) at our institution.*

5. Aneurysms of the internal carotid artery are dangerous lesions because of thromboembolism and, occasionally, rupture. The mortality-serious morbidity risk of surgical procedures is 4–10.8% and nerve injury is not uncommon. *Our aim is to treat* carotid pseudoaneurysms using stent-grafts.

6 Patients and Materials

6.1 Angioplasty of the innominate artery

Between January 1, 1981 and December 31, 1999, 89 innominate artery lesions [84 stenoses and 5 short (<1 cm in length) occlusions] were treated with angioplasty. The sex distribution of the patients was almost equal (44 female, 45 male); mean age was 49.0 years (range 21–72 years). Major symptoms included vertebrobasilar insufficiency (46 patients), upper limb ischemia (35 patients) and transient ischemic attacks (17 patients). The degree of stenosis was <60% of the arterial diameter in three patients with severe clinical symptoms, 60–90% in 49 patients and >90% in 32 patients; in five cases occlusions were treated. The initial diagnosis of innominate artery stenosis or occlusion was based on the clinical data, pulse palpation of the radial arteries, comparative blood pressure measurement on both arms, and carotid and vertebral duplex scans to identify a carotid postocclusive Doppler spectrum and/or subclavian steal phenomenon. The diagnosis was always confirmed with angiography. PTA was usually performed in the same session. Antegrade ipsilateral vertebral artery flow was found in 47 patients. In 42 cases subclavian steal syndrome was observed. Angioplasty was carried out via a femoral artery puncture in all but three cases, when axillary artery was utilized. Before the intervention, anticoagulation and platelet aggregation inhibition was achieved by 5000 U heparin i.v., 100 mg sodium pentosan polysulfate i.v., and 125 mg/day aspirin per os. Balloons of a diameter equal to that of the innominate artery just beyond the lesion were chosen for dilatation (9–12 mm). In case of technical difficulties in traversing the curved stenotic origin of the innominate artery, a long guiding catheter was inserted and predilation with a 3–4 mm PTCA balloon was achieved. A control post-angioplasty angiogram was then performed to confirm a satisfactory radiographic result. Aspirin (125 mg daily) was continued (provided there was no contraindication) for at least 6 months after PTA.

Patients were usually discharged 1 day after PTA and asked to come back for a follow-up examination (clinical examination including pulse palpation; blood pressure measurements on both arms; subclavian, common carotid and vertebral artery duplex

scan on both sides) 6 weeks, 3 months and 6 months after PTA and yearly thereafter. Duplex scan examination has been available at our clinic only since 1985; therefore early duplex scan follow-up of the first four patients in 1981 and 1984 was not possible. Technical success was defined as successful angioplasty of the innominate artery lesion with a <50% residual stenosis. Clinical success was based on the clinical examination, including the patients' own assessment of the symptoms. During the follow-up examinations, the innominate artery was considered to be open without significant stenosis if the right radial pulse was palpable, the blood pressure difference between the two arms was <30 mmHg and the flow in the vertebral artery was antegrade (38, 39).
For statistical analysis, the Kaplan–Meier method was employed to calculate cumulative primary and secondary patency rates (SPSS, version 9.0, Chicago, IL, USA).

6.2 Endovascular treatment of proximal common carotid artery lesions

Between January 1, 1994 and December 31, 2006, 153 percutaneous transluminal angioplasties (PTA) including six repeat PTA [rePTA]/stenting procedures one in the follow-up period) were performed on 147 consecutive patients with significant proximal common carotid artery (pCCA) stenosis. Eighty-four percent of the lesions were ostial stenoses, 14% proximal stenoses, and 2% combined. Proximal CCA stenosis was diagnosed by catheter angiography following an initial duplex screening. Inclusion criteria for endovascular treatment were ≥70% luminal diameter stenosis in patients with ipsilateral ischemic neurologic symptoms or >85% stenosis in asymptomatic patients. The decision for treatment was made by consensus between the interventional radiologist, the vascular surgeon, and/or the neurologist. Informed consent of patients was obtained before the procedure in all patients. The average diameter stenosis was 81.5%. Patient age ranged from 21 to 83 years (mean=60.6 years). The group included 76 men and 71 women. The majority of patients had atherosclerotic lesions, 10 patients had stenoses due to irradiation, and one had Takayasu arteritis. There were 32 common carotid artery interventions performed on the right and 121 on the left. Forty-six patients were symptomatic and 101 patients were asymptomatic, including 57 patients with contralateral carotid or vertebrobasilar symptoms and 44 patients with no neurological symptoms. Presenting symptoms in the symptomatic group were amaurosis fugax on

the ipsilateral side (n=9), hemispheric symptoms (n=27), and aphasia in (n=10) patients. Greater than 50% stenoses and/or occlusions in other supraaortic arteries were diagnosed in 124/153 (81.0%) of the cases. We additionally treated 3 innominate artery stenoses, 13 ipsilateral internal carotid artery stenoses, 1 contralateral external carotid artery stenosis, and 3 contralateral subclavian artery stenoses in one stage together with pCCA PTA.

Before the intervention, anticoagulation and platelet aggregation inhibition was achieved by 70 U/kg heparin i.a., and 125 mg/d aspirin p.o. Sodium pentosan polysulfate (100 mg). Angioplasty was carried out via femoral artery puncture in all but one case when the entry site was the axillary artery. Over the 13 years, details of the technique have changed with the availability of new devices. Additionally, some of the variations in technical details were lesion and operator dependent. A 7F introducer guide (typically MPA 1, Cordis) was advanced to the aortic arch. The pCCA lesion was negotiated using a selective cerebral catheter (Headhunter or JB2, Cordis) and a 0.035 inch hydrophilic guidewire (Terumo angled). The size of the angioplasty balloons were chosen based on the diameter of the CCA beyond the lesion (7–9 mm), with a length appropriate to the lesion (20 or 40 mm) (Wanda, Boston Scientific). In case of technical difficulties in traversing the curved stenotic origin of the CCA, occasionally a 0.014 inch guidewire was used to traverse the stenosis and predilation with a 4.0 x 20 mm PTCA balloon (4.0 x 20 mm, Maverick, Boston Scientific) was performed. Finally, completion angiography of the treated lesion and the intracranial circulation of the treated carotid artery in two projections were performed. A stent was implanted in 108 cases. An embolic protection device was used in 16 cases (FilterWire EZ 190 cm, Boston Scientific): 13 in the left carotid artery (3 ostial and 10 proximal stenoses), and 3 in the right carotid (3 proximal stenoses). In 13 cases, neuroprotection was used because of simultaneous internal carotid artery stenting. Until 2002, protection devices were not available at our institution. Life long administration of acetylsalicylic acid was continued after the PTA. Thirty-six patients were on dual antiplatelet therapy (three patients on acetylsalicylic acid + clopidogrel [75 mg per os] and four patients on acetylsalicylic acid + ticlopidine per os [2 x 250 mg/day]). Patients were usually discharged 1 day after the PTA and scheduled for a follow-up examination at 1, 3, 6, 12 months, and every 6 months thereafter.

One hundred fifteen out of 147 patients (78.2%) (undergoing 120/153 [78.4%] successful procedures) had follow-up visits that included carotid duplex scanning and a neurological examination. Clinical follow-up was performed up to 7 years, and mean follow-up time was 24.7 months. Follow-up was carried out by an independent neurologist and results obtained through reviewing the medical records and clinical notes of the patients. New relevant neurological symptoms, such as occurrence of stroke or death were assessed as complications of the procedure.

Technical success was defined as less than 30% residual diameter stenosis on the completion angiogram. A two- or threefold increase in value of peak systolic velocity by carotid duplex examination referred to a 50% or 70% diameter stenosis, respectively. Since direct visualization by carotid duplex during follow-up was not always possible, we refer to the patency rate rather restenosis-free patency rate in our analysis.

The Kaplan-Meier method was employed to calculate cumulative primary and secondary patency rates (SPSS, Chicago, Ill), and the log rank test was used to compare cumulative patency rates between PTA and PTA/stent groups. The occurrence of TIA, stroke, or death was monitored during in-hospital stay (24 to 48 hours) (periprocedural), at 30 days (perioperative), and through the time to the most recent follow-up.

6.3 ICA stenting protocol

Neurological examination, carotid duplex scan, magnetic resonance imaging or computed tomography of the head, and complete diagnostic cerebral angiography were performed on all patients. Stenosis was measured according to NASCET methodology with the distal, normal vessel serving as the reference diameter. Aspirin (100 mg) and clopidogrel (Plavix, 75 mg) were given for at least 3 days before the procedure. Heparin (10,000 U) was administered intra-arterially at the beginning of the procedure; patients with primary lesions received routine prophylactic i.v. atropine (0.5 mg) before balloon dilation. The femoral artery was punctured; in case of iliofemoral occlusion brachial access was utilized. The common carotid artery (CCA) was catheterized with a 4F catheter over a 0.035 inch wire. A 0.035 inch stiff Jindo wire (Cordis) was advanced into the external carotid artery; the sheath and the diagnostic catheter were exchanged for an 8F guiding sheath, which was positioned proximal to the lesion. Quantitative

angiography was performed to precisely measure the stenosis and the diameter of the distal internal carotid artery (ICA) and accurately size the balloons required. The stenosis was crossed with FilterWire EX (Boston Scientific), and the filter was opened. Very severe lesions were predilated with low profile balloons. The stent was deployed across the stenosis and subsequently dilated with a 5 or 6 mm Ultrasoft balloon (Boston Scientific). Completion angiography was performed on the bifurcation and ipsilateral intracranial vessels in three planes: posteroanterior, 45º oblique, and lateral. Technical success was defined as the ability to successfully stent the lesion with residual stenosis of less than 30%. The sheath was removed and the vessel was closed by percutaneous closer device. Patients were discharged on either the first or second day after the procedure. Besides permanent administration of Aspirin, clopidogrel was continued for 6 weeks (40). Patients were scheduled for a follow-up carotid duplex scan at 3, 6, and 12 months.

6.4 High-resolution CT and angiographic evaluation of NexStent wall adaptation

Forty one patients (14 female and 27 male) underwent stenting of 42 carotid arteries at our department. Inclusion criteria were based on those of the NASCET and ACST, which specified that patients with symptomatic or asymptomatic carotid stenosis of at least 70% were eligible. The stenosis treated was found on the left side in 20 cases and on the right side in 22 cases; the mean stenosis was 84±8%. Nine of the 41 patients were symptomatic; 10 lesions were restenosis after carotid surgery. The mean age of the patients was 65±10 years.

CTA examinations were performed by an eight-channel multidetector computed tomographic system (General Electric Lightspeed Ultra) with the following scanning parameters: slice thickness, 1.25 mm; pitch, 0.625; rotation time, 0.5 s; tube voltage, 120 kV; and automatic tube current modulation, resulting in values between 100 mA and 300 mA, depending on the patient's constitution. Scanning range was designed to cover the pre- and poststent segment of the carotids sufficiently, without exposing the patient to unnecessary X-ray exposure. Therefore, an approximately 10-cm-long helical acquisition was performed between the midcourse of the common carotids and the skull base. Eighty to 100 ml of nonionic contrast material with 370 mg/100 ml iodine

concentration was administered by a flow rate of 4 ml/s. Bolus tracking (SmartPrep) was used for scan initiation. Postprocessing of the scan data was performed on a General Electric Advantage Windows 4.2 workstation. Oblique and curved multiplanar reformations were generated manually and by the semiautomatic Vascular Analysis program.

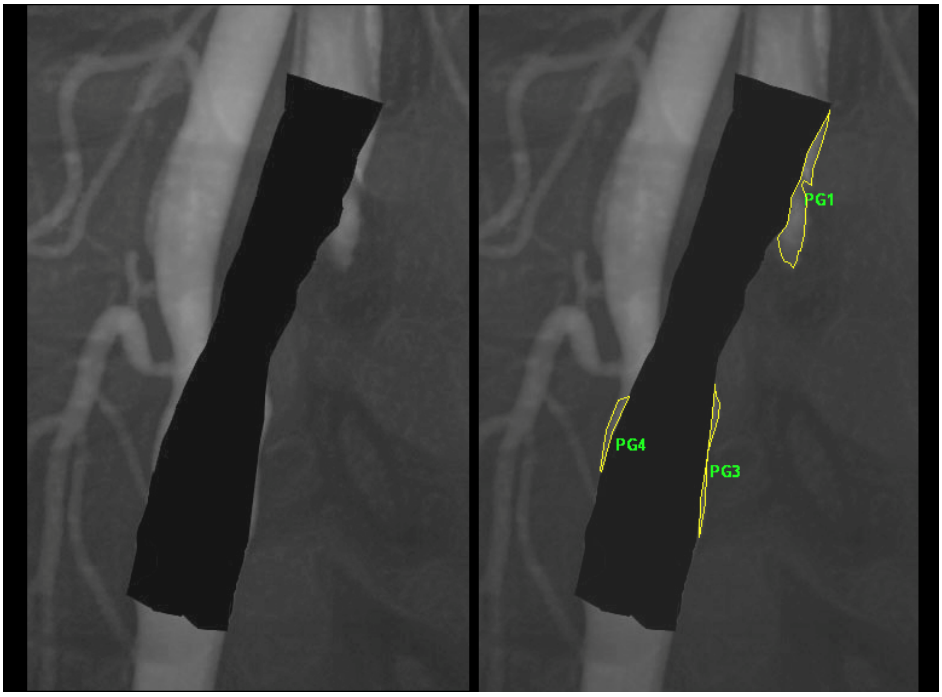


Figure 3. Measurement of incomplete apposition on angiographic image

CTA helped to quantify plaque calcification and evaluate of wall apposition and proper overlapping (no protrusion or infolding) of the stent layers. Plaque calcification was measured by using the method described by McKinney et al (41). Statistical calculations were performed by GraphPad Prism (GraphPad Software Inc.). The relationship between the amount of plaque calcification and the residual stenosis after stenting was tested by Spearman's rank correlation. The adaptation between stent and vascular anatomy were evaluated on angiograms with the following criteria: (1) stent coverage of the plaque; (2) stent-induced kinking of the ICA; and (3) apposition (free area between stent and vessel wall). Angiographic images were calibrated and measured by Image-Pro Express software (Media Cybernetics Inc.). The lack of apposition between stent

filaments and vessel wall was measured as contrast filled area outside of the stent in the carotid bulb and in the regions of former plaque ulcerations (*Figure 3*). For the measurement projection, the largest visible gap between the stent and the wall was selected.

6.5 Early restenosis after eversion carotid endarterectomy versus carotid stenting

Data were retrospectively collected from our database, listing all patients with severe stenosis of the internal carotid artery (ICA), treated between 1st of January and 31st of December in 2004 at the Department of Cardiovascular Surgery, Semmelweis University. We collected patients who underwent CEA or CAS during this period to ensure a mean follow-up time of less than 2 years, since early restenosis is known to develop within this time. The patient population was nonselective and consecutive. During the mentioned period, 206 CAS procedures were performed on 201 patients and 479 CEA were undertaken on 453 patients.

All patients underwent preoperative Duplex ultrasound (US) before carotid revascularization. All carotid Duplex scans were performed by an experienced radiologist using the color scanner and a 7.5 MHz probe (Toshiba, Aplio, Model SSA-700A). The common carotid (CCA), ICA and external carotid arteries (ECA) on both sides were examined in the standard fashion. The spectral measurements were taken with a Doppler probe at an angle of 50° to 60°. Velocities were measured in the distal CCA and the ICA. The diagnostic criteria for ICA stenosis was based on peak systolic velocities (PSV), end diastolic velocities (EDV) as well as internal carotid artery : common carotid artery (ICA/CCA) PSV ratios and modified to detect carotid stenosis at the 70% level, in accordance with the recommended intervention threshold from the Carotid Endarterectomy Trialists (42, 43). Blood flow and compliance are altered in the stented carotid artery, and existing velocity criteria overestimate the degree of restenosis; defining adequate criteria is critical to noninvasively assess the restenosis rate after CAS (44). After US examination, an additional neurological examination was performed by an independent neurologist for all patients.

ICA stenting protocol was described in details in section 7.3. Wallstent were used in 90% of cases, Precise and Xact stent were used in 5–5%. During the study period eversion CEA was the treatment of choice for carotid surgery. The CEA was performed under general anesthesia as described previously. Briefly, the ICA was obliquely transected at its origin in the carotid bulb and was everted cranially, than the plaques were removed. This was followed by endarterectomy of the common and ECAs. After this, the ICA flap was reinserted in its original place (45). Indication for CEA was in accordance with the American Heart Association guidelines (46). After evaluation of the risk factors, patients received adequate medical treatment before and after surgery, in addition to currently accepted anticoagulant and antiplatelet prophylaxis.

Follow-up: First, the baseline clinical parameters and perioperative results were collected from the database of a total of 685 carotid interventions. Patients were then contacted by mail or telephone and were invited to a control carotid Duplex US examination. Of the 479 CEA cases and 206 CAS cases we identified a subgroup of 368 CEA cases (in 347 patients) and 144 CAS cases (in 140 patients) with complete follow-up (18.4 months mean follow-up time, range 6 to 38 months) for determining the early restenosis rates. All patients gave informed consent and the study was approved by the Ethical Committee of Semmelweis University.

There were 368 carotid endarterectomy cases in 347 patients (21 patients with bilateral CEA at different time intervals), among them 180 were right-sided and 188 were left-sided CEA, 362 were due to primary carotid stenosis and 6 due to carotid reoperation (in these 6 patients with recurrent carotid stenosis a CAS procedure was impossible to perform because of the tortuosity of the CCA).

The CAS group consisted of 144 ICA stenting cases in 140 patients (4 patients with bilateral stenting at different time intervals), among them 100 ICA stenoses were of primary origin, whereas 44 ICA stenoses were restenotic.

Perioperative complications and early restenosis: Cardiological complications included tachyarrhythmia, bradyarrhythmia, hypotension, hypertension and angina. Primary endpoints of the study included early restenosis of the treated artery. The mean follow-up time for CEA and CAS patients were 17.9 months (range 6–38 months) and 19.8 months (range 6–36 months), respectively (P=NS). The evaluation of carotid restenosis was performed by US at the Department of Cardiovascular Surgery of the

Semmelweis University of Budapest. The diagnostic criteria for ICA restenosis were based on PSV, EDV as well as ICA/CCA PSV ratios. Restenoses were further categorized as mild (<50%), moderate (50–69%) and severe (≥ 70%).

US velocity criteria for restenosis after carotid endarterectomy: ICA restenosis lower than 50% was diagnosed when ICA PSV was less than 125 cm/sec. Additional criteria included ICA/CCA PSV ratio <2.00 and ICA EDV <40 cm/s. ICA restenosis between 50–69% was diagnosed when ICA PSV was 125–230 cm/sec. Additional criteria included ICA/CCA PSV ratio of 2.00–4.00 and ICA EDV of 40–100 cm/s. ICA restenosis over 70% but less than subtotal occlusion of the vessel was diagnosed when the ICA PSV was greater than 230 cm/s. Additional criteria included ICA/CCA PSV ratio >4.00 and ICA EDV >100 cm/s. In cases of subtotal occlusion of the ICA, the diagnosis was established primarily by demonstrating a markedly narrowed lumen at color or power Doppler US. These criteria had been established according to the Society of Radiologists in Ultrasound Consensus Conference and were internally verified (47).

US velocity criteria for restenosis after carotid stent placement: Stented carotid arteries were examined within the ICA stent at three sites (proximal, mid, and distal) as well as distal to the stent. PSV was obtained from ICA velocities within the stent. End-diastolic velocity values were also determined. The ICA/CCA ratio was calculated from the PSV within the stent and the distal CCA velocity. A <50% ICA instent restenosis was diagnosed when ICA PSV was less than 225 cm/s. Additional criteria included ICA/CCA PSV ratio <2.50 and ICA EDV <75 cm/s. A 50–69% ICA instent restenosis was diagnosed when ICA PSV was 225–350 cm/s. Additional criteria included ICA/CCA PSV ratio of 2.50–4.75 and ICA EDV of 75–125 cm/s. A ≥70% ICA instent restenosis but less than subtotal occlusion of the ICA was diagnosed when the ICA PSV was greater than 350 cm/s. Additional criteria included ICA/CCA PSV ratio >4.75 and ICA EDV >125 cm/s. In cases of near occlusion of the ICA, the diagnosis was established primarily by demonstrating a markedly narrowed lumen at color or power Doppler US (48).

Statistical analysis: Data were collected in MS Excel 2003 and were analyzed with the Statistica 7.1 and SPSS 13.0.1 statistical software products. Categorical variables were reported as absolute numbers and percentages, and continuous variables as medians and interquartile ranges. In cases when the variables exhibited non-Gaussian distributions

we used non-parametric tests in the analysis. Categorical values were compared using the chi-square test and Fischer's exact test. Continuous variables between the two groups were compared using the Mann-Whitney U test. A stepwise logistic regression model was used to analyze the effect of baseline characteristics on any observed association with early restenosis rates. Freedom from restenosis rates was also estimated and illustrated with the Kaplan-Meier method, using log-rank test for comparison of groups. All analyses were performed two-tailed, and $P<0.05$ was considered as significant.

6.6 Stent graft treatment of carotid pseudoaneurysms

Case 1 was a 66-year-old man who underwent ultrasound guided aspiration cytology due to enlarged lymph nodes in the right submandibular region. Six months later the patient returned to the hospital with a pulsatile mass at the right mandibular angle. Carotid ultrasound showed extravasation at the origin of the right ICA into a 2.5–3 cm^2 diameter pseudoaneurysm and diagnosed a left internal carotid artery (ICA) occlusion. Contrast-enhanced computer tomography confirmed the diagnosis and described a 4.2x3.2 cm^2 pseudoaneurysm medial to the right carotid bifurcation, containing thrombus. Angiography verified the left ICA occlusion; the middle cerebral artery on the left side was filled through the left posterior communicating artery. We localized the neck of the aneurysm on the proximal ICA just distal the bifurcation.

Case 2 was an 81-year-old asymptomatic man presented with a slowly growing mass on the left side of the neck. He underwent carotid endarterectomy 23 years ago and had a long history of ischemic heart disease. Carotid duplex scan showed a large pseudoaneurysm at the bifurcation. The subsequent angiogram confirmed the diagnosis and the size of the aneurysm was measured 4 cm in diameter.

Informed consent was obtained from the patients prior to the endovascular procedure. We used local anesthesia to be able to monitor the neurological status of the patients. The right femoral artery was punctured and a 4F sheath was placed into the femoral artery to introduce a diagnostic Headhunter catheter. The patients received 5000 units of Heparin; a 300 cm long Jindo guidewire was advanced into the ICA and the diagnostic catheter was removed. The 4F sheath was replaced by a 10F introducer. Due to the lack

of appropriate length 10F guiding catheter, the left femoral artery was punctured and a 4F Headhunter catheter was introduced to the aortic arch to provide access for control angiogram. The 50 mm long 10 mm diameter Wallgraft was advanced into the ICA on the exchange wire and deployed across the neck of the aneurysm. After deployment the stent was dilated using an appropriate size PTA balloon to assure fixation to the wall. Control angiography was obtained at the end of the procedure. The large introducer sheath was removed and the bleeding was controlled using mechanical compression. The 4F sheath was left overnight in the patient. The heparin was discontinued and the patients were observed in the intensive care unit for 12 h. The patients were placed on daily oral administration of 325 mg aspirin.

All study protocols were approved by the institutional review board of the Semmelweis University, Budapest, Hungary.

7 Results

7.1 Angioplasty of the innominate artery

The technical success rate was 96.6%, in two cases postdilation angiography showed more than 50% residual stenosis (a stent was not available at the time of the dilation of these patients). On one other occasion, the procedure was stopped before the dilatation because the patient lost consciousness. There were no lethal complications during the procedures. There was one major complication: a left occipital lobe infarction in a patient with an occluded left common carotid and left subclavian artery that was considered to be a high operative risk; PTA was therefore chosen as a minimally invasive intervention. As the patient lost consciousness during the procedure, the PTA was stopped before the actual dilation. A CT scan performed 2 days after the procedure showed infarction in the left occipital lobe. One year after the unsuccessful procedure the symptoms (dizziness) of the patient remained the same as preprocedurally and no new neurologic symptom has developed due to the occipital lobe infarction. Other complications of innominate artery PTA included puncture site thrombosis that needed an operation in two cases (2%) and transient neurologic symptoms in four patients (4%). Clinical follow-up, including objective data (blood pressure measurements on both upper extremities), is available for 56 (63%) patients. There were six patients with altered flow velocity pattern in the right subclavian artery, but the blood pressure difference between the two arms was less than 30 mmHg and these patients had no relevant symptoms; therefore angiography was not indicated. There were three patients with a blood pressure difference >30 mmHg. One had no relevant symptoms. In the remaining two cases with relevant symptoms angiography proved more than 70% restenosis; both were successfully treated with re-PTA. Further follow-up showed an open innominate artery without significant restenosis 14 and 30 months following re-PTA. Cumulative primary patency was 98±2% at 6 months, 95±3% at 12 months, and 93±4% at 16–117 months (*Figure 4*). Secondary patency was 100% at 6 months, 98±2% at 12–117 months. The mean primary and secondary patency time was 32.8±3.61 and 33.5±3.58 months, respectively. Based on the clinical examination

including the patients' own assessment of the symptoms, 34 (61%) patients became asymptomatic, 18 (32%) showed improvement and only four (7%) did not improve.

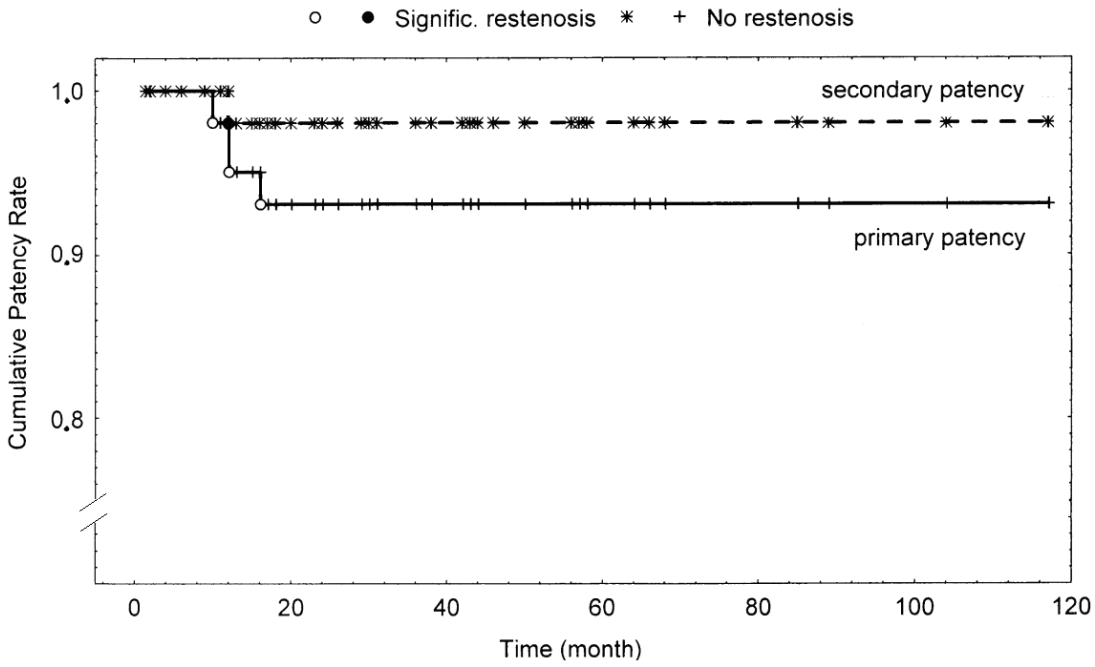


Figure 4. Kaplan–Meier analysis of patency rate for 50 innominate artery interventions, excluding initial failures.

7.2 Endovascular treatment of proximal common carotid artery lesions

The initial technical success rate was 98.7% (151 of 153 lesions in 147 patients). In two cases, the angioplasty was not successful: in one case it was impossible to cross the lesion with a guidewire, while in the second occasion, the procedure was stopped before the dilatation was done because of ipsilateral TIA (the patient did not undergo a second attempt of endovascular therapy).

There were no procedure related deaths. Eight neurological complications (5.2%) occurred during the hospital stay: 3/153 (2%) ipsilateral major strokes during the procedure, 3/153 (2.0%) ipsilateral, 1/153 (0.7%) contralateral TIAs within 4 hours of the intervention.

One hundred fifteen out of 147 (78.2%) patients, representing 120/153 (78.4%) successful procedures were available for follow-up evaluation. Eleven unrelated deaths (gastrointestinal and hepatic malignity) occurred 35 days to 52 months following the procedure.

More than 50% diameter restenosis was detected in 11/115 (9.6%) patients: 51% to 69% diameter restenoses n=2; 70% to 99% stenoses n=6; occlusion n=3. Eight patients (7.0%) had angiography. Angiography revealed one 50% to 69% stenosis, and there was no indication for rePTA in this patient. Seventy percent to 99% restenosis was detected in seven patients (in one patient, CDS underestimated the degree of stenosis). Successful rePTA was done in six cases; one patient refused the offered intervention.

Follow-up of rePTA patients revealed restenosis in 3 cases at 14, 16, and 18 months following rePTA. Two of these were 50% to 69% secondary restenosis with no indication for further intervention. One patient was offered endovascular therapy; this patient did not consent to the procedure by the end of the follow-up period.

Two asymptomatic patients showed new neurological symptoms: one contralateral TIA (19 months postprocedure) and one minor stroke (52 months postprocedure). The cumulative primary patency rate was 97.9%±2.1% at 1 year, 82.0%±7.1% at 4 years, and 73.5%±12.7% at 84 months. The cumulative secondary patency rate was 100% at 1 year, 88.0%±7.0% at 4 years, and 88.0%±7.0% at 84 months (*Figure 5, A*). The mean primary and secondary patency times were 23.9 and 24.9 months, respectively. In the PTA-only group, the primary patency rate was 97.2%±3.6% at 1 year, 86.5%±11% at 4 years, and 79.1%±11% at 84 months. In the PTA + stent group, the primary patency rate was 96.0%±2.5% at 1 year and 88.2%±5.3% at 4 years and 58.1%±12% at 74 months In the PTA + stent group, longest follow-up was 74 months (*Figure 5, B*). Log-rank test showed no statistical difference in primary (P=0.825) (*Figure 5, B*) and in secondary (P=0.680) (*Figure 5, C*) cumulative freedom from restenosis between PTA alone (n=34) or PTA/stent (n=84) (*Figure 5*).

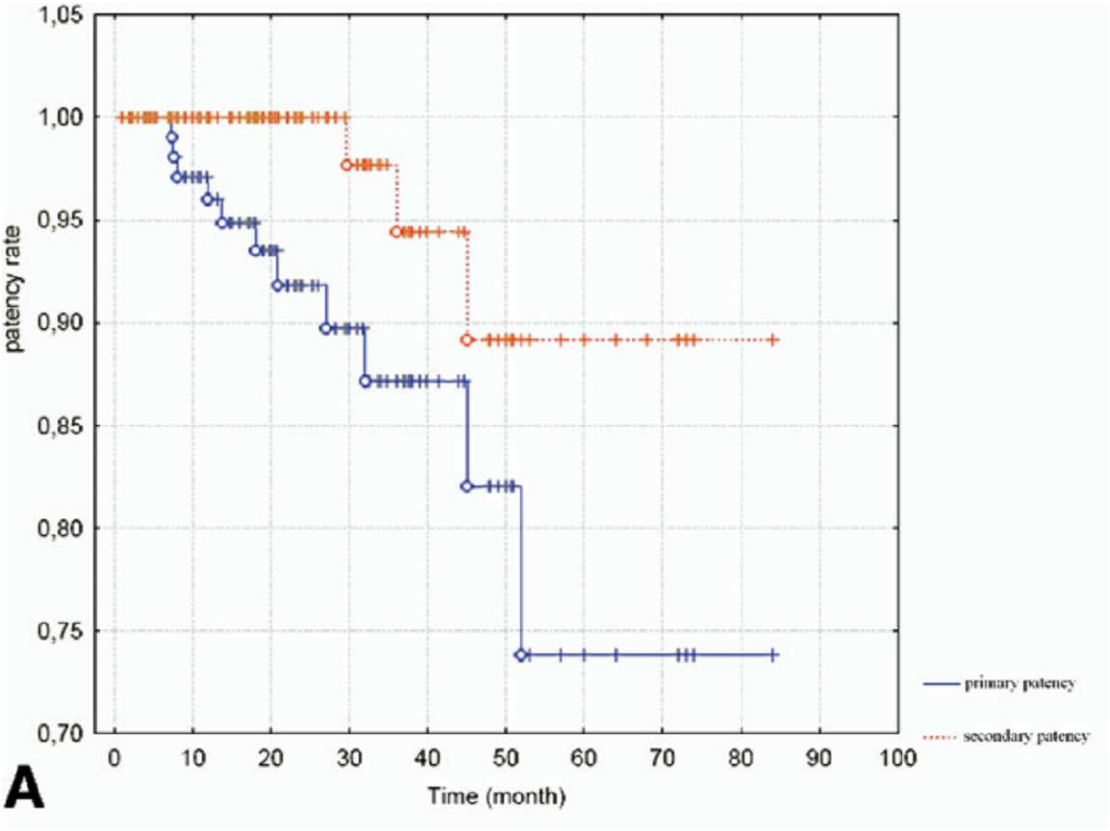
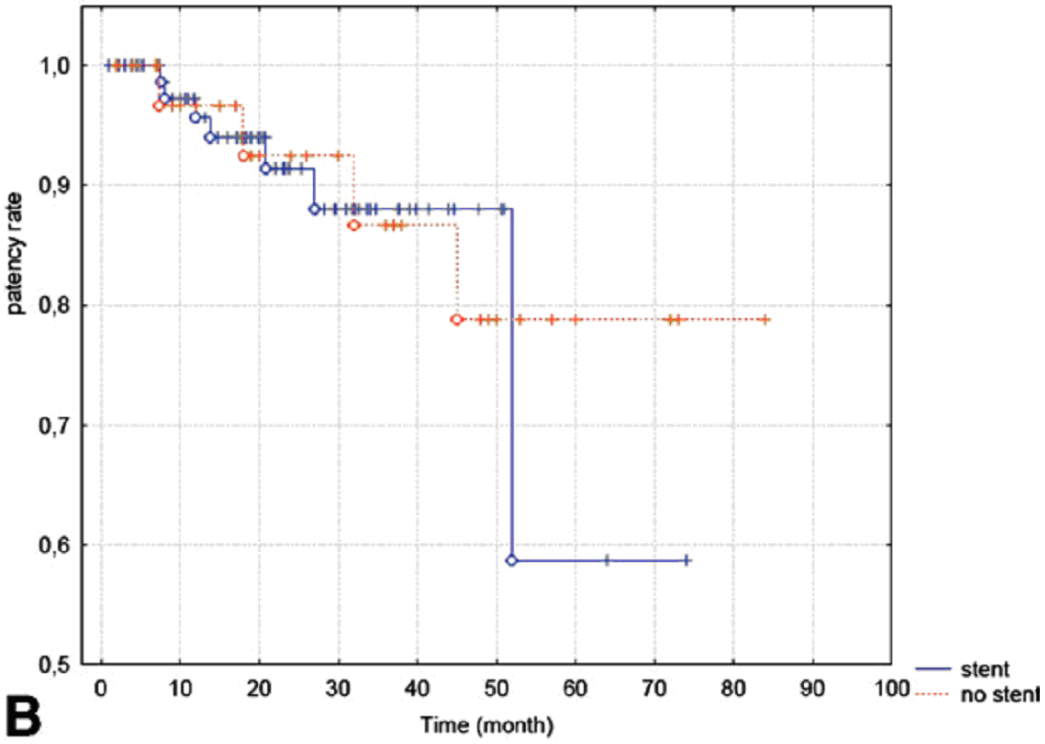


Figure 5. A, Kaplan-Meier analysis of cumulative patency rate for 120 proximal common carotid artery interventions, excluding initial failures.



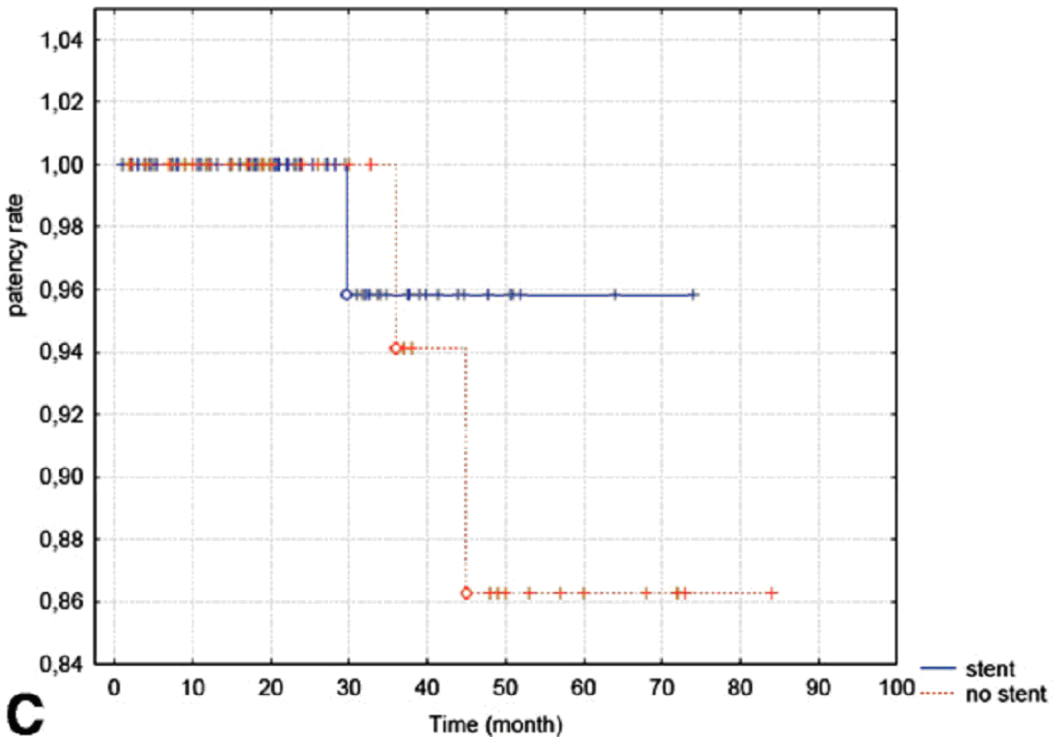


Figure 5. B, Kaplan-Meier curves of primary cumulative patency rate for 34 proximal common carotid artery angioplasty and 86 proximal common carotid artery stent implantation. Log rank test was used to compare primary cumulative patency rate between PTA and PTA/stent groups. (P=0.825). C, Kaplan-Meier curves of secondary cumulative patency rate for angioplasty and stent implantation. Log rank test was used to compare secondary cumulative patency rate between PTA and PTA/stent groups (P=0.680).

7.3 High-resolution CT and angiographic evaluation of NexStent wall adaptation

Forty-two ICAs of 41 patients were treated endovascularly with NexStent. All procedures were performed with a distal protecting device; the technical success rate was 100%. Stenosis before the procedure was 84±8%. After stenting, residual stenosis was 15.7±7%. Predilation before stent deployment was used in four cases. We noticed transient ischemic attack during the procedures of two asymptomatic patients. One patient had prolonged bradycardia and hypotension. There was one case of stent misplacement; the stent was placed too distally, which required placement of a second stent. Twenty-five bifurcations had straight anatomy; in 12 cases slight and in 5 cases significant tortuosity was noticed. Control angiography showed one poststent angulation

and one kink formation, both noticed in patients with significant tortuosity, but these did not result in significant stenosis. Patchy calcification was seen in 12 cases and large calcified areas were noticed in 13 cases. The residual stenosis and the amount of calcification showed weak correlation (Spearman correlation coefficient=0.345, P=0.0154). Plaque ulceration was identified in seven cases. Postprocedure angiography and CTA showed good coverage of the lesions, and in all cases, the stent properly covered the entire length of the treated lesion. The edges of the stent did not show dehiscence from the vessel wall except in one case, when a non-ostial ICA lesion was treated and the stent did not completely cross the bifurcation. Incomplete stent apposition, with visible gaps between the stent and the wall, was identified and measured on angiographic images in 12 cases. Six of them were associated with the seven ulcerative lesions (*Table 1*). The unrolling of the stent was complete in all cases; there was no layer protrusion or infolding into the lumen.

Table 1. Measurement of NexStent wall apposition

Patient no.	**Gap size (mm^2)**	**Ulceration present**
2	3.2	No
3	7.3	Yes
4	3.9	No
5	12.9	Yes
9	4.9	No
15	5.0	No
20	0.8	Yes
25	6.3	No
33	10.1	Yes
34	6.2	Yes
36	6.0	No
41	19.0	Yes

7.4 Early restenosis after eversion carotid endarterectomy versus carotid stenting

Twenty-four neurological complications (5.01%) occurred among patients involved in the CEA group: 7/479 (1.46%) major strokes, 8/479 (1.67%) minor strokes and 9 (1.88%) transient ischemic attacks (TIA). One (0.21%) acute myocardial infarction (AMI), 9 hematomas (1.88%) and 5 cranial nerve injuries (1.04%) were also noted in this group of patients. In the CAS group, among all patients (206) involved in the study, one major stroke (0.48%), 3 minor strokes (1.46%), 18 TIAs (8.74%) and one AMI (0.48%) were recorded. Two deaths were noted in the CEA group (0.42%) and one in the CAS group (0.48%). According to the relevant complications, significantly higher incidence of TIA was found after CAS than after CEA. In Table 2 are reported the complication rates only for the patients followed-up. Regarding these patients no differences between those of the CEA and CAS groups were noted in terms of age and gender distribution and degree of carotid stenosis. Comparing concomitant diseases, a higher incidence of hypertension and peripheral arterial disease were reported in the CEA group, and a higher incidence of arrhythmias and malignant diseases were found in the CAS group. According to the SAPPHIRE definition, incidence of high risk patients was significantly different between the two groups. There were no differences in relevant laboratory parameters (Table 2).

The percentage of ICA stenosis was similar between CEA and CAS groups before intervention. Overall, there was no significant difference in the frequency of symptomatic lesions between the two groups: 45.10% of CEA patients and 36.10% of CAS patients had preprocedural symptoms. With regard to the transient neurological symptoms (TIA, amaurosis fugax) the difference also did not reach the significant level (21.70% vs. 24.30% for the CEA and CAS groups, respectively, P=NS.). These results are summarized in Table 2.

Table 2. Preoperative characteristics and perioperative complications of patients followed-up

	CEA (N=368)	CAS (N=144)	P value
Age	67.2 (59.3-74.1)	65.8 (57.4-74.0)	P=0.39
Gender (male)	56.25% (207/368)	62.5% (90/144)	P=0.10
Symptomatic	45.1% (166/368)	36.1% (52/144)	P=0.06
T1A/AFX	21.7% (80/368)	24.3% (35/144)	P=0.53
Stenosis grade	90% (80-90)	90% (85-90)	P=0.98
High risk patient*	46.74% (172/368)	70.83% (102/144)	P<0.05
Hypertension	86.7% (319/368)	69.4% (100/144)	P<0.05
CAD	32% (118/368)	38.8% (56/144)	P=0.14
PAD	31.8% (117/368)	15.9% (23/144)	P<0.05
DM	27.4% (101/368)	22.91% (33/144)	P=0.29
Heart valve disease	3.53% (13/368)	4.86% (7/144)	P=0.48
Arrhythmia	2.9% (11/368)	7.6% (11/144)	P=0.02
Malignant disease	2.2% (8/368)	5.5% (8/144)	P=0.04
Statin usage**	52.26% (150/287)	56.63% (47/83)	P=0.48
Laboratory parameters †			
White blood cell count (M/L)	7.7 (6.3-9.3)	7.3 (6.3-7.9)	P=0.07
Red blood cell count (G/L)	4.4 (4.1-4.8)	4.5 (4.0-4.9)	P=0.80
Hemoglobin (g/dL)	13.4 (12.4-14.4)	13.6 (12.6-14.6)	P=0.48
Hematocrit (%)	39.0 (35.9-41.5)	39.5 (36.3-43.0)	P=0.35
Platelet count (M/L)	243.0 (196.0-295.0)	229.0 (198.0-266.0)	P=0.21
Creatinine (Imol/L)	90.0 (77.0-107.0)	88.0 (76.0-111.0)	P=0.79
Urea (mmol/L)	6.8 (5.5-8.3)	7.0 (5.9-9.6)	P=0.14
Protein (g/L)	75.1 (70.3-79.3)	74.5 (72.2-77.5)	P=0.83
Glucose (mmol/L)	6.6 (5.5-8.9)	6.0 (5.3-7.2)	P=0.08
Bilirubin (Imol/L)	8.6 (6.8-11.2)	9.0 (6.7-11.6)	P=0.78
Cholesterol (mmol/L)	5.4 (4.6-6.5)	5.6 (4.7-6.3)	P=0.83
Triglycerides (mmol/L)	1.8 (1.2-2.4)	1.8 (1.4-2.3)	P=0.75
Perioperative complications			
TIA	2.2% (8/368)	7.6% (11/144)	P<0.05
Minor stroke	0.8% (3/368)	2.1% (3/144)	P=0.23
Major stroke	0.8% (3/368)	0% (0/144)	P=0.27
Cardiovascular complications	1.1% (4/368)	4.1% (6/144)	P=0.02

Values presented in percentage (absolute numbers) and median (interquartile ranges). Statistical test used: Mann-Whitney U test (age and laboratory parameters) and chi-square test (gender, symptoms, concomitant diseases); *Including at least one of the following risk factors: contralateral carotid occlusion, recurrent stenosis, age>80 yr, ischemic heart disease; **Data of statin usage were available of approximately 80% of CEA patients and 60% of CAS patients; † Laboratory data were available of approximately 70% of CEA patients and 40% of CAS patients

Significantly more transient neurological (TIA: 2.20% vs. 7.60% for the CEA and CAS groups, respectively, P <0.05) and cardiovascular (1.10% vs. 4.10% for the CEA and CAS groups, respectively, P <0.05) symptoms occurred after CAS than after surgery. No difference between groups in terms of minor stroke (0.80% vs. 2.10% for the CEA and CAS groups, respectively, P >0.05) and major stroke (0.80% vs. 0% for the CEA and CAS groups, respectively, P >0.05) was observed (Table 2).

CEA: In the CEA group, the mean follow-up time was 17.9 months. The number of patients participating in follow-up was relatively high: 76.80% (368/479). Moderate (50–69%) restenosis occurred in 11.41% (42/368), whereas the incidence of severe (≥ 70%) restenosis was 10.05% (37/368) in the CEA group. Further evaluation regarding the side of restenosis revealed no difference between right-sided and left-sided CEA (data are not shown).

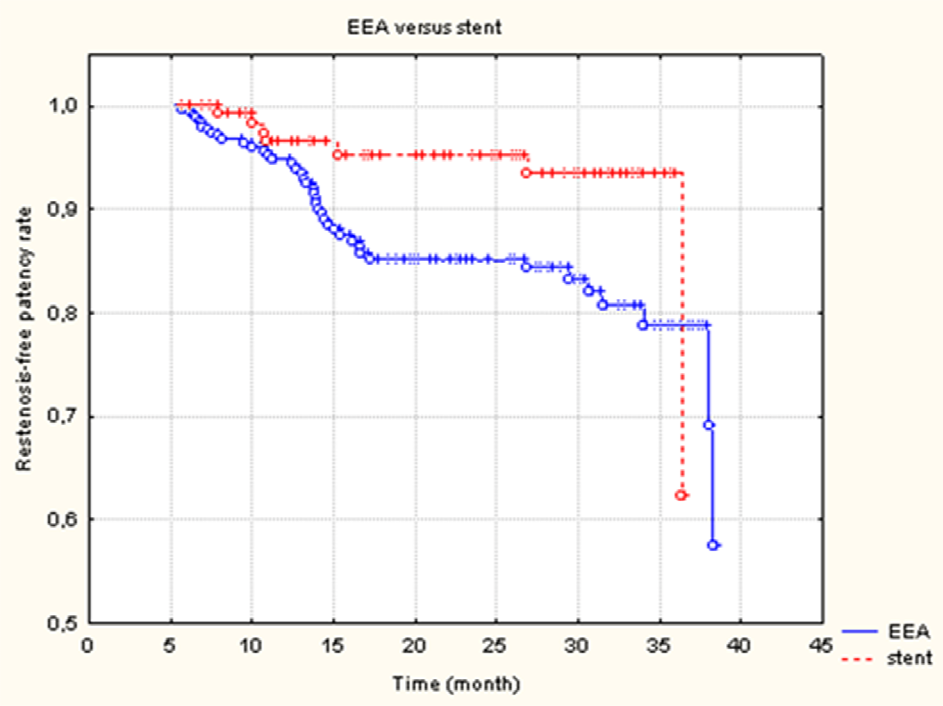
CAS: For the CAS group, the mean follow-up time was 19.8 months. The follow-up proportion of CAS patients was 69.90% (144/206), which did not differ significantly from that of the CEA patients. Moderate (50–69%) restenosis occurred in 4.86% (7/144) of this group. Severe (≥ 70%) restenosis occurred in 3.47% (5/144) of the CAS group. Further results – according to the type of the treated lesion – are summarized in Table 3. Incidence of instent restenosis of greater than 50% was higher in patients stented for postendarterectomy restenosis than in subjects stented for primary stenosis (13.6% vs. 6%). However, the difference was not statistically significant.

Table 3. Restenosis in the CEA and CAS groups at the end of the follow-up (18.4 months)

Restenosis	CEA	CAS	
		Primary stents	Post EEA stents
Moderate (50-69%)	42/368	4/100	3/44
Severe (≥70%)	37/368	2/100	3/44
Overall above 50%	79/368	6/100	6/44

Restenosis in the CEA versus CAS group: Evaluation with the Kaplan-Meier life table analysis showed a significant difference in freedom from both moderate (50–69%) and severe (≥ 70%) restenosis between the CEA and CAS groups in favor of the stent (Figure 6). The difference has become more apparent when severe restenosis (P=0.006) was compared with moderate restenosis (P=0.025). After further adjustment of data according to lesion type treated with stent results were as follows: there was a greater difference in the incidence rates of moderate (50–69%) restenosis between CEA and those CAS patients who underwent treatment with a primary stenosis (primary stents) (P=0.016). In case of severe restenosis the statistical significance was even more pronounced (P=0.002) when CEA was compared with primary stenting (Figure 7).

Logistic regression analysis was performed to assess variables associated with moderate and severe restenosis. Univariate analysis showed that female gender was associated with severe restenosis irrespectively of the interventional technique (OR: 2.02 [CI: 1.07–3.80], P=0.028). The odds ratio was found to be higher when only those patients were selected who underwent CEA (OR: 2.61 [CI: 1.28–5.32], P=0.006). No such association was found for the CAS group or for male patients.



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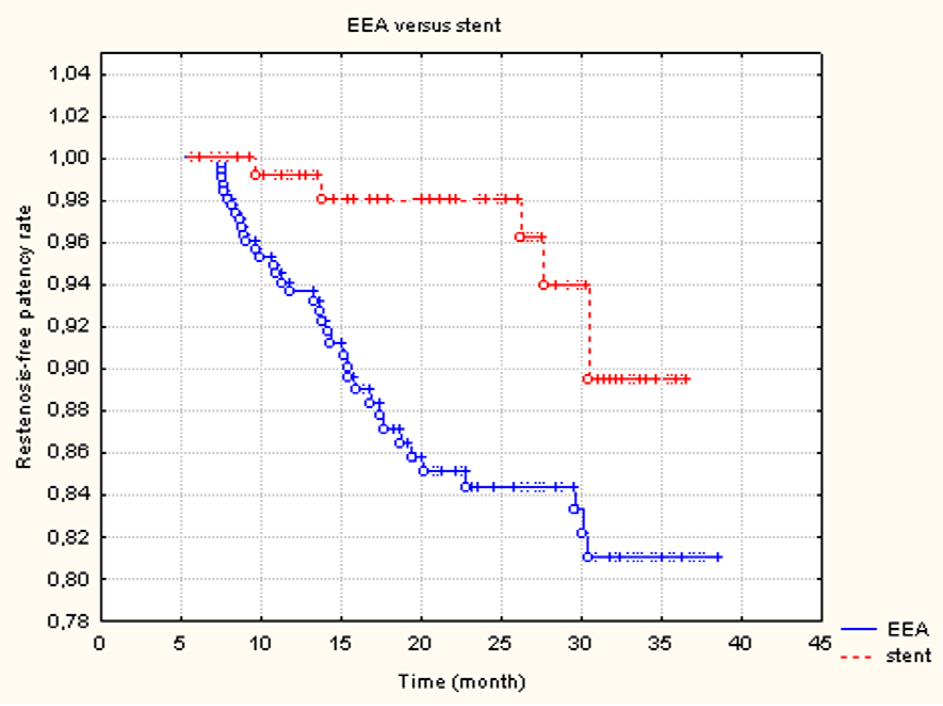
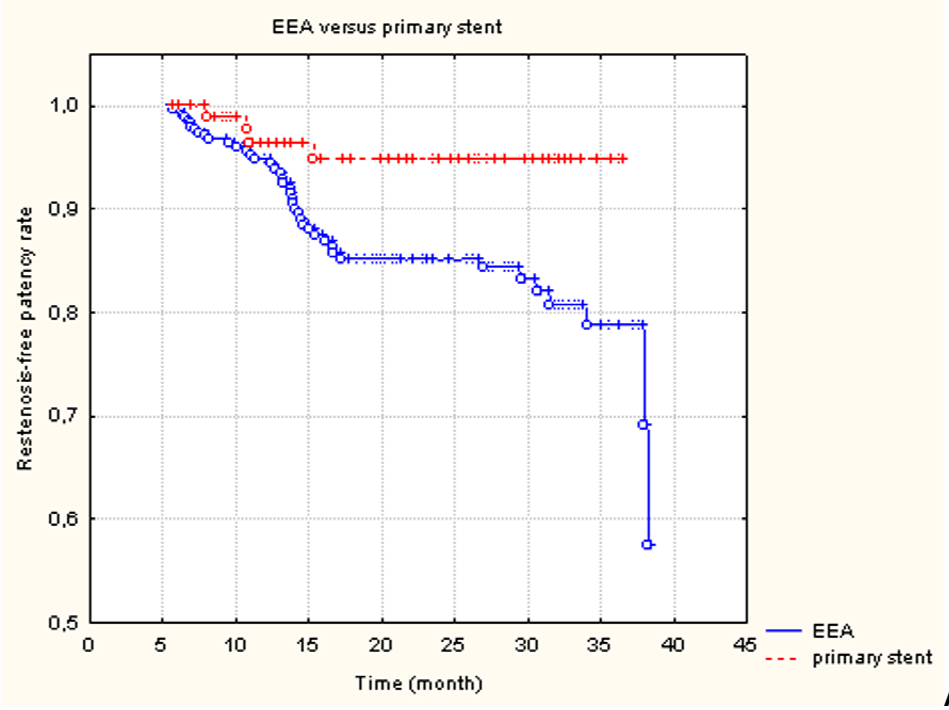


B

Figure 6. Freedom from restenosis, comparison of all CEA and all CAS cases.
A) Kaplan-Meier analysis of moderate (50-69%) restenosis for CEA and CAS groups (P=0.025);
B) Kaplan-Meier analysis of severe (≥70%) restenosis for CEA and CAS groups (P=0.006).



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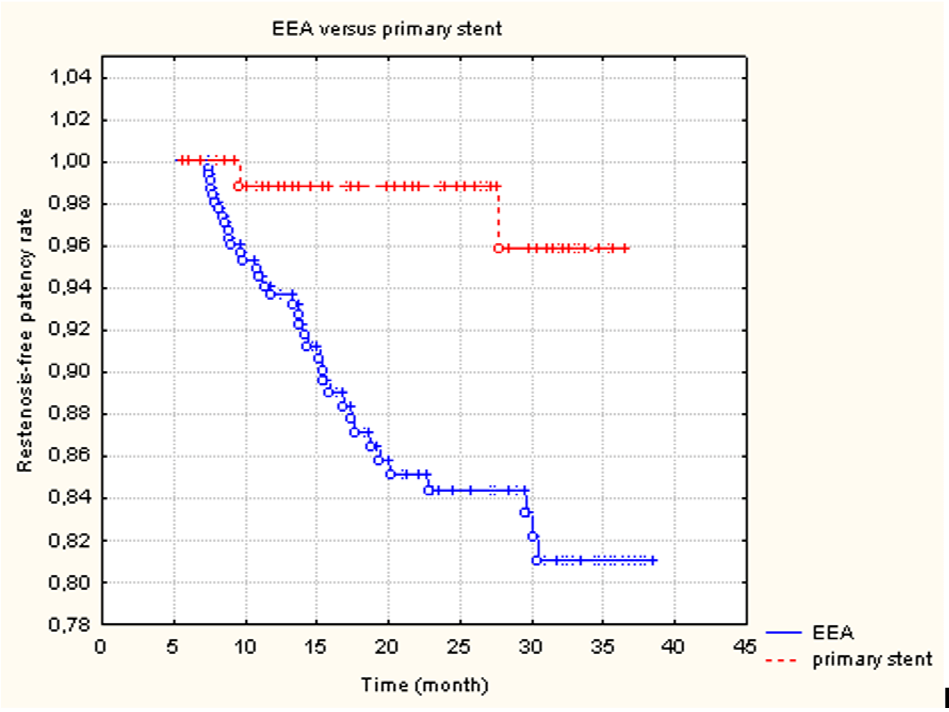

B

Figure 7.-Freedom from restenosis, comparison of all CEA and primary CAS cases.
A) Kaplan-Meier analysis of moderate (50-69%) restenosis for CFA and CAS groups (P=0.016);
B) Kaplan-Meier analysis of severe (≥70%) restenosis for CEA and CAS groups (P=0.002)

7.5 Stent graft treatment of carotid pseudoaneurysms

Case 1. Control angiography on the following day of the procedure showed no contrast extravasation into the aneurysm and filling of the ECA was delayed. The patient was discharged on the third day. The patient remained asymptomatic at the 6 weeks, 6 months and 1 year follow-up examinations. Duplex US demonstrated patent carotid artery with continued obliteration of the pseudoaneurysm during the follow-up period.

Case 2. Postprocedural angiography still showed filling of the aneurysm sack after the deployment. A control angiography 5 h after the intervention showed no filling of the pseudoaneurysm. On the following day the patient complained of dyspnoe, cardiology consultation found signs of heart failure but no major cardiac event. Blood pressure remained in the normal range; control carotid duplex scan 2 days later confirmed patency of the graft and showed no extravasation. However, 3 days later repeated duplex examination was performed because of amaurosis of left eye and revealed occlusion of the endograft. Follow-up neuro exams showed no neurological symptoms.

8 Discussion

8.1 Angioplasty of the innominate artery

Innominate artery stenosis or occlusion can be responsible for cerebral, ocular or upper limb ischemia. Symptomatic lesions of the innominate artery that result from obstruction of blood flow to the common carotid and subclavian arteries or embolization from incomplete occlusions with ulcerations need operative treatment (49). No prospective comparison of innominate artery PTA with surgery has been reported. Lesions of the innominate artery have been treated via the transthoracic or extrathoracic route. Mortality of the transthoracic group varies between 3% and 16%; extrathoracic surgical procedures have an associated lower mortality, but nevertheless have a high complication rate (11-16). Percutaneous therapy for occlusive arterial disease may have several advantages over standard surgical therapy, including its minimally invasive nature, greater patient acceptance, avoidance of general anesthesia and lower cost-per-unit treatment. PTA of the innominate artery has been done in most centers in a relatively small number of cases (n=13 in one study (50), n<18 in the other published studies (38, 50-54).

Due to the higher complication and mortality rate of surgery, and the good patency results without any mortality of PTA, at our clinic all innominate artery stenoses and short occlusions (less than 1 cm in length) as well as occlusions with medical contraindications for surgery are currently treated with PTA. Surgery is indicated only in the case of unsuccessful PTA or long segment occlusion (38, 50, 51, 53, 55). This approach has gradually changed since the 1980s. The indication has always been a joint decision by the vascular surgeon and interventional radiologist. The increasing number of innominate artery PTA per year and the decreasing number of innominate artery operations per year during the last 19 years (*Figure 8*) underscore the above concept.

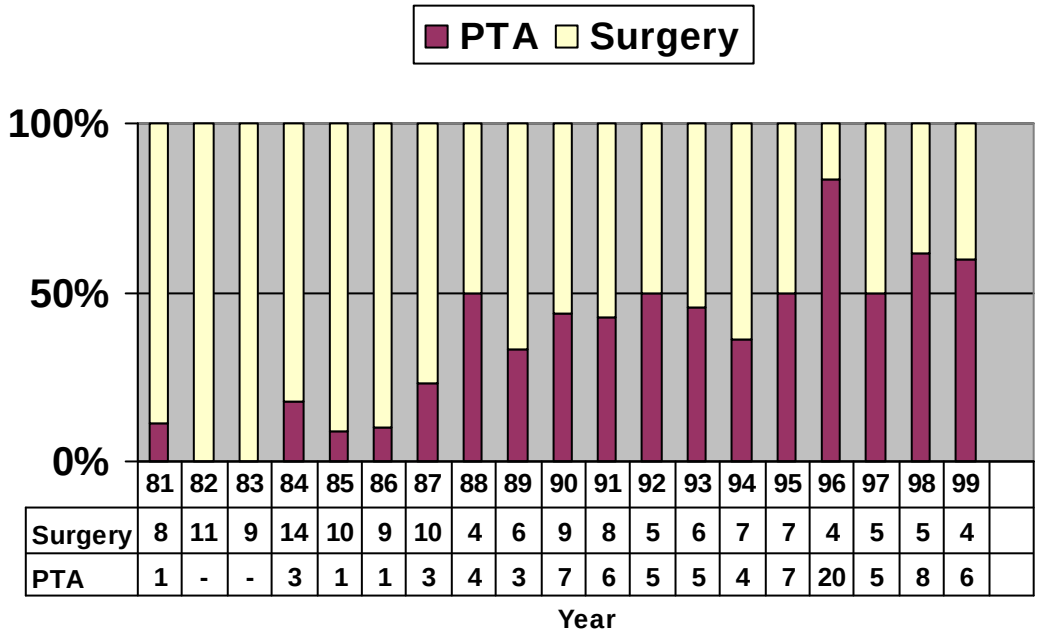

Figure 8. Number of angioplasties and surgical treatment of innominate artery stenoses and occlusions between 1981 and 1999 at the Clinic of Cardiovascular Surgery, Faculty of General Medicine, Semmelweis University, Budapest, Hungary

Innominate artery occlusion is frequently associated with stenoses of other brachiocephalic arteries (11, 56) . In contrast to the male predominance observed in other atheromatous lesions, innominate artery stenoses and occlusions occur with equal frequency in both sexes, as suggested by the literature (11-13) and confirmed by our study. The mean age was lower than expected, the distribution spreading even between 30 and 70 years, with an average of 49 years. This suggests that arteritis - besides atherosclerosis - is the cause of the stenosis or occlusion of the innominate artery in a larger percentage of cases than in lower limb or renal artery stenoses or abdominal artery aneurysm.

Primary stenting or stenting lesions with significant residual stenosis following PTA has been very common for most vascular beds during the last 5–10 years. Until 1996, stent implantation was not available in Hungary. In the 39 cases between 1996 and 1999 there was only one post-PTA angiography that showed significant residual stenosis; thus we performed only one stent implantation, which eliminated the residual stenosis in this case. In a recent study, a Palmaz stent was employed in 26 patients with supraaortic artery stenoses, including eight innominate artery stenoses, along with surgical exposure

of either the common carotid or the brachial artery; initial success rate was 92.8%, and 85% of the vessels remained patent, including initial failures, during a mean follow-up period of 27 months (52) (patency rate excluding initial failures was 91.7%). The patency rate of this stent study is not better than our results (93.6% excluding initial failures, mean follow-up period 32.4±3.5 months) with only one stent implantation out of 89 patients. This suggests that, for the innominate artery, primary stent deployment is not mandatory; however, it may often eliminate significant residual stenosis following suboptimal balloon dilation.

Earlier reports as well as our study showed that the risk of embolization during innominate PTA is low (50, 51, 55, 57). In our series of 89 innominate PTAs, the only major complication was due to either ischemia or embolization - these two causes were indistinguishable. In the study by Dorros et al. (51) on 30 subclavian and three innominate arteries, they reported that 89% of the patients became asymptomatic, 9% improved and 4% showed not change. These figures are comparable to the results achieved by our group. In the other reports, small number of innominate artery PTAs (n=2–13) are reported together with PTA of other supraaortic (usually subclavian) arteries (n=20–80) without giving separate follow-up data for the innominate artery, and therefore these studies are not comparable with our results. Combined patency rates of subclavian and innominate arteries range from 43% for occlusions up to 100% for stenoses at variable follow-up periods. The good patency rate in the case of the innominate artery is most likely because of its large size and high flow.

PTA should be the treatment of choice in cases of symptomatic innominate artery stenosis and a short occlusion (less than 1 cm in length); surgery is indicated if PTA (and/or stent insertion) is unsuccessful or in the case of long occlusion.

8.2 Endovascular treatment of proximal common carotid artery lesions

Before the era of endovascular therapy, surgical treatment was the only option in the management of occlusive disease of pCCA. Surgical revascularization of pCCA and other supraaortic trunk lesions is an effective and durable treatment; however, the mortality/morbidity rate associated with the transthoracic approach can be as high as 16% (*Table 4*) (10).

Table 4. Surgical revascularization of supraaortic trunk lesions

Author	Year	No. of patients; cases	Trial type	Primary success rate	Indication	Postproc antiplatelet therapy
Berguer et al (58)	1999	173;182	Retrosp (extra-anatomic)	100%	>75% stenosis; 82% of patients symptomatic: cerebrovascular ischemia (66%), hand ischemia (13%), LIMA steal that lead to angina or congestive heart failure after LIMA CABG (3%)	unknown
Berguer et al (10)	1998	98;100	Retrosp (transthoracic)	100%	87% symptomatic: cerebrovascular ischemia in 83%; upper extremity ischemia 4%	single

Table 4 continued

Author	Non neurol compl	Neurol compl periprocedural	30 days all stroke/death	Restenosis rate	Follow-up
Berguer et al (58)	Asymptomatic graft occl.: 2%; AMI: 3%;Pulm compl: 5%; graft infection: 1%	Death: 0,5% Stroke: 3,8%	4.30%	Primary: 5 years: 9%, 10 years: 18%	mean 53±5 months
Berguer et al (10)	2 asymptomatic graft occlusions, 3 nonfatal MI, 7 significant pulmonary complications, 3 sternal wound infections, 1 recurrent laryngeal nerve injury	Death: 8% Stroke: 8%	16%	Primary: 5 years: 6%, 10 years: 12%	mean 51±4.8 months

The introduction of extra-anatomic repair reduced the mortality rate of surgical repair of CCA to 4.3% (*Table 4*) (58).

Nevertheless, having introduced the balloon dilation method at our department in the early eighties, the operative reconstructions of CCA was minimized to the cases of CCA occlusions or multiple lesions of the supraaortic vessels. In addition, surgery is indicated in the case of unsuccessful endovascular therapy.

Data on endovascular treatment of pCCA lesions are scarce. There is only one other study on transfemoral elective stenting of 42 proximal common carotid artery lesions (*Table 5*) (59). In that study, the periprocedural neurological complications rate was 4.7% (two minor strokes) with an additional death due to retroperitoneal hemorrhage within 24 hours of the procedure, leading to a 7.1% 30-day all stroke/death rate. However, the authors claimed that all 30-day procedure-related neurological events and

deaths occurred in the first 2 years of the 5-year period studied, and expected further reductions in periprocedural events with experience and improved techniques, such as use of protection devices (59).

The neurological complication rate in the current study was lower (3/115, 2.6%); however, our study is retrospective, and follow-up was not available for all patients due to the long time-span (13 years) of treatment. An alternative option for treatment of pCCA lesions is synchronous carotid endarterectomy and retrograde endovascular treatment of the common carotid artery stenosis (combined treatment) (*Table 5*). There are numerous reports concerning this approach (n=10), but all represent small patient cohorts (range 6-23), therefore, any conclusion from these studies are limited. Carotid bifurcation stenting is routinely done under dual antiplatelet therapy. On the contrary, dual antiplatelet therapy was not routinely used in many of the published studies of pCCA endovascular procedures, including this report. However, use of dual antiplatelet therapy and protection devices, when technically possible, may further reduce the number of neurological complications associated with pCCA endovascular treatment.

Table 5. Endovascular treatment of pCCA lesions

Author	Year	No. of patients; cases	Trial type	PTA only/ PTA+stent	Primary success rate	Indication	Postproc antiplatelet therapy
Percutaneous PTA/stent							
Chio et al (59)	2003	37;42	Prosp	0/42	95%	>50% stenosis	u
Current study	2007	147;153	Retrosp	45/108	98.6%	31.2% of patients symptomatic 68.7% asymptomatic	Double
Surgical and retrograde PTA/stent							
Peterson et al (60)	2006	9;9	Retrosp	0/9	100%	80% of patients symptomatic (>90% sten)	Double
Payne et al (61)	2006	8;8	Retrosp	8/0	100%	Severe inflow disease	Aspirin only
Allie et al (62)	2004	23;23	Prosp	0/23	97%	Various	u
Grego et al (63)	2003	10;10	Retrosp	0/10	87%	12.5% TIA; 37.5% non focal cerebral symptoms	Aspirin only
Macierewicz et al (64)	2000	6;6	Retrosp	0/6	100%	67% asymptomatic 33%cerebral ischemia	Aspirin only
Arko et al (65)	2000	8;8	Retrosp	0/8	100%	62.5% TIA; 7.8% non disabling stroke; 7.8% amaurosis	Double
Levien et al (66)	1998	20;20	Retrosp	0/20	97%	43% TIA; 20.5% amaurosis; 6.8% retinal emboli; 29.7% asymptomatic	Aspirin only
Sullivan et al (53)	1998	11;11	Prosp	0/11	92,9%	42.8% TIA; 57.1% asymptomatic	Aspirin only
Queral et al (52)	1996	6;6	Prosp	0/6	92.3%	16.6% amaurosis; 83.3% TIAs	Aspirin only
Motarjeme (50)	1996	8;8	Retrosp	8/0	93%	u	Aspirin only

Table 5 continued

Author	Non neurol compl	Neurol compl periproc	30 days all stroke/death	Restenosis rate	Follow-up month
Percutaneous PTA/stent					
Chio et al (59)	2.7% retroperitoneal hemorrhage	2 minor strokes	3/42 (7.1%)	Primary 24 months: 5.1%	mean 24
Current study	5.2%	3 major strokes; 4 TIAs	3/104 (2.8%)	Primary 12 months: 4.2%; at 48 months: 19,7%	mean 24.9
Surgical and retrograde PTA/stent					
Peterson et al (60)	0%	0	0	Primary 12 months: 0,00%	mean 12
Payne et al (61)	0%	0	0	Primary 24 months: 12.5%	mean 24
Allie et al (62)	0%	0	0	Primary 12 months: 8.6%	mean 34
Grego et al (63)	0%	0	0	0.00%	u
Macierewicz et al (64)	0%	0	0	Primary 18 months: 16.6%	median 20
Arko et al (65)	25% wound hematomas	1 hypoglossal palsy	0	Primary 23 months: 0.0%	mean 23.6
Levien et al (66)	4.5% hematoma	0	0	Primary 12 months: 9%	u
Sullivan et al (53)	3.4% hematoma 1.1% AV fistula 1.1% pseudoaneurysm	1 major stroke	2/14 (14.2%)	Primary 14,3 months: 16.0%	mean 14.3
Queral et al (52)	0	0	0	Primary 48 months: 15%	mean 27
Motarjeme (50)	0	1 major stroke	1/8 (12.5%)	Primary 12 months: 0%	mean 60

The principal advantage of stent placement in the treatment of carotid artery stenoses is its impact on immediate outcome. The stent serves to limit embolization of atherosclerotic debris liberated during the PTA procedure. In addition, it reduces elastic recoil and prevents propagation of intimal dissections created during the procedure. However, there is no evidence that stenting is superior to angioplasty alone for proximal CCA lesions; current practice, however, includes primary stenting in most cases for the reasons discussed above (*Figure 9*).

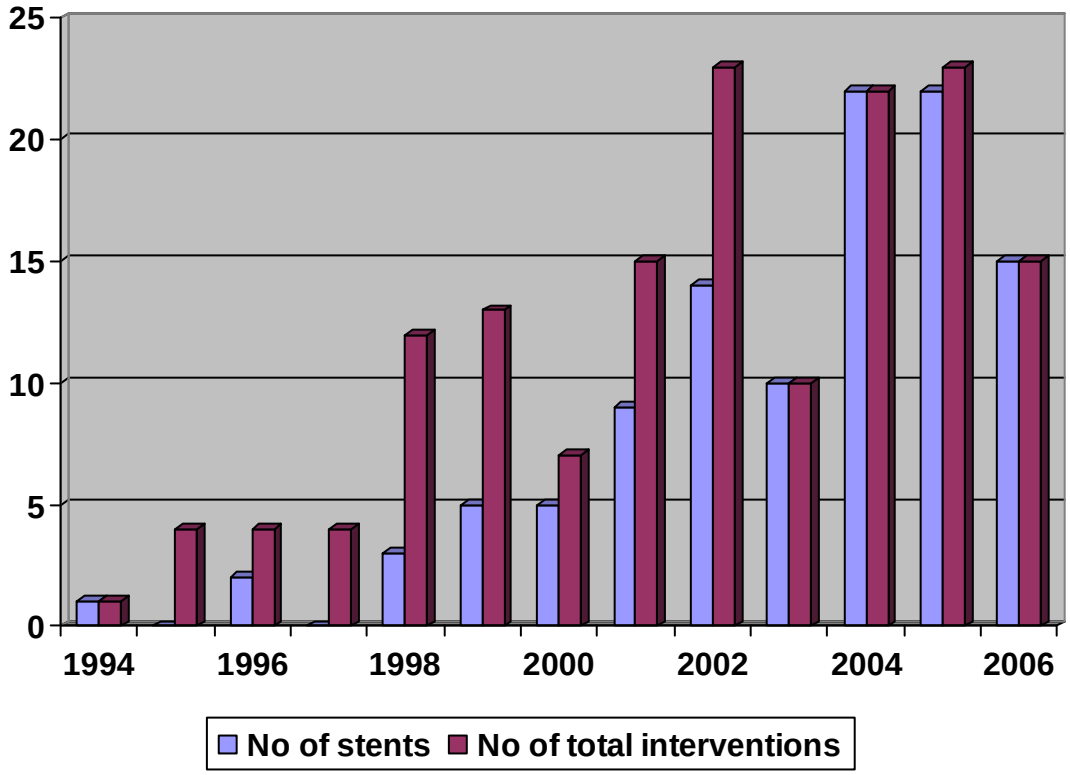

Figure 9. Number of stents and total interventions annually

Restenosis, although an issue in essentially all vascular interventions, has not been a major problem in lesions involving the carotid bifurcation or the adjacent internal carotid artery. In a recent review, a 5.5% incidence of restenosis at 12 months and 3% of repeat angioplasty for restenosis with a mean follow-up time of 26 months was described (67).

Our restenosis and rePTA rates for the pCCA are in a similar range. Moreover, stent placement has not changed the restenosis rate significantly in our study (Figure 5, B and C). The main limitation of this study lies in its retrospective nature. In addition, due to the long period studied (1994-2006), the population was not homogeneous as to whether or not stents, protection devices, and/or dual antiplatelet therapy were used. For the same reason, follow-up is missing for 22% of the patients; however, procedural and in-hospital clinical outcomes were available for all 153 treatments. The number of restenoses, especially those below 70%, may also be underestimated due to the limitations of duplex scan examinations in direct visualization of CCA origins. The lack

of significant differences in the restenosis-free patency rate in our study between angioplasty alone and angioplasty stenting may also be due to the relatively small sample size and the overall excellent patency rate.

8.3 High-Resolution CT and Angiographic Evaluation of NexStent

Several in vivo and in vitro studies have examined the physical properties of self-expandable stents (68, 69). Nitinol stents have higher radial force than Wallstent, which represents an advantage in the treatment of calcified lesions. Tortuous target vessels require flexible open-cell stents, which accommodate to the curves without changing the anatomy; their structure provides better wall apposition. Although open-cell stents have improved conformity with the anatomy, their structure and less radial force cannot completely prevent plaque protrusion, which may be a source of emboli. Retrospective analysis of carotid stenting cases showed higher neurological postoperative complication rate in symptomatic patients (70, 71). A recent retrospective study (72) did not prove the superiority of a specific stent cell design. Several factors, including vessel tortuosity, may influence the procedure complication rate; therefore, only a large randomized trial would be able to provide scientifically valid data.

All stents on the market are tubular structures except NexStent, which is specifically designed for carotid lesions. A study that used intravascular ultrasound and histological examination of the stent using a porcine model was published in 2006 (73). The animal study used the CCA and showed good conformability of the stent in different-sized vessels with minimal vessel injury and intimal proliferation.

By means of data from 41 NexStent procedures, we evaluated the immediate anatomic result after the treatment. The target stenosis was localized close to the carotid bifurcation in all cases; the data obtained via angiography and CTA showed good vessel lumen expansion. The radial force was large enough to prevent insufficient dilation or recoil in case of calcified plaques. Gaps between the stent and the wall are frequently seen as a result of plaque ulceration and the larger diameter of the carotid bulb. In our study, plaque ulceration was a strong predictor of incomplete stent apposition. Outside the ulcerations, a lack of apposition between the stent filaments and endothelial surface was demonstrated in the carotid bulb, especially at the edge of eccentric plaques. We

were not able to find cases with incomplete unrolling of the stent or infolding of the inner layer, which might have resulted in delayed endothelization. The nontubular closed-cell stent provided adequate expansion and wall adaptation.

8.4 Early restenosis after eversion carotid endarterectomy versus carotid stenting

Sample size and follow-up proportion were higher (74%) than those published in most other single-centre studies. This sample involved 685 (206 CAS, 479 CEA) patients and 512 (144 CAS, 368 CEA) of them were followed-up by US over a mean follow-up period of 18.4 months, which reflects the timeframe for developing early restenosis. (74, 75)

Higher incidences of arrhythmias and malignant diseases were found in the CAS group. It reflects that patients with higher risk are considered for endovascular intervention rather than for open carotid surgery. An increased number of TIA was observed after CAS. It can be explained by the lack of general anesthesia which may obscure the signs of transient neurological symptoms, but a higher rate of embolization can not be excluded either.

These results showed that both moderate (50-69%) and severe (≥70%) restenosis occurred statistically less frequently in the CAS than in the CEA group. These findings are also in accordance with the results of Cao et al. They showed a 6.4% restenosis (≥50%) rate after CAS which is more favorable than after CEA (7.9%) within an 18-month mean follow-up time. In the current study the 3.47% incidence of severe restenosis after CAS is in agreement with previously published data (76). Bergeron et al. suggested a time- dependent increase of restenosis after CAS, resulting in a 3.7% restenosis rate at 2 years, the present results are in harmony with their data (77, 78). Contrary to the current findings and to those of most other trials, Christiaans et al. (79) reported on a considerable higher instent restenosis rate. In this trial involving a sample size of 217 CAS patients they found a 21% instent restenosis rate at 24 months. These authors published 14% instent restenosis rate in the same population at 3 days after intervention, which may actually reflect the proportion of residual stenosis. In other trials the investigators report on lower instent restenosis rate (80-82). In the SAPPHIRE study carotid revascularization

was repeated in fewer patients who had received stents than in those who had undergone endarterectomy (28).

Setacci et al. (83) found previous ipsilateral CEA to be a risk factor for developing instent restenosis after CAS. In accordance with their findings, our study showed the same tendency, namely, restenosis of more than 50% occurred in 13.6% of CAS cases (6/44) with prior endarterectomy and 6% of CAS cases (6/100) with primary stenosis (P=NS). De Borst et al. analyzed the restenosis in patients stented for postendarterectomy stenosis and found 19% instent restenosis (≥50%) rate, which is also comparable with our results (84). By contrast, Skelly et al. did not find previous ipsilateral carotid endarterectomy as a risk factor for instent restenosis (78).

Carotid endarterectomy patients in this cohort underwent eversion type CEA, which is superior to conventional CEA regarding restenosis rate (85) (conventional CEA is no longer routinely performed at the department since 1993). The incidence of restenosis after CEA is known to vary over a wide range from 1% to 37%. The result of this study of 10.05% severe restenosis rate after eversion CEA is also comparable to those published in other studies (86, 87). Brothers et al. reported >80% restenosis in 6% of cases for eversion endarterectomy at 36 months, which is also similar to the data reported in this study (88). It has to be taken into consideration that in Brothers' study 80% restenosis was considered significant for severe restenosis. The lack of concordance in restenosis rates defined in various studies is likely to be explained by variations in definition criteria and follow-up.

The authors found an increased risk for severe restenosis in female patients which is consistent with the findings of Hugl et al. (89) The increased risk for restenosis in female patients was found in the whole patient population, irrespective of the revascularization procedure. A higher odds ratio was found for only the endarterectomized female patients compared to the whole group (CAS and CEA together). No such association was found in male patients and in overall stented patients.

In comparison to other studies on this topic, this trial differs principally in two points: 1) the authors focused explicitly on the early restenosis, i.e. the restenosis that develops within 2 years after CEA and stenting, and reflects primarily intimal hyperplasia, in contrast to late restenosis due to progressive atherosclerosis (74, 75); 2) the authors had a relatively high follow-up proportion with a close follow-up range, resulting in an acceptably low

standard deviation in the follow-up time. Contrary to other studies which have compared restenosis between CEA and CAS in general, apart from an overall comparison between the two groups, the authors compared CEA patients to a subgroup of CAS patients with primary carotid stenosis, which resulted in a more significant difference between restenosis rates of CEA and CAS. This adjustment of data is sensible, seeing as most of the CEA's were done on primary stenosis, but a considerable amount of CAS's were done on patients with postendarterectomy restenosis. In order to compare restenosis caused by similar pathogenesis, CEA should be compared with only the primary CAS cases.

To explain the lower restenosis rate in the CAS versus the CEA group, it has to be taken into consideration that CEA denudates the intima and part of the media by removing the atherosclerotic plaque of the vessel wall, exposing a new surface composed mainly of smooth muscle cells and local inflammatory cells. In addition, during the CEA procedure cross clamping of the carotid artery is performed for a short period of time, which leads to ischemia/reperfusion injury of the carotid artery (35, 36, 90). These pathological processes do not occur in stented carotid arteries. During the CAS procedure no intima denudation takes place and no ischemia/reperfusion injury due to cross clamping occurs, which ultimately does not trigger neointima formation. This hypothesis was supported by a recent work that showed how an immediate complement activation could be seen after CEA and it was related to the time of clamping of the carotid artery during the surgery. However, no such complement activation was found in patients who underwent CAS (36). Further studies are needed to support the hypothesis that inflammation and early complement activation due to ischemia/reperfusion injury has a pathophysiological role in the development of restenosis following CEA and that the lack of complement activation in the CAS group contributes to the lower restenosis rate observed in these patients. The tendency towards a higher incidence of restenosis in carotid arteries stented for postendarterectomy stenosis also shows that stent deployment in a preexistent neointimal hyperplastic lesion may potentiate an ongoing process.

8.5 Stent-graft treatment of carotid pseudoaneurysms

Aneurysms of the extracranial carotid artery are rare and may occur spontaneously or due to trauma (91-95). Treatment of extracranial carotid artery aneurysms depends on the location and size of the aneurysms. Conservative treatment cannot prevent the further growth and rupture of aneurysm and carries the risk of hemorrhages. Seventy percent of those patients who did not undergo surgery later died later of aneurysm related complications. Ligature of the internal carotid artery had an associated stroke rate of 12–40% (91, 92, 94). Reconstructive surgery is performed using grafts or less frequently direct end-to-end anastomosis. Resection and patch angioplasty may be another surgical option in some cases. The difficulty of the surgery depends on the size and location of the aneurysm, adequate exposure and control of the distal ICA is often difficult. The mortality-serious morbidity risk of these procedures is 4–10.8% and nerve injury is not uncommon (91, 93, 94).

Graft covered stents have a very low porosity and are ideal for the treatment of aneurysms, AV fistulas and vascular injuries since the lesions are immediately excluded from the circulation. The first transfemoral endovascular aortic aneurysm exclusion was reported by Parodi in 1991 (96). Since then clinical experience has been accumulated using stent-grafts for the treatment of a variety of vascular pathologies (97-100).

The currently available peripheral stent-grafts are PET, PTFE or polyurethane covered stainless steel or nitinol stents. Since of balloon expandable stents are prone to be deformed or collapsed and due to the diameter difference between the CCA and ICA, self-expandable stents are advised for use in the carotid bifurcation. Synthetic grafts have been successfully used by vascular surgeons for more than 30 years in large-diameter applications like the aorta or in the aortoiliac region; however, the patency rates of small-diameter vascular grafts are low. Several studies have reported favorable immediate and long-term results using PTFE grafts for carotid reconstruction (101, 102).

The Wallgraft endoprosthesis is a PET covered self expandable stainless steel stent; we choose Wallgraft because it is flexible, low profile and it conforms well to the different diameter of the CCA and ICA. Reviewing the literature seven papers were found describing 17 cases of carotid aneurysm treatment in 16 patients using Wallgraft (103-

110). The immediate result was excellent in all cases without complication. Fourteen patients were followed up to 24 months; two patients refused the further cooperation. Ultrasound follow-up detected patent vessel in 12 cases at the last exam. Only one author reported an occlusion and a late graft stenosis (109). One of these patients had bilateral carotid bifurcation aneurysms 10 years after carotid endarterectomy on both sides. The aneurysms were treated by Wallgraft; 5 months later the patient suffered a stroke and the ultrasonography confirmed occlusion of the left carotid artery. In the other case 10 months after the treatment routine follow-up angiography detected asymptomatic 50% stenosis.

PTE and PTFE are highly thrombogenic materials. Animal studies described a marked inflammatory vessel wall response to the PET coating of the endografts (111-113). The endothelialization was delayed compared to bare stents and the endothelial layer was thicker. These unfavorable attributes may be responsible for the neointima formation in certain clinical cases (109). Appropriate antiplatelet medication is important to prevent early occlusion. Unfortunately Clopidogrel was not available at the time of our procedures, which might have helped preventing the reocclusion in Case 2.

9 Novel findings

1. We have confirmed in a large series of innominate artery angioplasties that it is a safe and effective procedure with an excellent initial success rate, without any lethal complication, with a lower complication rate than the surgical option and with a similar long-term patency rate as surgery.

2. We published the largest study on transfemoral angioplasty of ostial and proximal common carotid artery stenosis. The primary technical success rate is high (98.7%) with a 2.5% 30-day all stroke/death rate. These results should help vascular surgeons and interventional radiologists to consider risk versus benefit when deciding treatment options for ostial and proximal common carotid artery significant stenoses. This study should also draw attention to the lack of data on natural history or effect of best medical treatment alone for these lesions, making evidence-based decision making currently impossible for treatment of symptomatic or asymptomatic ostial and proximal common carotid artery significant stenoses.

3. Good plaque coverage and proper overlapping of the rolled sheet was achieved in all cases. The longitudinal flexibility of the stent is limited, as for all other closed-cell stents; in tortuous vessels, kink formation may occur. The stent provided adequate expansion and wall adaptation. We found weak correlation between the residual stenosis and the amount of plaque calcification, and plaque ulceration was a good predictor of incomplete stent apposition.

4. Our results showed that both moderate (50-69%) and severe (≥70%) restenosis occurred statistically less frequently in the CAS than in the CEA group. We found an increased risk for severe restenosis in female patients, irrespective of the revascularization procedure. A higher odds ratio was found for only the endarterectomized female patients compared to the whole group (CAS and CEA together). We compared CEA patients to a subgroup of CAS patients with primary carotid stenosis, which resulted in a more significant difference between restenosis rates of CEA and CAS. This adjustment of data is sensible, seeing as most of the CEA's were done on primary stenosis, but a considerable amount of CAS's were done on patients with postendarterectomy restenosis. In order to compare restenosis caused by similar pathogenesis, CEA should be

compared with only the primary CAS cases. An increased number of TIA was observed after CAS. Incidence of early restenosis after CAS was less common than after CEA.

5. The use of Wallgraft for the management of carotid artery aneurysms is an alternative to surgical repair in certain situations: major co-morbidity, hostile neck and contraindications to surgery. The relatively low incidence of these carotid lesions makes difficult to collect enough clinical information to be able to determine the optimal indication and assess the complication rate. While the technical success rate is good, the long-term effectiveness is still uncertain. Postoperative surveillance is extremely important to detect restenosis or thrombosis.

10 References

1. Mohr JP, Caplan LR, Melski JW, et al. The Harvard Cooperative Stroke Registry: a prospective registry. Neurology 1978; 28:754-762.

2. Nagy Z, Magyar G, Óváry C. Magyarországi stroke-betegek epidemiológiai vizsgálata. Agyérbetegségek 2000; 6:2-10.

3. Kesteloot H, Sans S, Kromhout D. Dynamics of cardiovascular and all-cause mortality in Western and Eastern Europe between 1970 and 2000. Eur Heart J 2006; 27:107-113.

4. Poirier J, Gray F, Escourolle R. Frequency and severity of atherosclerotic lesions in the arterial cervicocerebral tree. Philadelphia: WB Saunders, 1990.

5. Matsunaga N, Hayashi K, Sakamoto I, et al. Takayasu arteritis: MR manifestations and diagnosis of acute and chronic phase. J Magn Reson Imaging 1998; 8:406-414.

6. Park JH, Chung JW, Im JG, Kim SK, Park YB, Han MC. Takayasu arteritis: evaluation of mural changes in the aorta and pulmonary artery with CT angiography. Radiology 1995; 196:89-93.

7. Tanigawa K, Eguchi K, Kitamura Y, et al. Magnetic resonance imaging detection of aortic and pulmonary artery wall thickening in the acute stage of Takayasu arteritis. Improvement of clinical and radiologic findings after steroid therapy. Arthritis Rheum 1992; 35:476-480.

8. Werdelin L, Juhler M. The course of transient ischemic attacks. Neurology 1988; 38:677-680.

9. Johnston SC, Rothwell PM, Nguyen-Huynh MN, et al. Validation and refinement of scores to predict very early stroke risk after transient ischaemic attack. Lancet 2007; 369:283-292.

10. Berguer R, Morasch MD, Kline RA. Transthoracic repair of innominate and common carotid artery disease: immediate and long-term outcome for 100 consecutive surgical reconstructions. J Vasc Surg 1998; 27:34-41; discussion 42.

11. Brewster DC, Moncure AC, Darling RC, Ambrosino JJ, Abbott WM. Innominate artery lesions: problems encountered and lessons learned. J Vasc Surg 1985; 2:99-112.

12. Cherry KJ, Jr., McCullough JL, Hallett JW, Jr., Pairolero PC, Gloviczki P. Technical principles of direct innominate artery revascularization: a comparison of endarterectomy and bypass grafts. J Vasc Surg 1989; 9:718-723; discussion 723-714.

13. Melliere D, Becquemin JP, Benyahia NE, Ecollan P, Fitoussi M. Atherosclerotic disease of the innominate artery: current management and results. J Cardiovasc Surg (Torino) 1992; 33:319-323.

14. Herring M. The subclavian steal syndrome: a review. Am Surg 1977; 43:220-228.

15. Azakie A, McElhinney DB, Higashima R, Messina LM, Stoney RJ. Innominate artery reconstruction: over 3 decades of experience. Ann Surg 1998; 228:402-410.

16. Kieffer E, Sabatier J, Koskas F, Bahnini A. Atherosclerotic innominate artery occlusive disease: early and long-term results of surgical reconstruction. J Vasc Surg 1995; 21:326-336; discussion 336-327.

17. Motarjeme A, Keifer JW, Zuska AJ. Percutaneous transluminal angioplasty of the brachiocephalic arteries. AJR Am J Roentgenol 1982; 138:457-462.

18. Theron J, Courtheoux P, Henriet JP, Pelouze G, Derlon JM, Maiza D. Angioplasty of supraaortic arteries. J Neuroradiol 1984; 11:187-200.

19. Beneficial effect of carotid endarterectomy in symptomatic patients with high-grade carotid stenosis. North American Symptomatic Carotid Endarterectomy Trial Collaborators. N Engl J Med 1991; 325:445-453.

20. Randomised trial of endarterectomy for recently symptomatic carotid stenosis: final results of the MRC European Carotid Surgery Trial (ECST). Lancet 1998; 351:1379-1387.

21. Endarterectomy for asymptomatic carotid artery stenosis. Executive Committee for the Asymptomatic Carotid Atherosclerosis Study. Jama 1995; 273:1421-1428.

22. Halliday A, Mansfield A, Marro J, et al. Prevention of disabling and fatal strokes by successful carotid endarterectomy in patients without recent neurological symptoms: randomised controlled trial. Lancet 2004; 363:1491-1502.

23. Kerber CW, Cromwell LD, Loehden OL. Catheter dilatation of proximal carotid stenosis during distal bifurcation endarterectomy. AJNR Am J Neuroradiol 1980; 1:348-349.

24. Tsai FY, Matovich V, Hieshima G, et al. Percutaneous transluminal angioplasty of the carotid artery. AJNR Am J Neuroradiol 1986; 7:349-358.

25. Freitag G, Freitag J, Koch RD. [Percutaneous transluminal angioplasty of carotid stenoses]. Röfo 1984; 140:209-212.

26. Kachel R, Endert G, Basche S, Grossmann K, Glaser FH. Percutaneous transluminal angioplasty (dilatation) of carotid, vertebral, and innominate artery stenoses. Cardiovasc Intervent Radiol 1987; 10:142-146.

27. Endovascular versus surgical treatment in patients with carotid stenosis in the Carotid and Vertebral Artery Transluminal Angioplasty Study (CAVATAS): a randomised trial. Lancet 2001; 357:1729-1737.

28. Yadav JS, Wholey MH, Kuntz RE, et al. Protected carotid-artery stenting versus endarterectomy in high-risk patients. N Engl J Med 2004; 351:1493-1501.

29. Mas JL, Chatellier G, Beyssen B, et al. Endarterectomy versus stenting in patients with symptomatic severe carotid stenosis. N Engl J Med 2006; 355:1660-1671.

30. Eckstein HH, Ringleb P, Allenberg JR, et al. Results of the Stent-Protected Angioplasty versus Carotid Endarterectomy (SPACE) study to treat symptomatic

stenoses at 2 years: a multinational, prospective, randomised trial. Lancet Neurol 2008; 7:893-902.

31. Meier P, Knapp G, Tamhane U, Chaturvedi S, Gurm HS. Short term and intermediate term comparison of endarterectomy versus stenting for carotid artery stenosis: systematic review and meta-analysis of randomised controlled clinical trials. Bmj; 340:c467.

32. Lattimer CR, Burnand KG. Recurrent carotid stenosis after carotid endarterectomy. Br J Surg 1997; 84:1206-1219.

33. Horrocks M. When should I reoperate for recurrent stenosis? : Harcourt Publishers Ltd, 2000.

34. Frericks H, Kievit J, van Baalen JM, van Bockel JH. Carotid recurrent stenosis and risk of ipsilateral stroke: a systematic review of the literature. Stroke 1998; 29:244-250.

35. Szabó A, Laki J, Madsen HO, et al. Early rise in serum VEGF and PDGF levels predisposes patients with a normal MBL2 genotype to restenosis after eversion endarterectomy. Stroke 2007; 38:2247-2253.

36. Széplaki G, Hirschberg K, Gombos T, et al. Early complement activation follows eversion carotid endarterectomy and correlates with the time of clamping of the carotid artery. Mol Immunol 2008; 45:3289-3294.

37. Rugonfalvi-Kiss S, Dosa E, Madsen HO, et al. High rate of early restenosis after carotid eversion endarterectomy in homozygous carriers of the normal mannose-binding lectin genotype. Stroke 2005; 36:944-948.

38. Insall RL, Lambert D, Chamberlain J, Proud G, Murthy LN, Loose HW. Percutaneous transluminal angioplasty of the innominate, subclavian, and axillary arteries. Eur J Vasc Surg 1990; 4:591-595.

39. Maggisano R, Provan JL. Surgical management of chronic occlusive disease of the aortic arch vessels and vertebral arteries. Can Med Assoc J 1981; 124:972-977.

40. Sacco RL, Adams R, Albers G, et al. Guidelines for prevention of stroke in patients with ischemic stroke or transient ischemic attack: a statement for healthcare professionals from the American Heart Association/American Stroke Association Council on Stroke: co-sponsored by the Council on Cardiovascular Radiology and Intervention: the American Academy of Neurology affirms the value of this guideline. Circulation 2006; 113:e409-449.

41. McKinney AM, Casey SO, Teksam M, et al. Carotid bifurcation calcium and correlation with percent stenosis of the internal carotid artery on CT angiography. Neuroradiology 2005; 47:1-9.

42. Elgersma OE, van Leersum M, Buijs PC, et al. Changes over time in optimal duplex threshold for the identification of patients eligible for carotid endarterectomy. Stroke 1998; 29:2352-2356.

43. Rothwell PM, Eliasziw M, Gutnikov SA, et al. Analysis of pooled data from the randomised controlled trials of endarterectomy for symptomatic carotid stenosis. Lancet 2003; 361:107-116.

44. Lal BK, Hobson RW, 2nd, Goldstein J, Chakhtoura EY, Duran WN. Carotid artery stenting: is there a need to revise ultrasound velocity criteria? J Vasc Surg 2004; 39:58-66.

45. Entz L, Járányi Z, Nemes A. Eversion endarterectomy in surgery of the internal carotid artery. Cardiovasc Surg 1996; 4:190-194.

46. Biller J, Feinberg WM, Castaldo JE, et al. Guidelines for carotid endarterectomy: a statement for healthcare professionals from a special writing group of the Stroke Council, American Heart Association. Stroke 1998; 29:554-562.

47. Grant EG, Benson CB, Moneta GL, et al. Carotid artery stenosis: gray-scale and Doppler US diagnosis--Society of Radiologists in Ultrasound Consensus Conference. Radiology 2003; 229:340-346.

48. Stanziale SF, Wholey MH, Boules TN, Selzer F, Makaroun MS. Determining in-stent stenosis of carotid arteries by duplex ultrasound criteria. J Endovasc Ther 2005; 12:346-353.

49. Provan L. Arteriosclerotic occlusive arterial disease of brachiocephalic and arch vessels. Philadelphia: Saunders, 1989.

50. Motarjeme A. Percutaneous transluminal angioplasty of supra-aortic vessels. J Endovasc Surg 1996; 3:171-181.

51. Dorros G, Lewin RF, Jamnadas P, Mathiak LM. Peripheral transluminal angioplasty of the subclavian and innominate arteries utilizing the brachial approach: acute outcome and follow-up. Cathet Cardiovasc Diagn 1990; 19:71-76.

52. Queral LA, Criado FJ. The treatment of focal aortic arch branch lesions with Palmaz stents. J Vasc Surg 1996; 23:368-375.

53. Sullivan TM, Gray BH, Bacharach JM, et al. Angioplasty and primary stenting of the subclavian, innominate, and common carotid arteries in 83 patients. J Vasc Surg 1998; 28:1059-1065.

54. Vitek JJ, Raymon BC, Oh SJ. Innominate artery angioplasty. AJNR Am J Neuroradiol 1984; 5:113-114.

55. Motarjeme A, Gordon G. Percutaneous transluminal angioplasty of the brachiocephalic vessels: Guidelines for therapy. Int Angiol 1993; 12:260–269.

56. De Sobregrau RC, Lopez Collado M, Matas Docampo M, Rodriguez Mori A, Chavez Lopez J, Lisbona Sabater C. Surgery of the innominate artery. J Cardiovasc Surg (Torino) 1986; 27:31-37.

57. Nemes B, Dzsinich C, Bérczi V, et al. PTA and surgical revascularisation of the innominate artery. Cardiovasc Intervent Radiol 1998; 21(Suppl 1):S128.

58. Berguer R, Morasch MD, Kline RA, Kazmers A, Friedland MS. Cervical reconstruction of the supra-aortic trunks: a 16-year experience. J Vasc Surg 1999; 29:239-246; discussion 246-238.

59. Chio FL, Jr., Liu MW, Khan MA, Iyer SS, Roubin GS. Effectiveness of elective stenting of common carotid artery lesions in preventing stroke. Am J Cardiol 2003; 92:1135-1137.

60. Peterson BG, Resnick SA, Morasch MD, Hassoun HT, Eskandari MK. Aortic arch vessel stenting: a single-center experience using cerebral protection. Arch Surg 2006; 141:560-563; discussion 563-564.

61. Payne DA, Hayes PD, Bolia A, Fishwick G, Bell PR, Naylor AR. Cerebral protection during open retrograde angioplasty/stenting of common carotid and innominate artery stenoses. Br J Surg 2006; 93:187-190.

62. Allie DE, Hebert CJ, Lirtzman MD, et al. Intraoperative innominate and common carotid intervention combined with carotid endarterectomy: a "true" endovascular surgical approach. J Endovasc Ther 2004; 11:258-262.

63. Grego F, Frigatti P, Lepidi S, Bonvini S, Amista P, Deriu GP. Synchronous carotid endarterectomy and retrograde endovascular treatment of brachiocephalic or common carotid artery stenosis. Eur J Vasc Endovasc Surg 2003; 26:392-395.

64. Macierewicz J, Armon MP, Cleveland TJ, Gaines PA, Beard JD. Carotid endarterectomy combined with proximal stenting for multilevel disease. Eur J Vasc Endovasc Surg 2000; 20:572-575.

65. Arko FR, Buckley CJ, Lee SD, Manning LG, Patterson DE. Combined carotid endarterectomy with transluminal angioplasty and primary stenting of the supra-aortic vessels. J Cardiovasc Surg (Torino) 2000; 41:737-742.

66. Levien LJ, Benn CA, Veller MG, Fritz VU. Retrograde balloon angioplasty of brachiocephalic or common carotid artery stenoses at the time of carotid endarterectomy. Eur J Vasc Endovasc Surg 1998; 15:521-527.

67. Wholey MH, Jarmolowski CR, Wholey M, Eles GR. Carotid artery stent placement--ready for prime time? J Vasc Interv Radiol 2003; 14:1-10.

68. Berkefeld J, Turowski B, Dietz A, et al. Recanalization results after carotid stent placement. AJNR Am J Neuroradiol 2002; 23:113-120.

69. Tanaka N, Martin JB, Tokunaga K, et al. Conformity of carotid stents with vascular anatomy: evaluation in carotid models. AJNR Am J Neuroradiol 2004; 25:604-607.

70. Bosiers M, de Donato G, Deloose K, et al. Does free cell area influence the outcome in carotid artery stenting? Eur J Vasc Endovasc Surg 2007; 33:135-141; discussion 142-133.

71. Hart JP, Peeters P, Verbist J, Deloose K, Bosiers M. Do device characteristics impact outcome in carotid artery stenting? J Vasc Surg 2006; 44:725-730; discussion 730-721.

72. Schillinger M, Gschwendtner M, Reimers B, et al. Does carotid stent cell design matter? Stroke 2008; 39:905-909.

73. Kaneda H, Ikeno F, Lyons J, Rezaee M, Yeung AC, Fitzgerald PJ. Long-term histopathologic and IVUS evaluations of a novel coiled sheet stent in porcine carotid arteries. Cardiovasc Intervent Radiol 2006; 29:413-419.

74. Hunter GC. Edgar J. Poth Memorial/W.L. Gore and Associates, Inc. Lectureship. The clinical and pathological spectrum of recurrent carotid stenosis. Am J Surg 1997; 174:583-588.

75. Trisal V, Paulson T, Hans SS, Mittal V. Carotid artery restenosis: an ongoing disease process. Am Surg 2002; 68:275-279; discussion 279-280.

76. Setacci C, de Donato G, Setacci F, et al. In-stent restenosis after carotid angioplasty and stenting: a challenge for the vascular surgeon. Eur J Vasc Endovasc Surg 2005; 29:601-607.

77. Bergeron P, Roux M, Khanoyan P, Douillez V, Bras J, Gay J. Long-term results of carotid stenting are competitive with surgery. J Vasc Surg 2005; 41:213-221; discussion 221-212.

78. Skelly CL, Gallagher K, Fairman RM, et al. Risk factors for restenosis after carotid artery angioplasty and stenting. J Vasc Surg 2006; 44:1010-1015.

79. Christiaans MH, Ernst JM, Suttorp MJ, et al. Restenosis after carotid angioplasty and stenting: a follow-up study with duplex ultrasonography. Eur J Vasc Endovasc Surg 2003; 26:141-144.

80. Ouriel K, Hertzer NR, Beven EG, et al. Preprocedural risk stratification: identifying an appropriate population for carotid stenting. J Vasc Surg 2001; 33:728-732.

81. Robbin ML, Lockhart ME, Weber TM, et al. Carotid artery stents: early and intermediate follow-up with Doppler US. Radiology 1997; 205:749-756.

82. Willfort-Ehringer A, Ahmadi R, Gschwandtner ME, Haumer M, Lang W, Minar E. Single-center experience with carotid stent restenosis. J Endovasc Ther 2002; 9:299-307.

83. Setacci C, Pula G, Baldi I, et al. Determinants of in-stent restenosis after carotid angioplasty: a case-control study. J Endovasc Ther 2003; 10:1031-1038.

84. de Borst GJ, Ackerstaff RG, de Vries JP, et al. Carotid angioplasty and stenting for postendarterectomy stenosis: long-term follow-up. J Vasc Surg 2007; 45:118-123.

85. Cao P, Giordano G, De Rango P, et al. Eversion versus conventional carotid endarterectomy: late results of a prospective multicenter randomized trial. J Vasc Surg 2000; 31:19-30.

86. Reina-Gutierrez T, Serrano-Hernando FJ, Sanchez-Hervas L, Ponce A, Vega de Ceniga M, Martin A. Recurrent carotid artery stenosis following endarterectomy: natural history and risk factors. Eur J Vasc Endovasc Surg 2005; 29:334-341.

87. Sadideen H, Taylor PR, Padayachee TS. Restenosis after carotid endarterectomy. Int J Clin Pract 2006; 60:1625-1630.

88. Brothers TE. Initial experience with eversion carotid endarterectomy: absence of a learning curve for the first 100 patients. J Vasc Surg 2005; 42:429-434.

89. Hugl B, Oldenburg WA, Neuhauser B, Hakaim AG. Effect of age and gender on restenosis after carotid endarterectomy. Ann Vasc Surg 2006; 20:602-608.

90. Malek LA, Malek AK, Leszczynski J, et al. Carotid clamping time as a risk factor for early restenosis after carotid endarterectomy. Eur J Vasc Endovasc Surg 2005; 30:143-146.

91. El-Sabrout R, Cooley DA. Extracranial carotid artery aneurysms: Texas Heart Institute experience. J Vasc Surg 2000; 31:702-712.

92. McCann RL. Basic data related to peripheral artery aneurysms. Ann Vasc Surg 1990; 4:411-414.

93. McCollum CH, Wheeler WG, Noon GP, DeBakey ME. Aneurysms of the extracranial carotid artery. Twenty-one years' experience. Am J Surg 1979; 137:196-200.

94. Rosset E, Albertini JN, Magnan PE, Ede B, Thomassin JM, Branchereau A. Surgical treatment of extracranial internal carotid artery aneurysms. J Vasc Surg 2000; 31:713-723.

95. Winslow N. Extracranial aneurysmof the internal carotid artery. Arch Surg 1926; 13:689.

96. Parodi JC, Palmaz JC, Barone HD. Transfemoral intraluminal graft implantation for abdominal aortic aneurysms. Ann Vasc Surg 1991; 5:491-499.

97. Cragg AH, Dake MD. Percutaneous femoropopliteal graft placement. Radiology 1993; 187:643-648.

98. Criado E, Marston WA, Ligush J, Mauro MA, Keagy BA. Endovascular repair of peripheral aneurysms, pseudoaneurysms, and arteriovenous fistulas. Ann Vasc Surg 1997; 11:256-263.

99. Marks MP, Dake MD, Steinberg GK, Norbash AM, Lane B. Stent placement for arterial and venous cerebrovascular disease: preliminary experience. Radiology 1994; 191:441-446.

100. Hüttl K, Sebestyén M, Entz L, Molnár AA, Nemes B, Bérczi V. Covered stent placement in a traumatically injured vertebral artery. J Vasc Interv Radiol 2004; 15:201-202.

101. Castellani L, Benhamou AC, Angel F, Garces D, al Kassar T. Resection and reconstruction of the carotid bifurcation with polytetrafluoroethylene grafts; operative technique. Preliminary results in 25 procedures and indications. J Cardiovasc Surg (Torino) 1991; 32:426-435.

102. Becquemin JP, Cavillon A, Brunel M, Desgranges P, Melliere D. Polytetrafluoroethylene grafts for carotid repair. Cardiovasc Surg 1996; 4:740-745.

103. Amar AP, Teitelbaum GP, Giannotta SL, Larsen DW. Covered stent-graft repair of the brachiocephalic arteries: technical note. Neurosurgery 2002; 51:247-252; discussion 252-243.

104. Ellis PK, Kennedy PT, Barros D'Sa AA. Successful exclusion of a high internal carotid pseudoaneurysm using the Wallgraft endoprosthesis. Cardiovasc Intervent Radiol 2002; 25:68-69.

105. Mukherjee D, Roffi M, Yadav JS. Endovascular treatment of carotid artery aneurysms with stent grafts. J Invasive Cardiol 2002; 14:269-272.

106. Parodi JC, Schonholz C, Ferreira LM, Bergan J. Endovascular stent-graft treatment of traumatic arterial lesions. Ann Vasc Surg 1999; 13:121-129.

107. Kubaska SM, 3rd, Greenberg RK, Clair D, et al. Internal carotid artery pseudoaneurysms: treatment with the Wallgraft endoprosthesis. J Endovasc Ther 2003; 10:182-189.

108. Patel JV, Rossbach MM, Cleveland TJ, Gaines PA, Beard JD. Endovascular stent-graft repair of traumatic carotid artery pseudoaneurysm. Clin Radiol 2002; 57:308-311.

109. Smith TP, Alexander MJ, Enterline DS. Delayed stenosis following placement of a polyethylene terephthalate endograft in the cervical carotid artery. Report of three cases. J Neurosurg 2003; 98:421-425.

110. Terramani TT, Workman MJ, Loberman Z, et al. Adjunctive endovascular techniques in the management of postoperative carotid artery pseudoaneurysms--useful armamentarium for vascular surgeons--three case reports. Vasc Endovascular Surg 2003; 37:207-212.

111. Dolmatch BL, Dong YH, Trerotola SO, Hunter DW, Brennecke LH, LaBounty R. Tissue response to covered Wallstents. J Vasc Interv Radiol 1998; 9:471-478.

112. Hussain FM, Kopchok G, Heilbron M, Daskalakis T, Donayre C, White RA. Wallgraft endoprosthesis: initial canine evaluation. Am Surg 1998; 64:1002-1006.

113. Link J, Feyerabend B, Grabener M, et al. Dacron-covered stent-grafts for the percutaneous treatment of carotid aneurysms: effectiveness and biocompatibility--experimental study in swine. Radiology 1996; 200:397-401.

11 List of publications

Peer reviewed papers with relevance to the current work

Hüttl K, **Nemes B**, Simonffy A, Entz L, Bérczi V. Angioplasty of the innominate artery in 89 patients: experience over 19 years. Cardiovasc Intervent Radiol 2002; 25:109-114.

Nemes B, Járányi Z, Bérczi V, Hüttl K, Acsády G. Stent-graft Treatment of Carotid Pseudoaneurysms: Case Report and Review of the Literature. European Journal of Vascular and Endovascular Surgery 2005; 30:449.

Paukovits TM, Haász J, Molnár A, Szeberin Z, **Nemes B**, Varga D, Hüttl K, Bérczi V, Léránt G. Transfemoral endovascular treatment of proximal common carotid artery lesions: a single-center experience on 153 lesions. J Vasc Surg 2008; 48:80-87.

Hirschberg K, Dósa E, Hüttl K, Selmeci L, **Nemes B**, Szabó A, Merkely B, Acsády Gy, Entz L. Early restenosis after eversion carotid endarterectomy versus carotid stenting: a single-centre retrospective study. J Cardiovasc Surg (Torino) 2009; 50:655-663.

Nemes B, Lukács L, Balázs G, Dósa E, Bérczi V, Hüttl K. High-resolution CT and angiographic evaluation of NexStent wall adaptation. Cardiovasc Intervent Radiol 2009; 32:436-440.

Abstracts

Bérczi V, Szlávy L, Simonffy Á, **Nemes B**, Hüttl K. Angioplasty of the supraaortic arteries - a 18 year experience on 632 cases. Cardiovasc. Intervent. Rad. 1997; 20 Suppl 1:S83.

Nemes B, Dzsinich C, Bérczi V, et al. PTA and surgical revascularization of the innominate artery. Cardiovasc. Intervent. Radiol. 1998; 21 suppl. 1:231.

Bérczi V, Entz L, Gellér L, **Nemes B**, Simonffy A, Hüttl K. [Percutaneous angioplasty of the innominate artery in 89 patients: experience of 19 years]. Magy Seb 2001; 54 Suppl:19-23.

Bérczi V, Molnár AÁ, **Nemes B**, Varga D, Simonffy Á, Hüttl K. Az arteria carotis communis eredésének intervenciós radiológiai kezelése. Érbetegségek 2004; suppl.:E18.

Nemes B, Dósa E, Simonffy Á, Hüttl K. Az arteria carotis interna stentelése filteres embóliavédő használatával. Érbetegségek 2005; suppl.:16.

Entz L, Hüttl K, **Nemes B**. Az arteria anonyma angioplasztikája 129 betegen: 26 év tapasztalata. Érbetegségek 2006 suppl.:32.

Hüttl K, **Nemes B**. Direct stenting of an asymptomatic carotis artery stenosis with the NexStent Monorail Carotid Stent. Clinical Vision 2006; 18:1.

Hüttl K, **Nemes B**. Treatment of a soft, heterogenous carotid artery lesion in a symptomatic patient. Clinical Vision 2006; 18:6.

Hüttl K, Hirschberg K, Dósa E, **Nemes B**, Entz L. Retrospectiv tanulmány carotis interna sebészi és stentelése után kialakult restenosis arányának felmérésére és összehasonlítására. Cardiologica Hungarica 2008; 38 B35.

Nemes B. Proximalis embóliavédelemben végzett carotis stenteléssel szerzett tapasztalataink. Érbetegségek 2008; suppl.:73 E74.

Entz L, Szabó A, Járányi Zs, **Nemes B**, Hirschberg K, Dósa E, Hüttl K. Az a. carotis interna stenosisa: stentelés vagy endarterectomia – az érsebész nézőpontjából. Vascularis Neurológia 2009; suppl 1:28.

Hüttl K, Lukács L, **Nemes B**. Stent törés előfordulása anonyma intervenciós kezelését követően. Cardiologica Hungarica 2009; 39.

Nemes B. Carotis interna stentelés proximalis embóliavédelemben. Cardiologica Hungarica 2009; 39 A72.

Nemes B, Hirschberg K, Dósa E, Hüttl K. Az a. carotis interna stentelésével szerzett tapasztalataink, 1465 eset kapcsán. Vascularis Neurológia 2009; suppl 1:28.

Other publications

Peer reviewed papers

Nemes B, Szlávy L, Hüttl K, Repa I, Simonffy Á. Unusual cases of subclavian steal syndrome, their treatment by PTA. Subclavian steal syndroma atipusos formái és kezelésük percutan transluminalis angioplasztikával (PTA). Ideggyógyászati Szemle (Clin. Neurosci.) 1992; 45(9–10):306-312.

Hoffmann KR, Dmochowski J, Nazareth DP, Miskolczi L, **Nemes B**, Gopal A, Wang Z., Rudin S, Bednarek D. Vessel size measurements in angiograms: manual measurements. Med Phys 2003; 30:681-688.

Levy EI, Boulos AS, Hanel RA, Tio FO, Alberico RA, Fronckowiak MD, **Nemes B**, Paciorek AM, Guterman LR, Hopkins LN. In vivo model of intracranial stent implantation: a pilot study to examine the histological response of cerebral vessels after randomized implantation of heparin-coated and uncoated endoluminal stents in leooa blinded fashion. J Neurosurg 2003; 98:544-553.

Hüttl K, Sebestyén M, Entz L, Molnár AA, **Nemes B**, Bérczi V. Covered stent placement in a traumatically injured vertebral artery. J Vasc Interv Radiol 2004; 15:201-202.

Levy EI, Hanel RA, Howington JU, **Nemes B**, Boulos AS, Tio FO, Paciorek AM, Amlani S, Kagan-Hallet KS, Fronckowiak MD, Guterman LR, Hopkins LN. Sirolimus-eluting stents in the canine cerebral vasculature: a prospective, randomized, blinded assessment of safety and vessel response. J Neurosurg 2004; 100:688-694.

Rudin S, Wang Z, Kyprianou I, Hoffmann KR, Wu Y, Meng H, Guterman LR, **Nemes B**, Bednarek DR, Dmochowski J, Hopkins LN. Measurement of flow modification in

phantom aneurysm model: comparison of coils and a longitudinally and axially asymmetric stent--initial findings. Radiology 2004; 231:272-276.

Miskolczi L, **Nemes B**, Cesar L, Masanari O, Gounis MJ. Contrast injection via the central artery of the left ear in rabbits: a new technique to simplify follow-up studies. AJNR Am J Neuroradiol 2005; 26:1964-1966.

Hüttl K, **Nemes B**, Dósa E, Varga D, Bérczi V. A carotis szűkületek stenteléssel történő kezelése. Magyar Sebészet 2007; 60(1):488-493.

Published abstracts

Bérczi V, Szlávy L, Horváth G, **Nemes B**, Hüttl K. Transcatheter embolization of perpancreatic arterial pseudoaneurysm. Cardiovasc. Intervent.Rad. 1995; 18(suppl 1): S122.

Nemes B, Bérci V, Hüttl K. Successful embolisation of post papillotomy bleeding. Cardiovasc. Intervent. Rad. 1995; 18 (Suppl 1): S123.

Nemes B, Hüttl K, Simonffy Á, Bérczi V. Az iliaca rendszer stenosisának kezelése PTA-val. Magyar Radiológia 2000; Suppl 1: 5.

Hüttl K, Bérczi V, **Nemes B**, Simonffy Á. PTA szövődményeinek kezelése intervencionalis eszközökkel. Magyar Radiológia 2000; Suppl 1: 6.

Taheri S, Ashraf H, Fang YV, Naughton J, **Nemes B**, Orlick A. Experimental Myometrial Cell Patch Cardiomyoplasty. The American Journal of Cardiology 2003; 92.

Nemes B, Hüttl K. Intervenciós beavatkozások az érbeteg ellátásban. Érbetegségek 2004 suppl: R2.

Sótonyi P, Gősi G, Szabó A, **Nemes B**. Vesetranszplantáció aorto-iliacalis keringészavar esetén. Érbetegségek 2004 suppl: E18.

Nemes B, Rimely E, Hüttl K. Vena Cava Superior syndroma kezelése stenteléssel. Cardiologica Hungarica 2008; 38: B35.

E. Vano, J.J. Gallego, S. Pellet, **B. Nemes**, J.M. Fernandez-Soto, F. Giczi, R. Sanchez. Inluence of the X-ray system on patient doses in vascular radiology: results of a bicentric European study. Cardiovasc Intervent Radiol 2009; 32 Suppl 2: 401