Neuroradiology (2005) 47: 222–228
DOI 10.1007/s00234-005-1351-2

H. Henkes
E. Miloslavski
S. Lowens
J. Reinartz
T. Liebig
D. Kühne

Treatment of intracranial atherosclerotic stenoses with balloon dilatation and self-expanding stent deployment (WingSpan)

Received: 29 October 2004
Accepted: 7 December 2004
Published online: 15 March 2005

H. Henkes · E. Miloslavski
S. Lowens · J. Reinartz
Robert Janker Klinik, Villenstrasse 4-8,
53129 Bonn, Germany

H. Henkes (✉) · T. Liebig · D. Kühne
Klinik für Radiologie und Neuroradiologie,
Alfried Krupp Krankenhaus, Alfried
Krupp Strasse 21, 45117 Essen, Germany
E-mail: HHHenkes@aol.com
Tel.: +49-228-5306101
Fax: +49-228-5306184

Abstract The endovascular treatment of atherosclerotic intracranial arterial stenoses has previously been based on balloon dilatation or the deployment of a balloon expandable stent. Both methods have advantages (balloon: flexibility; balloon expandable stent: high radial force) and drawbacks (balloon: risk of elastic recoil and dissection; balloon expandable stent: limited flexibility, risk of injury to the vessel due to excessive straightening, overexpansion at ends of stent). A new combination of balloon dilatation, followed by the deployment of a self-expanding microstent has been applied in 15 patients with atherosclerotic arterial stenoses, symptomatic despite medical treatment. An anatomically and clinically adequate result was achieved in all patients. The initial degree of stenosis was 72% (mean). Balloon dilatation resulted in an average residual stenosis of 54% (mean), reduced further to a mean of 38% after stent deployment. Arterial dissection, occlusion of the target artery or symptomatic distal emboli was not encountered. In one patient, a side branch occlusion occurred after dilatation of a M1 stenosis, with complete neurological recovery. All patients were either stable or improved 4 weeks after the treatment. Recurrent TIA did not occur in any patient. Balloon dilatation and subsequent deployment of a self-expandable stent for the treatment of symptomatic intracranial arterial stenoses combines the advantages of both techniques and allows a rapid, clinically effective and technically safe treatment of these frequently challenging lesions.

Keywords Intracranial arterial stenosis · Cerebral ischemia · Balloon dilatation · Angioplasty · Stent · Self-expanding

Introduction

With widespread access to MRI, transcranial ultrasound and angiographic examinations, intracranial atherosclerotic arterial stenoses are increasingly identified as the cause of brain ischemia. Asymptomatic intracranial stenoses may be associated with a benign prognosis [1]. Atherosclerotic intracranial stenoses are found, however, in about 8–10% of the patients with stroke or TIA [2]. The annual stroke rate for these lesions is in the range of 7–8% [3, 4] and the prognosis for patients under medical treatment is even worse [5]. Not infrequently, intracranial arterial stenoses lead to stroke with permanent neurological deficit without preceding transient ischemic attacks. Patients with a symptomatic intracranial atherosclerotic stenosis are insufficiently protected against ischemic stroke by medication with platelet aggregation inhibitors [6]. Permanent anticoagulation with warfarin is accompanied by significant hemorrhagic risks and does not reliably prevent pro-

gression of atherosclerotic stenosis or from the occurrence of thrombotic vessel occlusion as the final step of this disease [6, 7].

The treatment of such stenoses by the use of balloon dilatation and stent implantation has been increasingly accepted during the last 10 years. Balloon dilatation without a stent runs the risk of an immediate vascular occlusion (either by so-called ''elastic rebound'' or ''elastic recoil'' or by arterial dissection). Dilatation with coronary balloon-expandable stents or variants thereof is sometimes technically difficult due to the limited flexibility of these stents, particularly in vessels of the anterior circulation. The previously reported occurrence of serious complications during (stent) dilatation of intracranial stenoses has prevented the general acceptance of this treatment modality.

The technique of endovascular coil occlusion of wide-necked intracranial aneurysms was advanced by the introduction of flexible self-expanding nitinol stents (Neuroform; Smart Therapeutics/Boston Scientific) [8]. These stents can atraumatically be inserted through, and released off, a wire-guided microcatheter. They adapt to the shape and anatomy of the target vessel much better than balloon-expandable stents.

In this study, we present the first clinical results of the endovascular treatment of intracranial atherosclerotic stenoses by a new procedural concept. The treatment starts with a stent-less balloon dilatation, followed by covering the previously dilated stenosis with a self-expanding nitinol stent (WingSpan; Smart Therapeutics/Boston Scientific). This stent is a reinforced modification of the Neuroform device. This technique was developed to decrease the procedural risks compared to pure balloon dilatation or the use of relatively rigid balloon-expanded coronary stents. Presuming that the occurrence of intimal hyperplasia and in-stent-stenosis are influenced by the adaptation of an implanted stent to the vessel wall and its radial force, improved long-term results can be expected from this implant.

Materials and methods

Fifteen patients (ten male, five female, mean age 64 years) with atherosclerotic stenoses of intracranial arteries were enrolled. These stenoses had caused ischemic clinical symptoms and/or infarcts while under medical therapy. All endovascular procedures were performed following the requirements of the clinical study of the WingSpan-system (Smart Therapeutics/Boston Scientific). The ethics committee of the University Duisburg-Essen approved the study. According to the protocol of this study, patients with intracranial arterial stenosis $>50\%$, symptomatic under medical therapy and with a brain ischemia attributable to this stenosis can be enrolled.

Medication

At the time of stent treatment, all patients were premedicated either by preceding administration of a combination of 100 mg ASA and 75 mg clopidogrel daily or by taking a loading dose of 500 mg ASA and 300 mg clopidogrel at least 2 days preceding the treatment, followed by the intake of the above mentioned daily dose. After introduction of a 6F femoral sheath into the right femoral artery, 5000 IU heparin and 500 mg aspisol were given intravenously. Following the procedure, a single subcutaneous dose of 0.8 ml low molecular heparin (Fraxiparin) was given on the day of treatment. On the 2 following days 0.6 ml Fraxiparin was administered subcutaneously twice a day. Additionally, permanent medications of 100 mg ASA per os daily and 75 mg clopidogrel per os daily were administered for 2 months.

Treatment technique

All procedures were performed by one of the authors (HH) under general intravenous anesthesia with complete relaxation using a high-resolution bi-plane DSA system (Philips Integris Allura 12/15). A 6F-guiding catheter (Guider softip; Target Therapeutics/Boston Scientific) was introduced through a femoral sheath into the target supraaortic vessel. An angiographic examination of the target vessel with the intracranial stenosis and of the distal vasculature was then performed.

From a series of projections, one, which showed the stenosis without foreshortening or overlap, was chosen. Two external markers (steel ball bearings with a diameter of 1 cm) were used for quantitative measurements of stenosis and target vessel diameter and length. Using the standard software of the DSA system, the narrowest diameter of the stenotic vessel, the length of the stenosis and the diameter of the target vessel proximal and distal to the stenosis was determined.

The stenosis was then crossed with an exchange microguidewire (0.014 in., 300 cm). The following microguidewires proved suitable: Transend 14 (Boston Scientific), Synchro 14 (Boston Scientific), *X*-celerator 14 (MTI/ev3). The introduction of the guidewire was limited to a position just far enough to provide a sufficient stability in the area of the stenosis, minimizing the risk of a vessel perforation with the guidewire tip.

The dilatation balloon was chosen in a way that its diameter at nominal pressure would not exceed 80% of the diameter of the vessel either proximally or distally to the stenosis, whichever was smaller. Generally, an ''over-the-wire'' balloon (Gateway, Boston Scientific) was used. In one patient, a coronary monorail balloon (Aqua, Cordis) was used.

The dilatation balloon was introduced until the stenotic vessel segment was covered. The manometer-con-

Table 1 Initial clinical findings and treatment results of 15 patients with symptomatic intracranial arterial stenoses, treated by balloon dilatation and subsequent implantation of a self-expanding stent. Risk factors: *AH* arterial hypertension, *DM* diabetes mellitus, *SM* smoking, *HL* hyperlipidemia, *FA* positive familial anamnesis, *ICA* internal carotid artery, *MCA* middle cerebral artery, *VA* vertebral artery, *BA* basilar artery

No.	Initials, age, gender	risk factors	Symptoms, medication	Localisation and dimensions of stenosis (%), diameter of the vessel, proximal to (prox) and in area of stenosis (sten)	Balloon, stent, residual stenosis (%)—post PTA—post stent duration of intervention	Procedural outcome, complications
1	IV, 78, f	AH, DM, HL	Recurrent severe TIAs under warfarin (INR 2.6)	ICA left (C4) 87% prox: 3.9 mm sten: 0.5 mm	B: 3.5/9 mm S: 4/20 mm PTA: 51% stent: 51% 22 min	No procedural complication
2	RM, 54, m	AH, SM, HL	Recurrent severe TIAs under warfarin, (INR > 2), later under ASA, clopidogrel and heparin	ICA left (C1) 80% prox: 2.4 mm sten: 0.5 mm	B: 2/15 mm S: 2.5/15 mm PTA: 63% stent: 37% 72 min	No procedural complication
3	WB, 62, m	DM, SM, HL	Motor dysfunction and parenchymal lesions arising under clopidogrel	ICA left (C4) 57% prox: 4.5 mm sten: 1.9 mm	B: 4/15 mm S: 4.5/15 mm PTA: 36% stent: 30% 48 min	No procedural complication
4	AF, 60, m	AH, DM, SM, HL, FA	Right-sided hemiparesis, cerebellum- and brain stem ischemia under ASA	BA 77% prox: 2.2 mm stent: 0.5 mm	B: 2.5/10 mm S: 3.0/20 mm PTA: 79% stent: 41% 81 min	No procedural complication
5	NO, 51, f	AH, DM	Recurrent MCA infarction under ASA	MCA right (M1) 61% prox: 2.2 mm sten: 0.8 mm	B: 1.5/15 mm S: 2.5/15 mm PTA: 64% stent: 23% 133 min	Transient renal failure, sepsis, ischemic brain lesion, transient increase of hemiparesis
6	US, 47, f	AH, SM	Recurrent TIAs under ASA, chronic headache and impaired cognition under warfarin	MCA right (M1) 71% prox: 3.3 mm stent: 0.9 mm	B: 1.5/15 mm S: 2.5/15 mm PTA: 76% stent: 46% 85 min	No procedural complication
7	JR, 75, m	AH	Recurrent TIAs under ASA	MCA right (M1) 82% prox: 3.5 mm stent: 0.7 mm	B: 2.0/15 mm S: 3.5/15 mm PTA: 68% stent: 48% 85 min	No procedural complication
8	MS, 80, f	AH, DM	Recurrent stroke and TIAs under heparin	VA left (V4) 69% prox: 2.7 mm stent: 0.9 mm	B: 2.25 /15 mm S: 4.5/20 mm PTA: 46% stent 30% 72 min	No procedural complication
9	AH, 54, m	AH, DM, SM	Recurrent TIAs under Heparin	BA 80% prox: 3.9 mm stent: 0.8 mm	B: 2.0/15 mm S: 4.0/20 mm PTA: 60% stent: 41% 45 min	No procedural complication
10	HGS, 67, m	AH, DM, HL	Recurrent brain stem TIAs under warfarin	BA 71% prox: 3 mm stent: 0.9 mm	B: 2.5/15 mm S: 3.5/15 mm PTA: 65% stent: 44% 42 min	No procedural complication
11	PS, 55, m	AH, HL	Recurrent stroke and TIAs under ASA	VA right (V4) 67% prox: 4.3 mm stent: 1.4 mm	B: 3.5/20 mm S: 4.5/20 mm PTA: 53% stent: 36% 55 min	No procedural complication
12	EW, 78, f	AH, DM, HL	Recurrent TIAs under ASA and Clopidogrel	BA 64% prox: 2.2 mm stent: 0.8 mm	B: 2.0/15 mm S: 3.5 /15 mm PTA: 13% stent: 11% 54 min	No procedural complication
13	EK, 64, m	AH, DM, HL	Recurrent TIAs and strokes under ASA	BA 83% prox: 3.6 mm stent: 0.6 mm	B: 2.5/15 mm S: 4.0/15 mm PTA: 48% stent: 43% 66 min	No procedural complication
14	KW, 64, m	AH, SM	Recurrent TIAs under heparin	VA right (V4) 55% prox: 3 mm stent: 1.3 mm	B: 3.0/15 mm S: 4.0 /15 mm PTA: 33% stent: 33% 20 min	No procedural complication
15	AK, 76, m	AH, HL	Recurrent TIA under ASA and clopidogrel	VA left (V4) 77% prox: 3.8 mm stent: 0.9 mm	B: 3.0/9 mm S: 4.0/15 mm PTA: 55% stent: 48% 20 min	No procedural complication

trolled vessel dilatation was performed very slowly for a maximum of 90 s until complete balloon inflation was achieved. With one exception, pressure of three atmospheres was sufficient for full balloon opening without a waist.

During deflation and withdrawal of the balloon, the guidewire was left in place. The dilatation results were angiographically documented and, finally, the self-expanding stent was introduced and deployed. For all patients, the diameter of the stent was chosen slightly larger than the diameter of the previously used balloon. The stent length was selected to completely cover the dilated stenosis with an overhang of at least a few millimeters on both sides. Approximately 10 min after deployment of the stent and withdrawal of the guidewire, a final angiographic examination terminated the intervention. The time period from the first to the last DSA run was registered as the duration of the procedure.

Results

The initial diagnostic findings and treatment results are summarized in Table 1. Figures 1 and 2 shows the treatments of a stenosis of the internal carotid artery and basilar artery, respectively.

In this series, the intracranial stenoses were located at the intracranial internal carotid artery ($n = 3$), the M1 segment ($n = 3$), the intracranial vertebral artery ($n = 4$) or the basilar artery ($n = 5$). In all patients, the passage and dilatation of the stenoses with the balloon catheter was successful. No dissection or elastic recoil was encountered. The high flexibility and the low profile of the Gateway balloon catheter significantly facilitated this part of the procedure. The introduction and deployment of the stents was performed readily, without any visible damage to the target vessels, with the high flexibility of the WingSpan stent proving clearly advantageous compared to balloon expandable stent systems. The balloon dilatation results were improved by WingSpan deployment to a variable extent, but there was usually a significant additional dilatation effect due to the stent.

The stenoses before the treatment were measured as 72% mean (minimum 55%, maximum 87%). After balloon dilatation the stenoses were reduced to 54%

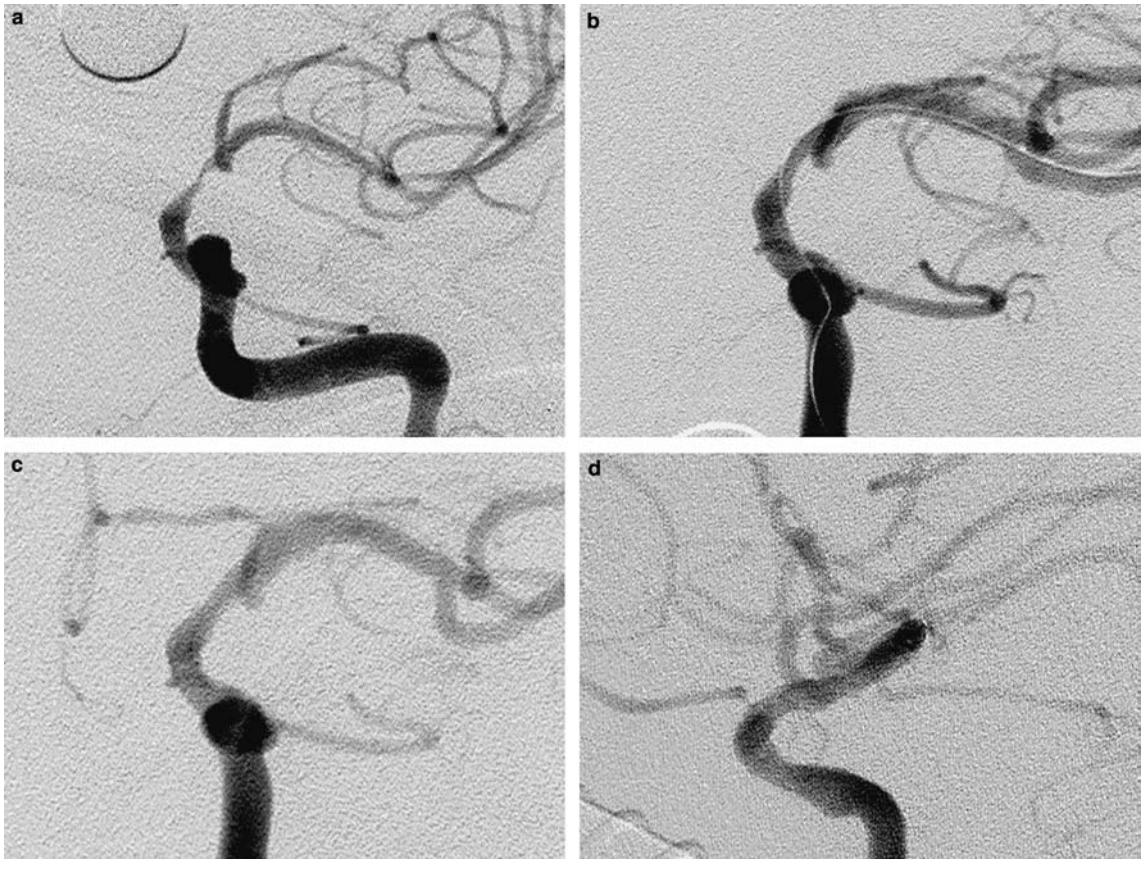

Fig. 1 Symptomatic high-grade stenosis of the left internal carotid artery proximal to the posterior communicating artery (*PcomA*). Angiography prior to the treatment (**a**), after balloon angioplasty (2/20 mm, 6 atm) (**b**), and after deployment of a self-expanding stent (**c**,**d**). Minor residual stenosis with unchanged opacification of the *PcomA*

mean (minimum 13%, maximum 79%) and after the stent deployment further reduced to 38% mean (minimum 11%, maximum 51%). The final reconstructed lumen proved sufficient to provide adequate blood flow in all patients. The procedure time from the first to the last DSA run was 60 min mean (minimum 20 min, maximum 133 min). In-stent thrombosis did not occur. In one patient with a MCA stenosis a MCA branch was occluded by the procedure, with a transient increase of a pre-existing hemiparesis. In the remaining 14 patients, the ischemic symptoms that were observed under antiaggregation or anticoagulation before the endovascu-

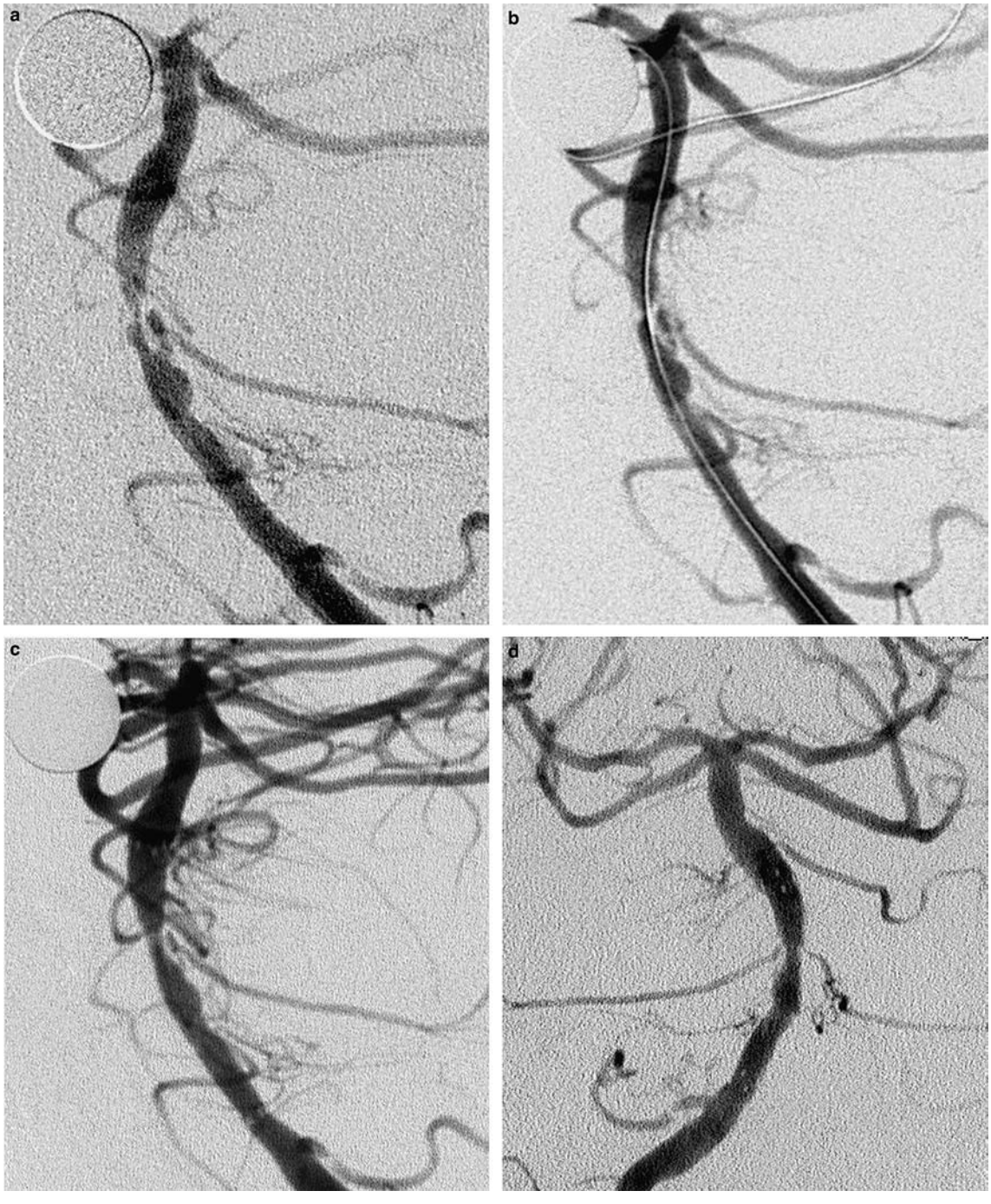

Fig. 2 Symptomatic near-occlusive stenosis of the middle basilar artery at the level of the origin of the anterior inferior cerebellar artery (*AICA*). Initial angiographic finding (**a**), the result after balloon dilatation (2/10 mm, 3 atm) with significant residual stenosis (**b**), and after deployment of a self-expanding stent (**c**) with residual stenosis. The stent covers both *AICA* origins without evident hemodynamic effect on them (**d**)

lar treatment did not recur after the WingSpan treatment.

Discussion

Intracranial atherosclerotic stenoses are a major risk factor for ischemic stroke. Bypass surgery proved ineffective for the treatment of ICA and MCA stenoses [9]. The ultimate cause of cerebral ischemia is related to the hemodynamic effect of the stenotic vessel segment. Thrombo-embolic events are of uncertain significance in this pathophysiology. This may explain why medical therapy with either antiaggregation or anticoagulant drugs is of limited efficacy. The medication with platelet aggregation inhibitors is accompanied by relatively minor side effects, but provides insufficient protection for the patient. More aggressive anticoagulation provides better protection from stroke, but is accompanied by a significant incidence of hemorrhagic complications [6].

Balloon dilatation of symptomatic intracranial stenoses without stent deployment has been carried out in specialized centers after the advent of single lumen balloon microcatheters since about 1992 with fairly good results [10–12]. High frequency of adverse events, as reported by Gupta et al. [13] with a 50% major complication rate and a 17% fatality rate, illustrate the potentially hazardous nature of these procedures. The main causes of adverse events are vessel dissection or perforation, elastic recoil, distal injury to the vessel wall from the microguidewire and embolic vessel occlusion.

With the availability of balloon expandable coronary stents, secondary stent deployment became an option in the case of insufficient effect of balloon dilatation or immediate vessel occlusion due to elastic rebound [14]. In order to avoid the variable outcomes of balloon-only procedures, several authors started to promote the primary use of balloon expandable coronary stents [15]. In a series of 34 patients with intracranial stenoses, stented by Lylyk et al. [16], the global morbidity rate was 18%, with a 6% neurologic morbidity rate and a 6% mortality rate. Jiang et al. [17] achieved good results in 42 symptomatic M1 stenoses, with a 10% total complication rate but incomplete follow-up data. In a recently published prospective study, far from ideal results were reported [18]. In three out of 61 patients of this series, the stent placement was not possible. At 6 months, follow-up 12 of 37 patients (32%) with intracranial lesions had a $>50\%$ restenosis. In the first 30 post-procedural days the stroke rate was 6.6%, with an additional stroke rate of 7.3% thereafter.

This device-related dilemma can be summarized as follows: balloon dilatation without a stent is technically easier, but provides insufficient control of dissection and elastic recoil while balloon-expandable stent deployment is associated with a significant risk of vessel injury, mainly due to over-sizing of the stent and dog-bone effect of the balloon.

When choosing both balloon and stent diameter, it always has to be kept in mind that an exponential relation between vessel diameter, cross-section area and blood flow volume exists. Due to this relation, doubling a vessel diameter will result in a 4-fold increase in blood flow. Since the risk of complications increases with the dilated diameter, intentional under-dilatation is a well-accepted strategy. For such an under-dilatation, balloon-expanded stents are not well suited, as there is a risk that an undersized stent will not be fixed to the vessel wall and will therefore move within the dilated vessel.

The passage of the previously dilated artery segment with the WingSpan stent-catheter over a microguidewire kept in place during the whole procedure seems in prospect more difficult than it finally proves. The rounded tip of the stent-catheter allows for atraumatic insertion, assuming that the guidewire is not accidentally withdrawn during removal of the balloon catheter or introduction of the stent. The stent itself is not radiopaque, but carries radiopaque markers on its distal and proximal ends, which allow accurate positioning. It was our impression that the WingSpan stent conforms very well to the vessel wall and, despite its limited radial force, makes sufficient contact with it.

Several limitations of these data must be mentioned. The high success and low complication rate in this series are partly due to the desirable physical properties of the device under investigation. Safety and efficacy may, however, vary significantly with both experience and skills of the operator and familiarity of the operator with the device. The restrictions placed on the use of the device, mentioned at the outset, are unlikely to be applied so rigorously in general clinical use. So far, no data can be given on the frequency of recurrent stenoses. For coronary lesions $>30\%$ restenosis rates after self-expanding stent implantation has been reported [19], however, these data may not be directly applicable to the intracranial arteries, where flow patterns are different and the radial force of the stent is lower. Only long-term follow-up will address these issues. Stent surface modification seems to be one possible way to improve long-term patency rates [20]. Experimental data have shown that self-expandable stenting alone reduces the rate of restenosis compared with balloon dilatation followed by stent deployment [21]. If this is also true for intracranial stenoses the use of a modified self-expanding stent with an increased radial force might yield reduced recurrent stenoses.

In conclusion, in the endovascular treatment of atherosclerotic intracranial arterial stenoses, intentional under-expansion should be the aim. The combination of balloon dilatation and subsequent deployment of a self-

expanding stent increases the safety of this procedure without compromising efficacy. Mid-term and long-term patency and stroke rates are pending.

Acknowledgements The authors are most grateful to Dr. H. Preiss for excellent anesthesiological service.

References

1. Kremer C, Schaettin T, Georgiadis D, Baumgartner RW (2004) Prognosis of symptomatic stenosis of the middle cerebral artery. J Neurol Neurosurg Psychiatry 75:1300–1303
2. Lutsep HL, Clark WM (2000) Association of intracranial stenosis with cortical symptoms or signs. Neurology 55:716–718
3. Marzewski DJ, Furlan AJ, St Louis P, Little JR, Modic MT, Williams G (1982) Intracranial internal carotid artery stenosis. Long term prognosis. Stroke 13:821–824
4. Petty GW, Brown RD, Whisnant JP, Sicks JD, O'Fallon WM, Wiebers DO (2000) Ischemic stroke subtypes. A population-based study of functional outcome, survival, and recurrence. Stroke 31:1062–1068
5. Thijs VN, Albers GW (2000) Symptomatic intracranial atherosclerosis. Outcome of patients who fail antithrombotic therapy. Neurology 55:490–497
6. Warfarin–Aspirin symptomatic intracranial disease (WASID) study group (1998) Prognosis of patients with symptomatic vertebral or basilar artery stenosis. Stroke 29:1389–1392
7. Meyring S, Jacoby N, Tillmann F, Henkes H, Leopold HC (2002) Local intra-arterial fibrinolysis of acute basilar artery occlusion under oral anticoagulation. Akt Neurol 29:203–207
8. Henkes H, Bose A, Felber S, Miloslavski E, Berg-Dammer E, Kühne D (2002) Endovascular coil occlusion of intracranial aneurysms assisted by a novel self-expandable nitinol microstent (Neuroform). Interv Neuroradiol 8:107–119
9. The EC/IC bypass study group (1985) Failure of extracranial–intracranial bypass to reduce the risk of ischemic stroke. Results of an international randomized trial. N Engl J Med 313:1191–1200
10. Berg-Dammer E, Henkes H, Weber W, Berlit P, Kühne D (1998) Percutaneous transluminal angioplasty of intracranial artery stenosis: clinical results in 24 patients. Neurosurg Focus 5, Article 13
11. Marks MP, Marcellus M, Norbash AM, Steinberg GK, Tong D, Albers GW (1999) Outcome of angioplasty for atherosclerotic intracranial stenosis. Stroke 30:1065–1069
12. Alazzaz A, Thornton J, Aletich VA, Debrun GM, Ausman JL, Charbell F (2000) Intracranial percutaneous transluminal angioplasty for arteriosclerotic stenosis. Arch Neurol 57:1625–1630
13. Gupta R, Schumacher HC, Mangla S et al. (2003) Urgent endovascular revascularization for symptomatic intracranial atherosclerotic stenosis. Neurology 61:1729–1735
14. Joseph GJ, Goldstein J, Cloft H, Tong F, Dion J (2000) Endovascular stenting of atherosclerotic stenosis in a basilar artery after unsuccessful angioplasty. Am J Radiol 174:384–385
15. Piotin M, Blanc R, Kothimbakam R, Martin D, Ross IB, Moret J (2000) Primary basilar artery stenting: immediate and long-term results in one patients. Am J Radiol 175:1367–1369
16. Lylyk P, Cohen JE, Ceratto R, Ferrario A, Miranda C (2002) Angioplasty and stent placement in intracranial atherosclerotic stenoses and dissections. Am J Neuroradiol 23:430–436
17. Jiang WJ, Wang YJ, Du B et al. (2004) Stenting of symptomatic M1 stenosis of middle cerebral artery. An initial experience of 40 of patients. Stroke 35:1375–1380
18. The SSYLVIA study investigators (2004) Stenting of symptomatic atherosclerotic lesions in the vertebral or intracranial arteries (SSYLVIA). Study results. Stroke 35:1388–1392
19. Foley DP, Rensing BJ, Pieper M et al. (1999) Clinical and quantitative angiographic outcomes following elective implantation of the self-expanding Wallstent for longer coronary artery lesions—final results of the Wellstent native study. Int J Cardiovasc Intervent 2:171–179
20. Meyer JM, Nowak B, Schuermann K et al. (2003) Inhibition of neointimal proliferation with 188Re-labeled self-expanding nitinol stent in a sheep model. Radiology 229:847–854
21. Harnek J, Zoucas E, Stenram U, Cwikiel W (2002) Insertion of self-expandable nitinol stents without previous balloon angioplasty reduces restenosis compared with PTA prior to stenting. Cardiovasc Intervent Radiol 25:430–436