Endovascular Treatment of Symptomatic Carotid Stenosis Using Stent Placement
Long-Term Follow-Up of Patients With a Balanced Surgical Risk/Benefit Ratio

Andreas Dietz, MD; Joachim Berkefeld, MD; Jacques G. Theron, MD; Thomas Schmitz-Rixen, MD; Friedhelm E. Zanella, MD; Bernd Turowski, MD; Helmuth Steinmetz, MD; Matthias Sitzer, MD

Background and Purpose—Carotid endarterectomy (CEA) is not necessarily beneficial in all patients with symptomatic high-grade (≥70%) internal carotid artery (ICA) stenosis. Independent risk factors modulate both the individual stroke risk under medical treatment and the combined stroke and death risk after CEA. Endovascular stenting of symptomatic ICA stenosis may be an alternative to CEA in patients with a balanced surgical risk/benefit ratio.

Methods—We included 43 patients (71% men; median age, 67 years) with a recently symptomatic ICA stenosis with ≥70% luminal narrowing in whom the individual sum of medical and surgical risk factors suggested a balanced surgical risk/benefit ratio (risk-modeling appraisal derived from the European Carotid Surgery Trial). After stenting of the stenosed ICA with distal balloon protection, the mean±SD follow-up, including clinical and ultrasonographic examinations, was 20±11.8 months, with a median number of examinations of 5 per patient.

Results—Recanalization of ICA stenoses was technically successful in 40 of 43 procedures (93%). Within the 30-day postinterventional period 1 death occurred (2.5%), and the combined stroke and death rate within follow-up was 5%. Except for 1 asymptomatic ICA occlusion, no restenosis ≥70% occurred during follow-up.

Conclusions—ICA stenting in symptomatic patients with a balanced surgical risk/benefit ratio is technically feasible, with a low periprocedural risk of stroke or death. Furthermore, the risk of future stroke and rate of significant restenosis during long-term follow-up appears to be low, suggesting that ICA stenting may be useful in carotid revascularization and stroke prevention. (Stroke. 2001;32:1855-1859.)

Key Words: angiography, digital subtraction ▪ carotid artery diseases ▪ carotid stenosis ▪ cerebrovascular disorders ▪ endovascular therapy ▪ stents ▪ ultrasonography

Carotid endarterectomy (CEA), performed with a low complication rate, is the only revascularization procedure of proven efficacy in symptomatic internal carotid artery (ICA) disease. It reduces stroke risk and overall mortality in patients with a recently symptomatic high-grade ICA stenosis, as defined by a transient ischemic attack (TIA) or minor stroke within the last 6 months attributable to a ≥70% narrowed ICA.1,2 Additionally, CEA may be effective in reducing the risk of TIA s, stroke, and overall mortality in patients with an asymptomatic ≥60% ICA stenosis or with a recently symptomatic ≥50% ICA stenosis.3,4 According to a meta-analysis, the average risk of stroke or death associated with CEA was 3.35% in asymptomatic ICA stenosis and 5.18% in symptomatic ICA stenosis.5 The Stroke Council of the American Heart Association has stated that for CEA the combined mortality and morbidity risk must be <3% for asymptomatic patients and <6% for symptomatic patients.6 Nevertheless, a positive risk/benefit ratio could not be achieved across all patients fulfilling the aforementioned criteria.7 In a post hoc analysis of the data of the European Carotid Surgery Trial, a risk-modeling appraisal revealed several independent risk factors modulating both individual 5-year stroke risk in case of medical treatment and 30-day stroke and death risk in case of surgery. The investigators found that the probability of an ipsilateral stroke within the next 5 years under medical treatment alone increases steadily with the individual number of the following independent risk factors: cerebral versus ocular clinical symptoms (1 point), plaque surface irregularity on intra-arterial angiogram (1 point), any ischemic event within the past 2 months (1 point), degree of stenosis 80% to 89% (1 point), or degree of stenosis 90% to 99% (2 points). In contrast, the individual risk of any fatal event (any stroke or death) within the first 30 days after...
CEA increases with the number of the following independent risk factors: female sex (−0.5 point), presence of peripheral arterial disease (−0.5 point), or a preoperative systolic blood pressure >180 mm Hg (−0.5 point) (Table 1). The net sum of individual risk factors in which the medical factors count positively and the surgical factors count negatively with the aforementioned point values may serve as an individual surgical risk/benefit score. A positive risk/benefit ratio favoring CEA was only present in case of a score of >4 in 1 individual, whereas the ratio was balanced below this threshold.

Endovascular treatment of ICA stenosis with the use of percutaneous transluminal angioplasty (PTA) with or without stent placement has been proposed as an alternative to CEA.8–11 Several case series have been published within the last years using PTA alone12,13 or combined with stenting of ICA stenosis.14–20 Overall, the procedure-related complication rates (death or stroke) ranged between 0% and 9.4%, with technical success rates between 86% and 100%. Follow-up data have not been provided by all studies, but if present they covered a 6- to 70-month period.12–14,16–18 Within this time frame, the combined rates of fatal events (death or stroke) ranged from 0% to 6.9%.12,17 Rates of significant restenosis (≥70%) have been reported to be as high as 16% in case of PTA alone and 4% in case of ICA stenting.13,17 Unfortunately, detailed preinterventional clinical characteristics of the treated patients have not been provided sufficiently in all reports. The majority of patients were asymptomatic, and general conclusions about safety and efficacy cannot be drawn from these series.

Therefore, endovascular treatment of ICA stenosis must be carefully evaluated for both safety and efficacy before its widespread use may eventually be recommended. Thus, a consensus statement of neurologists and vascular surgeons has called for safety and long-term efficacy data of endovascular carotid angioplasty before randomized, controlled studies can be initiated.8 Until now, prospectively collected long-term follow-up data that may elucidate the clinical outcome of endovascular stent placement have been rare.17,20

### Subjects and Methods

#### Patients

We included 43 consecutive patients (median age, 67 years; age range, 52 to 84 years) fulfilling the following criteria: (1) transient retinal or cerebral symptoms (TIA) or minor ischemic stroke within the past 120 days according to the criteria of the North American Symptomatic Carotid Endarterectomy Trial,21 attributable to (2) atherosclerotic stenosis of the ipsilateral ICA of ≥70% luminal narrowing based on color Doppler-assisted duplex imaging (CDDI) (cross-sectional area reduction; see below)22 and (3) an individual surgical risk/benefit ratio score <4, suggesting a balanced surgical risk/benefit ratio. Since July 1999, 25 patients were prospectively recruited. The remaining 18 patients were retrospectively identified from a larger sample of patients stented before this time (n=41). All patients were prospectively included into follow-up. This study was approved by the local ethics review committee and performed in accordance with the institutional guidelines. Written informed consent was given by each patient before study entry.

#### Intervventional Procedure

Technical feasibility of the procedure was assessed according to preoperative angiograms. The degree of ICA stenosis was confirmed on the basis of angiographic criteria.23 For correct selection of stent and angioplasty balloon size, the diameters of the normal common carotid artery (CCA) and ICA as well as of the residual...
lumen within the stenosis were measured angiographically and by high-resolution color duplex sonography. All carotid stent procedures were performed under local femoral anesthesia, and an anesthesiologist monitoring the vital functions as well as the interventional team communicated permanently with the patient. Self-expanding Wallstents (Schneider–Boston Scientific) were implanted under distal balloon protection of the ICA according to the technique described by Theron et al. To access the lesion from a transfemoral approach, a large-caliber (8F or 9F, depending on the stent subtype) guiding catheter was placed into the CCA below the stenosis. For temporary balloon occlusion of the ICA, the residual lumen was passed by a protection system that combines the functions of an exchange guidewire and a microballoon catheter. For the first 31 procedures, hand-mounted protection systems (3-m-long microcatheters [Cordis] with nondetachable latex balloons [Nycomed]) were used. After a steerable microguidewire with integrated balloon (Percu-Surge) became available, it replaced the aforementioned protection system. The protection balloon was inflated distal to the stenosis to occlude the ICA during the manipulations at the plaque. Predilation with a 3-mm PTA balloon catheter was performed before stent placement in tight stenoses with a residual lumen smaller than the diameter of the stent delivery catheter. After catheter exchange over the wire of the protection system, the stent was delivered across the stenosis. This step was followed by postdilation of the partly expanded stent with an angioplasty balloon adapted to the diameter of the normal ICA. After removal of the PTA balloon, the guiding catheter was advanced into the upper stent end. To eliminate potential emboli released during angioplasty and stent placement, 2×20 mL of blood was aspirated, and 40 mL of saline was injected to flush residual embolic particles into the territory of the external carotid artery. After that cleaning procedure, the protection balloon was deflated to restore the blood flow in the ICA. Control angiograms were performed to evaluate recanalization results and to exclude embolization into intracranial vessels.

Peri-interventional and Postinterventional Medical Treatment

Patients were preloaded with a combined antiplatelet treatment of aspirin (100 mg/d) and clopidogrel (75 mg/d) starting 5 days before intervention. In addition to antiplatelets, a heparin bolus of 150 IU/kg was given after placement of the arterial introducer sheath. For the prevention of bradycardia, 0.5 to 1 mg of atropine was administered immediately before each balloon dilation. After intervention, anticoagulation was continued with the use of heparin for 24 hours with individual dosages, leading to a 2.5-fold prolongation of the activated partial thrombin time compared with baseline preinterventional values. Combined antiplatelet therapy was continued for 3 months, and thereafter clopidogrel was stopped.

Follow-Up

All patients were scheduled to be seen 24 hours, 30 days, and 3, 6, 12, 24, and 36 months after intervention by a neurologist. Any stroke, TIA, myocardial infarction, or death constituted a clinical outcome event. In case of a stroke event, etiology (ischemic versus hemorrhagic) and location were clarified by the neurologist. Additionally, at each visit ultrasonographic evaluation of the stented ICA was performed by a sonographer according to a standardized protocol (see below).

Ultrasonographic Examinations

In all cases CDDI of the ICA was performed with a 7.5- to 10.0-MHz linear array scanner for B-mode gray scale images and a 5.0-MHz pulsed-wave transducer for superimposed simultaneous color-encoded blood flow information and at each follow-up after the intervention (Siemens SONOLINE Elegra Advanced, Siemens Medical Systems, Inc). The CDDI examinations included longitudinal and transverse views of the ICA at the level of the stenosis, allowing delineation of the normal (former) ICA lumen \( (A_N) \) as well as of the minimal residual “flow lumen” \( (A_S) \). With the use of transverse views of the narrowest part of the stenosis or after stent placement at the part of the narrowest flow lumen, the degree of luminal reduction was determined as the percentage of local cross-sectional area reduction: \((1 - (A_S/A_N)) \times 100\%\). Interobserver correlations have been determined previously and ranged between \( r = 0.76 \) and \( r = 0.90 \) (median \( r = 0.83 \); linear regression). Furthermore, categorization of ICA stenosis based on ultrasonographic and angiographic criteria revealed high concordance (number of stenoses classified by ultrasound/number of stenoses classified by angiography): \(<70%\); 0/0; 70% to 79%; 11/9; 80% to 89%; 15/16; 90% to 99%; 14/15. Additionally, angle-corrected systolic peak flow velocity was determined at the maximum of the stenosis preinterventionally and at the part of the narrowest flow lumen after stent placement. Complete vessel occlusion or a significant restenosis (\( \geq 70\% \) luminal narrowing) constituted vascular outcome events during follow-up.

Data Analysis

To display the postinterventional clinical course of the study population, Kaplan-Meier curves were drawn. Censor points were any TIA, ipsilateral TIA, any stroke, ipsilateral stroke, myocardial infarction, and nonstroke death. Preinterventional and postinterventional degrees of stenosis as well as peak systolic velocities were compared with a nonparametric test (Wilcoxon test).

Results

Technical Feasibility

Recanalization of ICA stenoses by stent placement was technically successful in 40 of 43 procedures (93%). In 3 patients extreme elongation or tortuosity of the aortic arch and its branches impeded the positioning of the stent delivery system, so that CEA was performed in these cases. In the 40 technically successful procedures, 8 Wallstents, 25 Easy Wallstents, and 9 Carotid Wallstents were implanted. Two of these cases required 2 overlapping Easy Wallstents to cover the entire plaque, respectively. Full balloon protection during predilation, stent deployment, and postdilation was feasible in 31 stent implantations. Partial balloon protection was confined to the last step of stent postdilation in 8 cases with impossible primary passage of the stenosis by the hand-mounted protection system and in 1 patient who did not tolerate ICA occlusion for \( >3 \) minutes.

Clinical Outcome

Of the 40 patients in whom stent placement was technically successful, none was lost to follow-up and none withdrew. The median follow-up was 22.7 months (mean \( \pm SD, 20.0 \pm 11.8 \) months), ranging from 31 days to 36 months; the median number of examinations was 5 (mean \( \pm SD, 4.5 \pm 1.5 \) per patient. Within the 30-day postinterventional period, 1 patient died of septic shock with disseminated intravascular coagulation 2 days after intervention. No patient had cerebrovascular symptoms or myocardial infarction. Therefore, the combined perioperative stroke and death rate was 2.5%. Within the entire follow-up, 1 patient (2.5%) suffered a hemorrhagic stroke contralateral to the stented ICA 108 days after intervention. Additionally, ipsilateral cerebral or retinal TIA occurred in 2 patients 246 and 337 days after intervention, respectively. There were no ipsilateral strokes, no myocardial infarctions, no contralateral TIAs, and no additional deaths during follow-up. Therefore, the combined event rate of any stroke or death was 5% across the entire follow-up. Including TIAs, the event rate was 10%. A Kaplan-Meier estimate of symptom-free survival is displayed.
in the Figure. Within the group of patients (n=23) stented before July 1999 and not included in the present analysis, the combined event rate of any stroke or death was 5% (1 death) across a median follow-up of 26.8 months (20 to 32 months).

Vascular Outcome
The mean±SD degree of ICA stenosis was reduced from 83.3±9.3% to 2.7±12.2% according to sonographic criteria at first follow-up (30 days) after stent placement (P<0.0001). Additionally, mean±SD peak systolic velocity dropped from 326.2±141.8 cm/s to 88.7±38.4 cm/s within the first 30 days (P<0.0001; Table 3). In 1 case the stented ICA was completely occluded by a local thrombus within the first 24 hours after stent delivery without clinical symptoms (Table 3). In another patient a residual stenosis (60% luminal narrowing) remained after treatment because of elastic recoil of the stent within a highly calcified plaque (Table 3). Across the entire follow-up, no significant restenosis (≥70% luminal narrowing) occurred.

Discussion
Stent placement for the treatment of symptomatic high-grade ICA stenosis was technically feasible in 40 of 43 cases (93%) of our series. Furthermore, 30-day mortality was 2.5%, and the combined overall stroke or death rate across a median follow-up of 22.7 months was 5%. No ipsilateral stroke occurred during follow-up. The patency rate of the stented ICA was 97.5%, 1 medium-grade residual stenosis (60% luminal narrowing) remained after stenting, and no significant restenosis occurred during follow-up. Thus, one may conclude from this series that stenting of high-grade ICA stenosis is technically feasible, successful, and possibly beneficial in symptomatic patients.

Four previous case series have reported 30-day mortality and morbidity rates of stenting in symptomatic patients with high-grade ICA stenosis.14,17,18,20 Combined stroke or death rates within the first 30 days after intervention ranged from 4.4% to 10.8%. Furthermore, long-term follow-up data (6 to 23 months) showed that the combined rate of any stroke or death ranged from at least 6.8% to 12.7% within follow-up in symptomatic patients. Reported patency rates of the stented ICA ranged from 89% to 100% in these series.5,14,17,18,20 As in the present series, no major cardiac event occurred within the first 30 days after intervention. Therefore, the reported rates of clinical and vascular outcome events in our series are at least as positive as those reported in the other studies.

A novel aspect of the present study is that patients were included on the basis of an established risk/benefit scoring system that allows prediction of both the mortality associated with CEA and the 5-year risk of ipsilateral major stroke.7 On the basis of this scoring system, all patients of the present study had an individual risk score of ≥4 points, indicating a balanced surgical risk/benefit ratio. Thus, CEA did not necessarily appear to be beneficial in these patients.7 The expected 30-day stroke or death rate in these patients was 3 of 40 (7.5%; 95% CI, 4% to 15%).7 In comparison, only 1 death and no occurrences of stroke (2.5%) were observed after stenting within the same time. On the other hand, the expected number of major ipsilateral strokes over 5 years under medical treatment alone was 11 of 40 (28%; 95% CI, 18% to 38%), 8 of which would be expected to occur within the first 2 years.7 In comparison, no major ipsilateral stroke occurred during the mean follow-up of almost 2 years in the study population.

The major purpose of the present study was to answer the question of whether stenting of high-grade ICA stenosis in

**TABLE 3. Ultrasonographic Characterization of ICA Index Stenosis Before and After Stent Delivery (n=40) at Second Follow-Up Visit (30 Days)**

<table>
<thead>
<tr>
<th>Degree of Luminal Narrowing, %*</th>
<th>Before</th>
<th>After</th>
</tr>
</thead>
<tbody>
<tr>
<td>70–79</td>
<td>10</td>
<td>1</td>
</tr>
<tr>
<td>80–89</td>
<td>15</td>
<td>0</td>
</tr>
<tr>
<td>90–99</td>
<td>13</td>
<td>0</td>
</tr>
<tr>
<td>Overall (95%)</td>
<td>38 (2.5%)</td>
<td>1 (2.5%)</td>
</tr>
</tbody>
</table>

*Degree of stenosis was based on cross-sectional luminal area measurements on transverse views at the narrowest part of the stenosis before and at the part of the narrowest flow lumen after stent placement using CDDI (see Subjects and Methods).12

†Angle-corrected systolic peak flow velocity at the narrowest part of the stenosis before and at the part of the narrowest flow lumen after stent placement (see Subjects and Methods). Values are mean±SD.
symptomatic patients with a balanced surgical risk/benefit ratio may provide a safe and effective alternative to CEA. We can conclude that the observed 30-day mortality (any stroke or death) of ICA stenting was low and may lie below that associated with CEA. Furthermore, the risk of concomitant cardiovascular events appears to be low. Additionally, stenting may be effective in reducing individual stroke risk, as suggested by our finding that during a mean follow-up of almost 2 years, the observed number of major ipsilateral stroke was zero, compared with an expected number of $>8$. Thus, the results of the present study may encourage the initiation of a randomized study comparing stenting with endarterectomy in symptomatic patients, particularly those with a balanced surgical risk/benefit ratio.

References


Endovascular Treatment of Symptomatic Carotid Stenosis Using Stent Placement: Long-Term Follow-Up of Patients With a Balanced Surgical Risk/Benefit Ratio
Andreas Dietz, Joachim Berkefeld, Jacques G. Theron, Thomas Schmitz-Rixen, Friedhelm E. Zanella, Bernd Turowski, Helmuth Steinmetz and Matthias Sitzer

Stroke. 2001;32:1855-1859
doi: 10.1161/01.STR.32.8.1855

Stroke is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
Copyright © 2001 American Heart Association, Inc. All rights reserved.
Print ISSN: 0039-2499. Online ISSN: 1524-4628

The online version of this article, along with updated information and services, is located on the World Wide Web at:
http://stroke.ahajournals.org/content/32/8/1855

Permissions: Requests for permissions to reproduce figures, tables, or portions of articles originally published in Stroke can be obtained via RightsLink, a service of the Copyright Clearance Center, not the Editorial Office. Once the online version of the published article for which permission is being requested is located, click Request Permissions in the middle column of the Web page under Services. Further information about this process is available in the Permissions and Rights Question and Answer document.

Reprints: Information about reprints can be found online at:
http://www.lww.com/reprints

Subscriptions: Information about subscribing to Stroke is online at:
http://stroke.ahajournals.org//subscriptions/