Clinical Predictors of Transient Ischemic Attack, Stroke, or Death Within 30 Days of Carotid Angioplasty and Stenting

Andreas Kastrup, MD; Klaus Gröschel, MD; Jörg B. Schulz, MD; Thomas Nägele, MD; Ulrike Ernemann, MD

Background and Purpose—Carotid angioplasty and stenting (CAS) is currently being assessed in the treatment of severe carotid stenosis. However, little data are available concerning patient-related factors affecting the risk of CAS. The purpose of this study was to identify potential clinical risk factors for the development of postprocedural deficits after CAS.

Methods—The clinical characteristics of 299 patients (217 men, 82 women; mean age 69±9 years) who underwent CAS for asymptomatic (n=129, 43%) or symptomatic (n=170, 57%) stenoses and the combined 30-day complication rates (any transient ischemic attack [TIA], minor stroke, major stroke, or death) were analyzed with logistic regression analysis.

Results—The overall 30-day TIA rate was 3.7%; the minor stroke rate was 5.3%, the major stroke rate was 0.7%, and the death rate was 0.7%. Although patients presenting with a hemispherical TIA or minor stroke had a significantly higher risk than asymptomatic patients (odds ratio [OR] 5.69; 95% confidence interval [CI], 2.03 to 19.57; P<0.001), the complication rates between patients presenting with a retinal TIA and asymptomatic patients was comparable (OR, 1.42; 95% CI, 0.13 to 9.09; P=0.6). Multivariate regression analysis revealed advanced age (OR, 1.06; 95% CI, 1 to 1.11; P<0.05), stroke (OR, 8; 95% CI, 2.6 to 24.4; P<0.01) or hemispherical TIA (OR, 4.7; 95% CI, 1.6 to 13.3) as presenting symptoms as independent clinical predictors of the combined 30-day outcome measures any TIA, stroke, or death.

Conclusion—Aside from advanced age and symptom status, the type of presenting event predicts postprocedural complications after CAS. When evaluating the outcome of CAS and comparing this treatment modality to surgery, patients should be stratified according to their presenting event.

Key Words: angioplasty ▪ carotid arteries ▪ carotid stenosis ▪ risk factors ▪ stents

Based on the results of several large randomized trials, carotid endarterectomy (CEA) is currently the accepted standard of treatment for patients with severe symptomatic and asymptomatic carotid stenosis.1 However, fueled by the encouraging results of several case series and small trials,2–4 carotid angioplasty and stenting (CAS) is currently evaluated as a potential therapeutic alternative to CEA.

The benefit of either CEA or CAS is highly dependent on the risk of procedural neurological complications and is eliminated when the combined 30-day stroke and death rates exceed ≈5% for patients with a transient ischemic attack (TIA), 7% for patients with a stroke, and 3% for asymptomatic patients, respectively.1 Therefore, identification of potential risk factors for both revascularization procedures is a key feature for patient selection and patient counseling.

For CEA, a number of patient-related risk factors for the development of perioperative neurological complications have been identified in the past few years. Among others, a symptomatic carotid stenosis, female sex, age, peripheral vascular disease, urgent CEA, diabetes, congestive heart failure, atrial fibrillation, occlusion of the contralateral internal carotid artery, and restenosis after CEA have been associated with an increased risk after CEA.5–10 Although the overall operative risk for symptomatic carotid stenosis was higher than for asymptomatic stenosis in a recent systematic review of the surgical literature, the risk of stroke or death resulting from CEA in symptomatic patients was highly dependent on the type of their presenting event.5 Surgery for cerebral TIA or stroke, for instance, was associated with a significantly higher risk than surgery for ocular events only.5

In contrast to the abundant literature on perioperative risks of surgery, data on clinical or angiographical predictors of stroke complicating CAS are sparse and controversial.11,12 Although evidence is accumulating that the combined stroke and death rate after CAS is higher in symptomatic than in asymptomatic patients,4 to the best of our knowledge the
influence of the type of presenting event in symptomatic patients on the outcome of CAS has not been studied to date. Therefore, the aim of this study was to analyze the impact of patient-related risk factors for the development of postprocedural complication after CAS in a consecutive series of patients.

Subjects and Methods

Patient Population
From June 1999 to August 2004, a total of 299 patients with high-grade carotid artery disease (CAD) (≥70% in symptomatic patients and ≥90% in asymptomatic patients assessed with ultrasound) were treated with CAS after a prospective protocol approved by our institutional ethics review board after giving informed consent. A multidisciplinary team comprising a vascular surgeon, an interventional neuroradiologist, and a stroke neurologist evaluated all patients. Initially, only patients with severe medical comorbidities and a high surgical risk were treated with CAS. Based on satisfactory preliminary results, patients suitable for either CAS or CEA were subsequently offered a choice of procedure after they had received detailed information about potential risks and benefits, as well as the investigational nature of CAS. With increasing personal experience and in line with 2 recent publications,14,15 patients with long and multiple coronary artery stenoses, severe peripheral vascular disease precluding femoral artery access, or with an extremely tortuous carotid artery anatomy were excluded from CAS during the course of the study period.

The outcome of the first 100 CAS patients and a subgroup analysis of 53 CAS patients has been published previously.14,15 Because it is a special policy of our hospital that principally all patients with a symptomatic and asymptomatic carotid stenosis are primarily admitted to the Department of Neurology and are routinely seen after CAS, all patients had received preprocedural and postprocedural neurological evaluations within our department. To document patency of the stent, an ultrasound follow-up study was performed routinely 1 to 2 days after CAS in all patients.

In all patients the diagnosis of a high-grade carotid artery stenosis was made by carotid duplex ultrasound using a combination of direct and indirect criteria and the presence and extent of intrastenotic and poststenotic turbulent flow. As a key feature, a stenosis ≥70% was diagnosed if the peak systolic velocity exceeded 200 cm/sec and ≥90% if the peak systolic velocity exceeded 300 cm/sec, respectively. In all patients, the presence of an internal carotid artery stenosis ≥70% was confirmed angiographically during the stent procedure using the European Carotid Surgery Trial criteria, respectively.11

Carotid Angioplasty and Stenting Procedure
In all patients, CAS was performed using a standardized protocol described in detail recently.14,15 With the exception of 8 cases, all procedures had been performed with the patient under conscious sedation.

A total of 117 patients were treated without cerebral protection devices, and in 182 patients filter-type embolic protection devices were used during the CAS procedures. According to physician preference and commercial availability, 2 different filter-type cerebral protection devices (Mednova Neuroshield; Johnson & Johnson-Cordis Angioguard Filter16 and several appropriately sized self-expandable stents (Johnson & Johnson-Cordis Smart/Precise; Boston Scientific Wallstent) were used in this study.

Definitions of Postinterventional Complication Rates
The definitions of postinterventional complication rates that occurred within 30 days were based on a previous study by Mathur et al11 and were defined as follows: (1) TIA, any neurological deficit (either ocular or cerebral) that resolved completely within 24 hours; (2) minor stroke, any new neurological deficit (either ocular or cerebral) that persisted for >24 hours and that either resolved completely within 7 days or increased the National Institutes of Health stroke scale <3 points; (3) major stroke, any new neurological deficit that persisted after 30 days and increased the National Institutes of Health stroke scale by ≥3 points; and (4) myocardial infarction, occurrence of a new Q-wave in ≥2 leads and the presence of elevated creatine kinase (CK) or CK-MB, or occurrence of a CK elevation >2-times upper limit of the normal in the presence of an elevated CK-MB.

Data Collection
In each patient, careful history taking and precise neurological examination including the National Institute of Health Stroke scale was performed by a stroke neurologist. In patients with symptomatic internal carotid artery stenosis, symptoms and timing of cerebral ischemic events and date and time of symptom resolution in the case of TIAs was recorded. Diagnosis of a hemispherical TIA was based on the classic definition of a transient focal neurological dysfunction of presumed ischemic cerebrovascular cause lasting <24 hours. A carotid stenosis was considered symptomatic if the patient had experienced an ipsilateral ocular or cerebral (transient or permanent) ischemic event within the past 6 months. A carotid stenosis that had not caused any stroke or TIA in the past 6 months was considered asymptomatic.

In all patients, the following cerebrovascular risk factors or comorbidities were recorded: hypertension, diabetes mellitus, hyperlipidemia, smoking (current or within the previous year), peripheral vascular disease, previous transient ischemic attacks or strokes, previous ipsilateral carotid endarterectomy, CAD, history of previous coronary bypass, valvular heart disease, and cardiac arrhythmias.

Statistical Analysis
Continuous values are expressed as mean±SD and nominal variables as count and percentages, respectively. The associations between potential clinical risk factors and the postprocedural complication rates within 30 days after CAS were first assessed by univariate methods and then by logistic regression methods. For comparisons of categorical data, 2-tailed χ² statistics with Yates correction and univariate Fisher exact test were used. The Fisher exact test was used when the predicted contingency table cell values were <5. A value of P<0.05 was considered to indicate a statistically significant difference.

Multiple logistic regression analysis was performed to determine independent predictors of postprocedural neurological deficits. Variables were considered for inclusion in the multivariate models if they were significant at the P<0.10 level in the univariate analysis. For this analysis, age was considered as continuous variable. The selected clinical variables were entered into the logistic regression model using the combined outcome measure (TIA, major or minor stroke, death) as dependent variable. Backward stepwise exclusion was performed using a criterion P>0.1 and with variables in the final model considered significant at P<0.05. All statistical analyses were performed with SPSS (Version 12; SPSS Inc.).

Results
The total study population consisted of 299 CAS patients (217 men, 82 women; mean age 69±9 years, range 49 to 90 years). One hundred twenty-nine patients (43%) were treated for asymptomatic CAD and 170 patients (57%) for symptomatic CAD, respectively. In the group of symptomatic patients, 37 (21%) had presented with an amaurosis fugax, 80 (47%) with a hemispherical TIA, and 54 (32%) with a minor stroke.

Table 1 summarizes the demographic and clinical characteristics of the patients, whereas Table 2 shows the postprocedural complication rates within 30 days. For the entire study population, the overall 30-day TIA rate was 3.7%; the minor stroke rate was 5.3%, the major stroke rate was 0.7%, and the death rate was 0.7%. All strokes were ischemic except...
There was one nonstroke-related death secondary to pneumonia 3 weeks after CAS in an 82-year-old patient. There were no cases of prolonged or permanent second-degree or third degree atrioventricular block. Moreover, no unstable angina, ventricular arrhythmia, or myocardial infarction occurred.

In this series, there were no significant differences in the combined complication rates (TIA, minor stroke, major stroke, or death) between patients treated without (11%) and with cerebral protection devices (9.9%) \((P=0.8, \text{ Fisher exact test})\) (Table 2). Therefore, the results of these subgroups were combined for further analyses.

Several clinical variables were significantly related to 30-day postprocedural complication rates in the univariate analysis (Table 3). Symptomatic patients had significantly higher overall complications rates than asymptomatic patients (15.3% versus 3.1% for the combined outcome measures any TIA, stroke, and death; \(P<0.01\)). The higher complication rate in symptomatic patients was mainly attributable to an increased risk in symptomatic patients with a TIA or stroke. Whereas symptomatic patients presenting with a hemispherical TIA or stroke had significantly higher complication rates than asymptomatic patients (18.6% versus 3.1% for the combined outcome measures any TIA, stroke, and death; \(P<0.001\)).

### TABLE 1. Patient Characteristics

<table>
<thead>
<tr>
<th></th>
<th>Symptomatic, No. (%)</th>
<th>Asymptomatic, No. (%)</th>
<th>Overall, No. (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total</td>
<td>170 (57)</td>
<td>129 (43)</td>
<td>299 (57)</td>
</tr>
<tr>
<td>Male</td>
<td>120 (70)</td>
<td>97 (75)</td>
<td>217 (67)</td>
</tr>
<tr>
<td>Female</td>
<td>50 (30)</td>
<td>32 (25)</td>
<td>82 (22)</td>
</tr>
<tr>
<td>Hypertension</td>
<td>138 (81)</td>
<td>112 (87)</td>
<td>250 (81)</td>
</tr>
<tr>
<td>Hyperlipidemia</td>
<td>84 (49)</td>
<td>72 (56)</td>
<td>156 (49)</td>
</tr>
<tr>
<td>Tobacco use</td>
<td>49 (29)</td>
<td>43 (33)</td>
<td>92 (28)</td>
</tr>
<tr>
<td>Diabetes</td>
<td>43 (25)</td>
<td>32 (25)</td>
<td>75 (22)</td>
</tr>
<tr>
<td>PVD</td>
<td>27 (16)</td>
<td>24 (19)</td>
<td>51 (15)</td>
</tr>
<tr>
<td>CAD</td>
<td>41 (24)</td>
<td>32 (25)</td>
<td>73 (21)</td>
</tr>
<tr>
<td>COPD</td>
<td>7 (4)</td>
<td>2 (2)</td>
<td>9 (3)</td>
</tr>
<tr>
<td>Contralateral carotid occlusion</td>
<td>12 (7)</td>
<td>29 (22)</td>
<td>41 (12)</td>
</tr>
<tr>
<td>Bilateral carotid disease</td>
<td>54 (32)</td>
<td>68 (53)</td>
<td>122 (34)</td>
</tr>
</tbody>
</table>

PVD indicates peripheral vascular disease; CAD, coronary artery disease; COPD, chronic obstructive pulmonary disease.

### TABLE 2. TIA, Stroke or Death Within 30 Days After CAS

<table>
<thead>
<tr>
<th>Unprotected CAS</th>
<th>Symptomatic, No. (%)</th>
<th>Asymptomatic, No. (%)</th>
<th>Overall, No. (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>TIA</td>
<td>5 (7.2)</td>
<td>0</td>
<td>5 (4.3)</td>
</tr>
<tr>
<td>Minor stroke</td>
<td>5 (7.2)</td>
<td>1 (2.1)</td>
<td>6 (5.1)</td>
</tr>
<tr>
<td>Major stroke</td>
<td>1 (1.4)</td>
<td>0</td>
<td>1 (0.8)</td>
</tr>
<tr>
<td>Death</td>
<td>1 (1.4)</td>
<td>0</td>
<td>1 (0.8)</td>
</tr>
<tr>
<td>Total events</td>
<td>12 (17)</td>
<td>1 (2.1)</td>
<td>13 (11)</td>
</tr>
</tbody>
</table>

Protected CAS

| TIA             | 0                    | 6 (7.4)               | 6 (3.3)          |
| Minor stroke    | 10 (9.9)             | 0                     | 10 (5.5)         |
| Major stroke    | 0                    | 1 (1.2)               | 1 (0.5)          |
| Death           | 1 (1)                | 0                     | 1 (0.5)          |
| Total events    | 11 (10.9)            | 7 (8.6)               | 18 (9.9)         |

PVD indicates peripheral vascular disease; CAD, coronary artery disease; COPD, chronic obstructive pulmonary disease.
the overall 30-day stroke and death rate in this series was 3.1% in asymptomatic patients, which is close to the 3% limit that the American Heart Association has established as an acceptable upper limit for combined postprocedural stroke and death for asymptomatic patients who undergo CEA. Excluding the 1 nonstroke related death secondary to pneumonia, the overall 30-day stroke and death rate was 9.4% in symptomatic patients, which is still above the recommended upper limit of 6% for patients who undergo CEA. However, our overall 30-day complication rate after CAS for asymptomatic patients appears to be similar to the early complication rate of 10% found in the Carotid and Vertebral Artery Transluminal Angioplasty Study, and of 7% to 8% found in other large case series. Moreover, it should be stressed that this series included many patients with contralateral carotid occlusion (14%), bilateral carotid disease (40%), and CAD (10%). These subsets have been shown to have a high incidence of perioperative complications when they undergo CEA. Finally, all patients had been evaluated by a neurologist, which could also have contributed to the high detection rate of postprocedural neurological complications.

This study has strengths but also several important limitations. First, because of the relatively small sample size and few observed peri-interventional complications, the generalizability of our results remains to be determined in larger randomized cohort of patients. Second, the selection criteria for CAS patients were modified during the course of the study period, so that patients with long and multiple carotid artery stenoses, severe peripheral vascular disease precluding femoral artery access, or with an extremely tortuous carotid artery anatomy were increasingly not treated with CAS. Because of this potential selection bias, we did not assess the impact of these angiographic factors on the neurological complication rate. Third, several potential clinical risk factors such as chronic obstructive pulmonary disease were only present in a minority of patients, so that this study might have lacked statistical power to adequately determine the relationship between these variables and the postprocedural complication rate after CAS. Finally, the field of endovascular therapy is subject to rapid technological advances. Although the postprocedural complication rates between patients treated without and with cerebral protection devices were similar in this series, a recent systematic analysis of a considerably larger data set has suggested that the use of cerebral protection devices can reduce thromboembolic complications during CAS. Therefore, the clinical risk factors for neurological complications after CAS might differ between patients treated with and without cerebral protection devices, which needs to be addressed in future studies.

In conclusion, this study stresses the importance of patient-related risk factors and particularly the presenting symptom in determining neurological complication rates after CAS. When evaluating the outcome of CAS and comparing this
References
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