Distribution and Outcome of Symptomatic Stenoses and Occlusions in Patients With Acute Cerebral Ischemia

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Objectives: To describe the distribution of steno-occlusive disease and the associated rate of recurrence in patients with acute cerebral ischemia.

Design: An inception cohort was prospectively recruited after an index event and followed up to assess recurrent stroke and death up to 1 year after the event.

Setting: Eleven German departments of neurology with acute stroke units.

Patients: A total of 4,157 patients who experienced an acute ischemic stroke or a transient ischemic attack and had complete cerebrovascular examination results. Follow-up information could be obtained in 85.3% of these patients.

Results: Symptomatic vessel occlusions were associated with a high mortality rate and were found most often in the proximal internal carotid artery (6.5% of patients), the M1 segment of the middle cerebral artery (3.7%), and the vertebral artery (3.0%). Symptomatic stenosis of 50% to 99% of the internal carotid artery was found in 308 patients (7.4%), and 272 patients (6.5%) had symptomatic intracranial stenosis. The highest rates of recurrent stroke during the first 3 days occurred in patients with symptomatic carotid and intracranial occlusions. Overall, 82 (8.0%) of 1,027 patients with symptomatic cerebrovascular disease experienced a recurrent stroke between day 4 and 1 year, but no significant differences in recurrent stroke rates could be found when comparing different locations of steno-occlusive disease.

Conclusions: Our study provides representative data on the distribution and outcome of steno-occlusive disease in patients with acute cerebral ischemia. In contrast to prior studies in more selected populations, the rate of recurrent stroke in patients with symptomatic intracranial stenosis was not elevated compared with that of patients without steno-occlusive disease.

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Since the introduction of noninvasive vascular diagnostic examinations, several observational and interventional studies have investigated risk factors and outcome of symptomatic cerebrovascular steno-occlusive disease. Race and sex could be consistently identified as independent predictors of the location (intracranial vs extracranial) of cerebral arteriosclerosis.1-3 Recently, the Warfarin-Aspirin Symptomatic Intracranial Disease study (WASID) showed no advantage of oral anticoagulation over high-dose aspirin in patients with symptomatic intracranial arterial stenosis.4 Nevertheless, the rate of ischemic stroke in that trial (20.4% in the aspirin group and 17.0% in the warfarin group during a mean follow-up of 1.8 years) was substantially higher than in other trials of secondary prevention of stroke in which aspirin or warfarin was evaluated, suggesting that intracranial stenosis is a high-risk disease for which alternative therapies are needed. Considering the existence of newer antiplatelet agents and fixed antiplatelet combinations and the fast development of intracranial angioplasty with and without stenting as alternatives to medical preventative treatment, knowledge about the natural recurrence rate in patients with intracranial stenosis is of particular interest.5,6 However, clinical interventional studies bear an inherent selection bias, and, to our knowledge, only 1 hospital-based study7 in a Chinese population has compared the outcome of patients with various forms of cerebrovascular steno-occlusive disease. We, therefore, investigated the exact location and outcome of cerebrovascular steno-occlusive lesions in a large, multicenter, consecutive, hospital-based cohort of patients with acute cerebral ischemia.
This study was part of a prospective validation of prognostic models for acute ischemic stroke that has been previously published.\(^6\) Enrollment of patients started on July 1, 2000, and was terminated on March 15, 2002. The 11 participating neurological departments (a complete list of members of the German Stroke Collaboration appears on page 1290) documented all patients admitted within 24 hours after an acute cerebrovascular ischemic event (ie, an ischemic stroke or a transient ischemic attack [TIA]). After the exclusion of 36 patients without cerebral imaging data to rule out primary intracerebral hemorrhage and other causes mimicking cerebral ischemia, 4637 patients were included in this analysis. Patients or their next of kin were informed about study participation, and informed written consent was obtained to forward personal data to the coordinating center. Data collection and management were approved by the Ethics Committee of the University of Duisburg-Essen, and aspects of data safety were approved by the responsible data protection state representative. Definitions of risk factors and comorbid conditions and data management have been previously described.\(^9\)

A complete cerebrovascular workup included conventional angiography, magnetic resonance angiography, or combined extracranial Doppler/duplex and transcranial Doppler/computed tomographic angiography. The criteria for quantification of stenosis depended on the examination technique and corresponded to frequently used reference values.\(^10,11\) Occlusion or stenosis of 50% or greater diameter reduction of the vertebral common carotid artery, the proximal internal carotid artery with 3 categories of stenosis (50%-69%, 70%-89%, and 90%-99%), the distal internal carotid artery (from the extracranial skull base to the intracranial bifurcation), the middle cerebral artery (main stem [M1] and proximal [M2 or M3] branches), the anterior cerebral artery, the posterior cerebral artery, or the basilar artery was diagnosed as being symptomatic by the treating neurologist if there was a cerebral infarction on computed tomographic/magnetic resonance imaging or (in the absence of a visible infarction) if clinical symptoms matched the supplied brain territory of the affected artery. According to Trial of Org 10172 in Acute Stroke Treatment (TOAST) criteria,\(^12\) a symptomatic stenosis or occlusion was classified as large-artery atherosclerosis (LAA) when no concurrent stroke causes (eg, cardioembolic, small-vessel disease, dissection, vasculitis, or coagulation disorders) were found. Early recurrent cerebral ischemia was defined as sudden worsening of neurological deficits with exclusion of intracerebral hemorrhage by cerebral imaging in case of persistent symptoms. In addition, recurrent TIA or stroke was assessed during follow-up performed predominantly via telephone interview by the coordinating center and blinded to baseline status and cerebrovascular pathological features. Follow-up was performed by the admitting hospital, if the patient had not given consent that personal data could be forwarded to the coordinating center. Outcome was assessed using the Barthel Index\(^13\) at 100 days (mean [SD], 107 [21] days) and 1 year (mean [SD], 371 [64] days) after the event or by confirmation of death. If patients self-reported a recurrent TIA or stroke, confirmation was sought from the treating general practitioner. If no follow-up information could be obtained from the patient, relatives, or the treating general practitioner, a query was sent to the local death registry. No complete follow-up information could be obtained from 231 (18.4%) of 1258 patients with steno-occlusive disease, which was mainly because of limited central funding and lack of staff in the participating hospitals. Patients without complete follow-up information were significantly older (\(P=.001\)) and had more severe initial neurological deficits (\(P<.001\)) than patients with complete follow-up information. The flowchart of patient inclusion is depicted in the Figure.

Statistical analysis was performed using a commercially available software program (SPSS, version 10.0; SPSS Inc, Chicago, Ill). If a single variable was not available for all patients, only valid cases were reported. If more than 1% of data were missing for any variable, the number of missing cases was additionally provided.

Of the 4637 patients admitted to the hospital within 24 hours after an acute cerebrovascular ischemic event, a complete cerebrovascular workup was documented in 4157 (89.6%). The median age of the patients was 67 years, and 43.2% were women. Cerebrovascular examinations consisted of Doppler/duplex ultrasonography in 99.4% (including transcranial Doppler ultrasonography in 96.7%, extracranial Doppler ultrasonography in 86.3%, and extracranial duplex ultrasonography in 82.8%), magnetic resonance angiography in 24.1%, conventional angiography in 4.2%, and computed tomographic angiography in 3.2% of these patients. The baseline characteristics of all patients with complete cerebrovascular workup information are presented in the Table.

Symptomatic extracranial and intracranial carotid (including common carotid) stenosis of 50% or greater was found in 379 patients (9.1%) and symptomatic occlusion of the carotid artery in 366 patients (8.8%). Intracranial symptomatic stenosis (excluding the internal carotid artery) was found in 272 patients (6.5%) and any symptomatic intracranial steno-occlusive disease in 611 patients (14.7%). No symptomatic stenosis-occlusive disease of 50% or greater could be detected in 2899 patients (69.7%). Symptomatic vessel occlusion of the common carotid artery was found in 19 patients (0.5%); of the proximal internal carotid artery, 269 patients (6.5%); of the distal internal carotid artery, 116 patients (2.8%); of the middle cerebral artery (M1 segment), 153 patients (3.7%); of the middle cerebral artery (M2 segment), 74 patients (1.8%); of the anterior cerebral artery, 6 patients (0.1%); of either verte-
Table. Baseline Characteristics and Outcomes of Patients With Symptomatic Cerebrovascular Steno-occlusive Disease*

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Carotid Artery (CCA/ICA)</th>
<th>MCA (M1 Segment) Occlusion</th>
<th>Basilar Artery Occlusion</th>
<th>Intracranial Stenosis</th>
<th>Any Steno-occlusive Disease</th>
<th>All Patients With Complete Workup Data</th>
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</table>
The German Stroke Study Collaboration includes the following collaborators, all from neurology departments at their affiliations, all in Germany: Christoph Hagemeister, MD, Krankenanstalten Gilead, Bielefeld; Christoph Kley, MD, Rheinische Kliniken Bonn, Bonn; Panagiotis Kostopoulos, MD, Universitätsklinikum des Saarlandes, Homburg; Vera Willig, MD, Universitätsklinikum Jena, Jena; Michael Goertler, MD, Universitätsklinikum Magdeburg, Magdeburg; Joerg Glahn, MD, Klinikum Minden, Minden; Kai Aulich, MD, Städtisches Krankenhaus Harlaching, München; Antje Kloth, MD, Universitätsklinik Rostock, Rostock; Thomas Mieck, MD, Bürgerhospital, Stuttgart; Matthias Riepe, MD, Universitätsklinikum Ulm, Ulm; Vesna Zegarac, MD, Universitätsklinik Essen, Essen.

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in patients with symptomatic intracranial stenosis generally does not seem elevated compared with that of patients without steno-occlusive disease. This should influence decisions about invasive treatment in these patients.

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REFERENCES