Short Communications

Prognosis of High-Risk Patients With Nonoperated Symptomatic Extracranial Carotid Tight Stenosis

J. Bogousslavsky, MD, P.A. Despland, MD, and F. Regli, MD

Forty-five patients with symptomatic (20 with transient ischemic attack, 25 with minor stroke) > 75% stenosis of the cervical internal carotid artery had no endarterectomy and received only medical therapy because the surgical risks (severe cardiac disease, chronic obstructive pulmonary disease, hypertension or diabetes with systemic complications, aortic aneurysm) were believed to be unacceptable. During follow-up (mean 48 months), occlusion of the internal carotid artery developed without symptoms in two patients and with symptoms in three patients. The cumulative stroke and/or death rate was 24% at 2 years and 50% at 6 years. The ipsilateral infarct rate was 10% after the first year, but decreased markedly thereafter (2.4% per year), and one third of these infarcts were probably lacunes due to hypertensive small vessel disease. Overall, stroke related to previously symptomatic internal carotid artery stenosis was not the major problem during follow-up but was largely overcome by other strokes and cardiac death. (Stroke 1988;19:108–111)

The prognosis of symptomatic occlusion of the internal carotid artery (ICA) has been evaluated in several studies 1-9 but that of symptomatic ICA stenosis is much less well known because most patients with ischemic events distal to a cervical ICA stenosis undergo a prophylactic carotid endarterectomy. The results from the medical group of the Joint Study 10 showed a 3.7% yearly rate of stroke, with a 7.4% per year risk of stroke and/or death. However, many patients included in that study had only vertebrobasilar symptoms with no ischemic events distal to the ICA stenosis. In the study by Busuttil et al. 11 167 nonoperated patients with an ICA stenosis had an annual stroke rate of 3.3% during 2½ years of follow-up; when only hemodynamic stenoses (on oculopneumo-plethysmography) were considered, this rate increased to 6.4% per year. In three studies, the prognosis of patients with a symptomatic intracranial ICA stenosis was evaluated; the stroke rate was 4–12% per year and the death rate was 10–17% per year. 12-14

We report follow-up data in a group of patients with a symptomatic tight ICA stenosis who were treated only medically because of contraindications for surgery.

Subjects and Methods

Between 1979 and 1986, 45 patients (34 men, 11 women, aged 58–72, mean 63.4, years) admitted to our department who had an ICA stenosis of ≥ 75% of the lumen diameter proximal to a recent (< 3 months) cerebral ischemic event were felt to have unacceptable risks for surgery; they were not operated on and were treated medically.

Twenty patients had been referred for ipsilateral transient ischemic attacks (TIAs) and 25 for an ipsilateral infarct with a minimal neurologic residuum (minor stroke); three patients had also experienced prior contralateral TIAs 1–4 years previous, one had suffered a prior contralateral infarct 2 years previous, and two had also had vertebrobasilar TIAs. Vascular risk factors were assessed according to criteria defined previously 15: 40 patients were regular cigarette smokers, 35 had hypertension, 20 diabetes mellitus, 14 fasting hypercholesterolemia, 11 a past myocardial infarct, and 14 angina pectoris without myocardial infarction. The carotid arteries were evaluated by Doppler ultrasonography with spectral frequency analysis (≥ 75% ICA stenosis: systolic peak > 8 kHz with spectral broadening, decreasing systolic window, and increased diastolic frequency) and angiography (Seldinger technique) with biplane views (comparison of lumen diameter at the level of maximal stenosis with that at the level of an apparently normal adjacent distal segment). An ulcer was visible on eight symptomatic ICA stenoses. Four patients had a tandem lesion with > 50% stenosis of the distal ICA or middle cerebral artery trunk. The contralateral ICA was occluded in four patients and stenosed in 15 patients (≥ 75% stenosis in 4, with a visible ulcer in 1; < 75% stenosis in 11, with a visible ulcer in 3).

The reasons for declining endarterectomy were severe chronic obstructive pulmonary disease in 12 patients, unstable ischemic heart disease in 11, severe chronic hypertension or diabetes with vascular or renal complications in 8, a combination of these disorders in 13, and an inoperable large aortic aneurysm in 1 patient. These contraindications were established for
each patient after discussion with the surgeons and anesthetists.

The patients were treated by their physicians with the best known medical treatment and were seen every 4–15 months in our department for neurologic and Doppler assessments. A cerebral computed tomogram (CT) was done in cases of delayed stroke. The duration of follow-up was 12–72 (mean 48) months. Thirty-two patients took 500 mg aspirin t.i.d. regularly, 10 were put on acenocoumarol, and 3 took only 375 mg dipyridamole t.i.d. because of intolerance to aspirin. Actuarial methods with Kaplan-Meier life tables were used to calculate the cumulative mortality and morbidity, starting at presentation.

Results

Mortality

Ten patients died during follow-up, which corresponded to an annual death rate of 5.6%. Two patients with coronary disease died during sleep and the exact cause of death was not established, but all other deaths were proven to be vascular (myocardial infarct in 6, ruptured aortic aneurysm in 1, pontine hemorrhage in 1). Three patients had a nonfatal myocardial infarct during follow-up.

Cerebrovascular Events

Fourteen patients had 15 strokes during follow-up, with an incidence of 7.8% per year (8.3% per patient per year). The cumulative stroke-free survival is schematized in Figure 1: the incidence of death or stroke was maximal during the first 2 years of follow-up (24% of the patients died or had a stroke); at the end of the follow-up, 50% of the patients were either dead or had suffered a stroke. The type of stroke during follow-up is shown in Table 1: 60% of the strokes were ipsilateral to the previously symptomatic ICA stenosis, so that at the end of follow-up 20% of the patients had suffered an ipsilateral infarct. It should be emphasized that the incidence of ipsilateral infarct was maximal during the first 12 months of follow-up (rate, 10%) and decreased subsequently (rate, 2.4% per year) (Figure 2). Among the ipsilateral infarcts, 4 involved the superficial territory of the middle cerebral artery, 2 involved both the deep and superficial territories, and 3 were small and limited to the deep (lenticulo-capsular) territory. As these three latter infarcts corresponded to a pure motor hemiparesis and as the patients had hypertension, a diagnosis of lacune was made. The functional disability due to a stroke was severe (inability to resume previous activities) in 3 of the 7 survivors with an ipsilateral stroke and in 1 of the 3 survivors with a nonipsilateral stroke. Among the other survivors, four resumed their previous activities with difficulty and two without difficulty. Seven patients also had TIs during follow-up: in two, TIAs distal to the ICA stenosis preceded an ipsilateral infarct and in five, TIAs occurred without a stroke (ipsilateral to the stenosis in 2, contralateral in 1, and vertebrobasilar in 2).

The occurrence of ipsilateral and nonipsilateral stroke was analyzed with respect to risk factors, type of presenting events (TIA or stroke), angiographic findings (ulcer, contralateral and intracranial disease), and antiocoagulant or antiaggregant therapy, but none of these factors were significantly associated with stroke during follow-up. An ulcer on the ICA stenosis did not reliably predict further cerebral ischemia. However, these negative findings may have been due to the small number of patients (Type II errors).

During follow-up, occlusion of the ICA stenosis was detected in five patients on sequential Doppler testing (18–60, mean 40, months after admission). Three had a simultaneous ipsilateral ischemic event (2

Table 1. Strokes During Follow-up

<table>
<thead>
<tr>
<th>Stroke type</th>
<th>Patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cerebral infarct distal to symptomatic internal carotid artery stenosis</td>
<td>9</td>
</tr>
<tr>
<td>Contralateral infarct</td>
<td>1</td>
</tr>
<tr>
<td>Contralateral infarct followed by brainstem infarct</td>
<td>1</td>
</tr>
<tr>
<td>Contralateral hemorrhage</td>
<td>1</td>
</tr>
<tr>
<td>Pontine hemorrhage</td>
<td>1*</td>
</tr>
<tr>
<td>Lateral medullary infarct</td>
<td>1</td>
</tr>
</tbody>
</table>

* Died of stroke.

FIGURE 1. Cumulative survival free from stroke (including nonstroke deaths).

FIGURE 2. Cumulative rate of infarction distal to symptomatic internal carotid artery stenosis.
strokes, 1 TIA). In two, no further ipsilateral ischemic event occurred.

Discussion
Our data show that these patients were actually high-risk patients since half of them were either dead or had suffered a stroke by the end of the follow-up. However, the annual incidence of delayed infarct distal to the previously symptomatic ICA stenosis remained rather low (< 5%) so that ipsilateral infarction was not the major long-term problem. Moreover, one third of these ipsilateral infarcts were probably lacunar and were less likely to be related to the ICA stenosis than to hypertensive small vessel disease.

As our study was not controlled, a possible role for endarterectomy in these patients cannot be inferred from our data. Perioperative stroke or death remain the most threatening complications of carotid endarterectomy. A review of the series published between 1975 and 1984 reported a 2.1% mortality and a 3.5% stroke rate. In the most recent studies, perioperative mortality varied between 0.9 and 2.8%, and the stroke rate was between 1.5 and 8.6%. These rates may increase considerably in patients with previous stroke, hypertension, and symptomatic ischemic heart disease, such as in our high-risk group. Also, the risk of postendarterectomy recurrent stenosis, which is 6–10% per year, is increased by the presence of vascular risk factors such as those in our patients, especially smoking. Even if no perioperative complications are encountered, carotid endarterectomy does not abolish the risk of delayed stroke, which varies from 1 to 4.7% per year, with approximately two thirds of the strokes being ipsilateral to the operated side. Vascular risk factors increase the risk of recurrent stroke. A definite answer to the question of endarterectomy in high-risk patients can be given only by a well-conducted randomized trial of endarterectomy in symptomatic patients. Whether prognosis in this group is comparable with that in surgical candidates who are not operated on can be determined only by future studies.

In our patients, the main risk was death from a vascular (mainly cardiac) cause, which obviously cannot be modified by endarterectomy. This finding suggests that in such patients, medical management of risk factors and heart disease may be the most useful therapy, especially during the first 2 years after the presenting events when the risks are maximal.

The progression of asymptomatic tight ICA stenosis toward occlusion is 2–8% per year and is not invariably associated with symptoms. The present study shows that occlusion of a previously symptomatic ICA stenosis may also occur without further cerebral ischemia. It remains to be studied whether reliable predictors of symptomless delayed occlusion can be found in these patients.

Acknowledgment
We thank Dr. A. Uske, neuroradiologist, CHUV, who supervised the angiographies.

**KEY WORDS** • carotid artery diseases • endarterectomy
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doi: 10.1161/01.STR.19.1.108

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