Internal Carotid Occlusion: A Prospective Study

R. Cote,* H.J.M. Barnett,* and D.W. Taylor†

SUMMARY Forty-seven patients with ICA occlusion and who presented either without any or only a mild neurological deficit were prospectively followed for an average of 34.4 months. During this period of time, 11 patients (23.5%) suffered a cerebral infarction in which two-thirds were ipsilateral to the occluded artery. The stroke rate distal to an occluded ICA artery was 5% per year. Twenty-four patients (51%) continued to experience TIA’s in the territory of the occluded artery. The mortality rate was low (8.5%) during follow-up. Whether extracranial-intracranial arterial bypass surgery will decrease the risk of cerebral infarction in this subgroup of patients is unknown. The International EC/IC Collaborative Trial may elucidate this point because this subgroup represents one of the randomization strata of that study.

Stroke Vol 14, No 6, 1983

THE SPECTRUM OF CLINICAL POSSIBILITIES after occlusion of an internal carotid artery ranges from that of an asymptomatic patient to one afflicted with a calamitous and fatal stroke.1 In those patients which present without symptoms or with no more than a mild neurological deficit, the clinician wishes to know the risk for further ischemic events so that the question of immediate and continuing management of the problem may be addressed. In this paper an attempt is made to define the risk in the nonsurgical management of such patients; these observations will provide a basis of comparison to be used in the evaluation of any additional and innovative forms of treatment, including extracranial-intracranial arterial bypass surgery.

Patients and Methods

During the Canadian Cooperative Study on platelet inhibitory drugs2 47 patients were identified by angiography to have an occlusion of the internal carotid artery. Only those patients with TIA or minor neurological residua were admissible for entry into this study and all 47 patients had experienced at least one cerebral or retinal ischemic attack in the three months prior to the entry. None were submitted to cerebral vascular bypass surgery. Those with coexisting conditions which might explain their symptoms, including patients with overt cardiogenic sources for emboli and patients likely to die from other illnesses within 12 months were excluded. The follow-up procedure included a neurological re-evaluation after one month and every three months thereafter. At each follow-up a neurologic history was obtained and full neurological and cardiovascular examinations were repeated. Because the patients were followed in a prospective manner, optimum accuracy in the adjudication of endpoints was obtained.

The absolute endpoints for the study were stroke and death. The cause of death was determined in every case. When stroke occurred it was correlated with the side of the occlusion, and its severity was recorded. The variety of stroke (hemorrhage, infarction) was also assessed. Stroke severity was graded according to its impact on the functional status. Three categories were used, minor (no impairment in activities of daily living), moderate (impairment in the activities of daily living but residing at home and out of bed for all or part of the day) or severe (bedridden or institutionalized). Transient ischemic attacks were recorded during the follow-up period.

Results

The forty-seven patients were followed for a period of five years from 1972 to 1977. The average follow-up was 34.4 months. The age of the patients ranged from 40 to 83 years with a mean of 58.9 years. There were 39 males and 8 females (table 1). Twenty-seven patients (57%) presented with transient ischemic attacks and 20 (43%) with minor neurological residua. Ten patients (21%) had no symptoms related to the occluded artery when first evaluated, but had TIA or partial stroke in the territory of the other internal carotid artery or the vertebral-basilar artery supply. When the clinical presentation was correlated with the side of the occluded artery, 22 patients (47%) had ipsilateral transient ischemic attacks and 15 patients (32%) presented with a minor stroke on the same side as the occluded artery (table 2).

Twenty-three patients (49%) had hypertension, 14 (30%) had cardiac disease (i.e. MI, angina, cardiac failure, cardiomegaly), 5 (11%) had diabetes and 7 (15%) had evidence of peripheral vascular disease. The origin of the internal carotid artery was the site of the atherosclerotic occlusion in 87% of cases. Other sites included, the ICA between its origin and the skull (6.5%) or the intracranial portion (6.5%). None of this series of patients had bilateral ICA occlusions.

Thirteen events considered to have cerebral infarction involving all vascular territories were recorded during the follow-up period. Two patients suffered more than one such event; considering the first stroke as an endpoint the total number of patients with cerebral infarction was 11 (23%). Therefore, 8% of the patients per year experienced a stroke, 7 (64%) of these infarctions occurred on the occluded side. Three of the strokes occurred on the contralateral side and 1 was in the vertebral-basilar distribution. For the observation period, there was a 15% ipsilateral stroke rate, 5% when adjusted on an annual basis. The median time from entry into the study to a stroke was 1.3 years (range 9 days to 3.8 years). No period of increased risk for cerebral infarction was noted during the follow-up period.
period. Of the 11 strokes, 3 were minor, 5 were moderate and 3 were severe. Of those patients with cerebral infarction, 5 entered the study with TIAs only and 6 entered with minor neurological residua. Twenty-three (49%) patients had angiographic evidence of additional atherosclerotic disease either in the external or common carotid arteries on either side; in 14 this was on the same side as the occluded artery. During follow-up, 9 (65%) of these 14 patients had an ischemic event beyond the ICA occlusion. This study was conducted before the ICA stump had been recognized as a cause of cerebral ischemia so that this aspect was not specifically examined.

Four (8.5%) patients died during the follow-up period: a mortality rate of about 3% per year. Two deaths were due to myocardial infarction, one was stroke-related and one suffered a non-vascular death. Twenty-four (51%) patients continued to experience TIAs in the territory of the occluded artery and overall 27 patients (57%) suffered at least one ischemic event beyond the ICA occlusion (i.e. TIA or stroke).

Twenty-eight patients had a carotid bruit; in 15 patients this was on the same side as the occluded artery and 9 (60%) of these 15 patients had angiographic evidence of atherosclerotic disease either in the common or external carotid artery ipsilateral to the occluded vessel. Nineteen patients had evidence on angiography of moderate to severe carotid stenosis (i.e. more than 30% narrowing) contralateral to the occluded artery. Six of these patients had a cerebral infarction during follow-up, 3 on the side of the occlusion and 3 ipsilateral to the carotid stenosis.

All 47 patients were followed closely with good control of the risk factors. At least 50% of the patients were treated with antiplatelet therapy (i.e. acetylsalicylic acid) during the follow-up period. In the ASA-treated group, 4 patients suffered a stroke and 1 died of myocardial infarction. Only 1 patient received a course of anticoagulant therapy and another was submitted to carotid surgery (i.e. repair of an internal carotid artery stump). These numbers are too small for any comment regarding the efficacy of any treatment program.

**Discussion**

Prognosis after occlusion of the internal carotid artery has been examined by different studies in the past (table 3). McDowell et al reported on 38 patients with internal carotid occlusion, who were available for follow-up; half of these were considered to have suffered either a moderate or severe stroke initially and 11 patients (29%) were treated with anticoagulant therapy. Finally the exact cause of death was not clear in all cases. Hardy et al followed 133 patients who survived a carotid artery occlusion of which more than 60% had some surgery performed on the occluded artery. A substantial number of those patients had a moderately severe neurological deficit and in almost half of the cases the cause of death was unknown.

Dyken et al over a short period prospectively followed a group of 43 patients with either common or internal carotid artery occlusion. Half of these patients had a moderate to severe neurological deficit and no specific details were given about the cause of death or the exact localization of subsequent ischemic events. The Joint Study of Extracranial Arterial Occlusion reported on 359 patients with unilateral carotid occlusion. Here again, a substantial number of patients had an initial severe deficit. Eighty-nine patients (25%) went on to have a new stroke, at least 35 being ipsilateral to the occluded artery but in 34 patients in whom the stroke was fatal, the vascular territory involved was not reported.

Although these early studies have given a reasonably good overall prognosis for patients with internal carotid occlusion, the information has been incomplete. None of the previous studies reported on the location of subsequent cerebral infarction with the exception of the Joint Study and even in this report considerable information was omitted. All of the earlier reports included a substantial number of patients who survived the occlusion with a severe or at least a moderate neurological deficit. In this group of patients, the prognosis may differ from that of less severely affected individuals. In a few of these studies patients were submitted to different types of therapeutic measures including vascular surgery and anticoagulant therapy, but no specific information was given on the accompanying mortality and morbidity. Finally, the chances of detecting new events in a vascular territory where a major stroke has occurred are probably limited; the ideal study should probably be restricted to patients suffering from TIAs or minor strokes.

Some additional and more complete data has been available more recently (table 4). In a retrospective review, Grillo and Patterson followed 37 patients with internal carotid occlusion who had survived a first stroke. Curiously all strokes occurred in the cerebral hemisphere opposite the occluded carotid artery. Patients with moderate and severe strokes were included in the study, although their exact number was difficult to evaluate. Fourteen of the patients underwent carotid endarterectomy because of disease in the opposite carotid artery.

Furlan et al in 1980 published a retrospective analysis of 138 patients with angiographically-proven carotid artery occlusion who had no or mild neurological

**Table 1 Age and Sex Distribution in 47 Patients with ICA Occlusion**

<table>
<thead>
<tr>
<th>Symptomatology</th>
<th>Female</th>
<th>Male</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>TIA</td>
<td>0</td>
<td>4</td>
<td>4</td>
</tr>
<tr>
<td>Minor stroke</td>
<td>2</td>
<td>14</td>
<td>16</td>
</tr>
<tr>
<td>Asymptomatic</td>
<td>3</td>
<td>15</td>
<td>18</td>
</tr>
<tr>
<td>Total</td>
<td>5</td>
<td>34</td>
<td>39</td>
</tr>
</tbody>
</table>

**Table 2 Clinical Presentation of 47 Patients with ICA Occlusion**

<table>
<thead>
<tr>
<th>Symptomatology</th>
<th>All vascular territories</th>
<th>Ipsilateral to occluded artery</th>
</tr>
</thead>
<tbody>
<tr>
<td>TIA</td>
<td>27 (57%)</td>
<td>22 (47%)</td>
</tr>
<tr>
<td>Minor stroke</td>
<td>20 (43%)</td>
<td>15 (32%)</td>
</tr>
<tr>
<td>Asymptomatic</td>
<td>0</td>
<td>10 (21%)</td>
</tr>
</tbody>
</table>
TABLE 3  Prognosis of Carotid Artery Occlusion — I

<table>
<thead>
<tr>
<th>Reference</th>
<th>Number of patients</th>
<th>Type of study</th>
<th>Patient population</th>
<th>Mean period of follow-up</th>
<th>Strokes during follow-up</th>
<th>Deaths during follow-up</th>
</tr>
</thead>
<tbody>
<tr>
<td>McDowell¹ (1961)</td>
<td>38</td>
<td>retrospective</td>
<td>major completed strokes included</td>
<td>24 months</td>
<td>3 (8%)</td>
<td>5 (13%)</td>
</tr>
<tr>
<td>Hardy² (1962)</td>
<td>133</td>
<td>retrospective</td>
<td>major completed strokes included</td>
<td>48 months</td>
<td>30 (23%)</td>
<td>51 (39%)</td>
</tr>
<tr>
<td>Dyken³ (1974)</td>
<td>43</td>
<td>prospective</td>
<td>half of patients with moderate to severe deficit</td>
<td>16.5 months</td>
<td>3 (7%)</td>
<td>6 (14%)</td>
</tr>
<tr>
<td>Fields⁴ (1976)</td>
<td>359</td>
<td>prospective</td>
<td>significant number of patients with initial severe deficit</td>
<td>44 months</td>
<td>89 (25%)</td>
<td>155 (43%)</td>
</tr>
</tbody>
</table>

The above studies give an overall stroke rate with no or incomplete reference to vascular territory involved.

residua. A small number of these patients (7%) had no symptoms of focal neurological disease and the carotid occlusion was an incidental finding. Two-thirds of the strokes occurred on the same side as the carotid occlusion equivalent to a 2% ipsilateral annual stroke rate for the first four years of follow-up. More than half the patients were treated with long-term anticoagulant therapy at one point during follow-up. Although the risk of death and cerebral infarction were clearly higher than for a normal population, the authors noted that the risk for stroke was approximately half the annual rate found in some other groups of patients suffering from transient ischemic attacks. Recently, Bogousslavsky et al.¹⁰ reported on 23 patients with occlusion of the internal carotid artery; in this retrospective study, 8 patients continued to experience TIAs but none of the 23 patients suffered a permanent stroke during follow-up.

Finally, three small studies¹¹⁻¹³ have looked prospectively at the prognosis of patients afflicted with internal carotid occlusion. Details of those studies are included in table 4.

In the present report, 47 patients were followed in a prospective manner for an average of 34 months. The data indicates that in this population the overall risk of stroke and death was 29.5% in this period of approximately three years. This compares well with the natural history of 295 untreated patients who were randomized in the Canadian Cooperative Trial: within three years, 30% of the patients suffered a stroke or were dead.¹⁴ The overall stroke rate ipsilateral to an occluded artery in the present study was 15% over 34 months; this is similar to an estimated stroke rate of 5% to 6% a year for groups of patients who suffer from TIAs.¹⁵ This would seem to indicate that patients with angiographically-proven ICA occlusions and who have no or mild neurological deficit have a similar outcome to those suffering from transient ischemic attacks or minor strokes in general. The data from this study indicates that 7 (63%) of the 11 strokes which occurred during follow-up were ipsilateral to the occluded internal carotid artery. This is comparable to the two-thirds figure reported by Furlan et al. Finally, more than 50% of the patients in this report continued to experience TIAs in the territory beyond the ICA occlusion. Bogousslavsky found this to occur in 34% of the patients in his retrospective study.

The prospective studies, including our own, suggest

TABLE 4  Prognosis of Carotid Artery Occlusion — II

<table>
<thead>
<tr>
<th>Reference</th>
<th>Number of patients</th>
<th>Type of study</th>
<th>Patient population</th>
<th>Mean period of follow-up</th>
<th>Strokes during follow-up</th>
<th>Deaths during follow-up</th>
</tr>
</thead>
<tbody>
<tr>
<td>Grillo⁸ (1975)</td>
<td>37</td>
<td>retrospective</td>
<td>majority having TIA or stroke</td>
<td>36 months</td>
<td>6† (16%)</td>
<td>10 (27%)</td>
</tr>
<tr>
<td>Samson¹¹ (1977)</td>
<td>7</td>
<td>prospective</td>
<td>TIA or minor stroke</td>
<td>17 months</td>
<td>2* (28%)</td>
<td>0</td>
</tr>
<tr>
<td>Barnett¹¹ (1978)</td>
<td>25</td>
<td>prospective</td>
<td>TIA or minor stroke</td>
<td>24 months</td>
<td>7* (28%)</td>
<td>—</td>
</tr>
<tr>
<td>Furlan⁹ (1980)</td>
<td>138</td>
<td>retrospective</td>
<td>TIA or minor stroke</td>
<td>60 months</td>
<td>11* (8%)</td>
<td>30 (21%)</td>
</tr>
<tr>
<td>Heyman¹² (1980)</td>
<td>13</td>
<td>prospective</td>
<td>TIA</td>
<td>24 months</td>
<td>7* (54%)</td>
<td>2 (15%)</td>
</tr>
<tr>
<td>Bogousslavsky¹⁰ (1981)</td>
<td>23</td>
<td>retrospective</td>
<td>majority having TIA or minor stroke</td>
<td>27 months</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Present study (1982)</td>
<td>47</td>
<td>prospective</td>
<td>TIA or minor stroke</td>
<td>34 months</td>
<td>7* (15%)</td>
<td>4 (8.5%)</td>
</tr>
</tbody>
</table>

The above studies give stroke rate ipsilateral to occluded artery.

* Ipsilateral stroke.
† Stroke in other vascular distribution.
an increased stroke rate compared to the retrospective analyses which in general show a lower rate of cerebral infarction during follow-up. An explanation for this difference could be the fact that a prospective analysis with regular follow-up is a very sensitive investigative tool and will permit the detection of minor strokes which otherwise could go undetected, especially those in which there is no permanent impact on the functional status of the patient. Furthermore, certain ischemic events including reversible ischemic neurological deficits (RIND) could easily be missed in a retrospective study due to their transient nature and the dependence upon the memory of the patients for a non-persistent event. In this study, 3 of the strokes recorded during follow-up were of a minor severity and did not affect the patients' functional status. Analysis of the data excluding minor strokes reduces the annual stroke rate in the vascular territory beyond an ICA occlusion from 5% to approximately 3%. Finally, a certain number of the reported studies have included patients with common carotid artery occlusion. In those cases the risk of further ischemic events distal to the occluded artery may be decreased because of the absence of an ipsilateral collateral channel via the external carotid artery thus preventing further embolic phenomena through this alternate pathway.

A few pathogenic mechanisms have been proposed to explain ischemic events in the territory of an occluded internal carotid artery. First there is evidence that a certain number of patients with ICA occlusion may present with ulcerative and/or stenotic disease in the ipsilateral common and/or external carotid arteries. These lesions may be considered as a source of thromboembolism causing ischemic events in the territory of the occluded artery through alternate channels (i.e. collateral circulation). Secondly, the presence of a 'stump' at the origin of the occluded artery has been reported as a source for embolic material through the external carotid artery. Thirdly, emboli may arise from the distal end of an occlusive thrombus in the ICA or there may be propagation of the existing ICA thrombus beyond the Circle of Willis causing further cerebral ischemia. Hemodynamic factors are believed to play a role in certain cases of cerebral ischemia beyond an occluded artery. Baron et al in a recent paper reported on a patient with ischemic events distal to an occluded ICA. The authors found zones of mismatch between the cerebral blood flow and the oxygen metabolism, calling this phenomenon the 'misery perfusion syndrome.' Interestingly, the ischemic events ceased and the 'misery perfusion syndrome' was reversed after STA-MCA anastomosis.

The mortality rate recorded in this report was relatively low, averaging approximately 3% per year; this was quite comparable to other recent studies. Higher mortality rates were recorded in the earlier studies; this could be explained by patient selection. The early studies often included patients with significant neurological deficits and an impaired functional status. Recent evidence suggests that the survival in such a group may be worse than for patients suffering from TIAs. Furthermore, differences in the occurrence and management of certain risk factors could explain certain variances in mortality. The Canadian Stroke Study excluded patients with prior evidence of recent myocardial disease or any heart disease likely to be considered a possible source of emboli. The most frequent cause of death in the present study was vascular-related and this is in agreement with previously published data.

Whether extracranial-intracranial arterial bypass surgery will improve the prognosis for patients suffering from ICA occlusion is unknown at the present time. Hopefully the International Cooperative Study of Extracranial-Intracranial Arterial Anastomosis will shed some light on this subject. One of the randomization strata in this study is the group of patients with internal carotid artery occlusion.

Conclusions

1. The risk of subsequent cerebral infarction distal to an occluded carotid artery is comparable to the one for patients suffering from TIAs and minor strokes in general.
2. Approximately two-thirds of strokes occurred ipsilateral to the occluded internal carotid artery.
3. During follow-up, three of the strokes were categorized as minor and did not impair the patient's functional status. Analysis of the data excluding those minor strokes would give us an annual stroke rate of 3% distal to an occluded internal carotid artery.
4. The mortality was low during the follow-up period and was comparable to recently published data. Vascular related causes accounted for the majority of deaths.
5. The possibility of reducing the risk of cerebral infarction distal to an occluded carotid artery by extracranial/intracranial bypass surgery is unproven. The International EC/IC Collaborative Trial has been designed to evaluate this form of treatment and a large cadre of patients with ICA occlusion is under surveillance in this trial.

Editors Note

In accordance with Stroke policy, this article was guest edited by Dr. J.P. Mohr.

References


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Internal carotid occlusion: a prospective study.
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Stroke. 1983;14:898-902
doi: 10.1161/01.STR.14.6.898
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Print ISSN: 0039-2499. Online ISSN: 1524-4628

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