Carotid Restenosis: Long-Term Noninvasive Follow-Up After Carotid Endarterectomy

Robert D. DeGroote, MD, Thomas G. Lynch, MD, Zafar Jamil, MD, and Robert W. Hobson II, MD

Recurrent stenosis has not been a primary consideration in the selection of patients for carotid endarterectomy. We have studied the incidence of postoperative restenosis retrospectively in 265 patients following 310 carotid endarterectomies. Two hundred fourteen patients (248 endarterectomies) were examined at 6–12 month intervals using ocular pneumoephysmography, spectral analysis, and B-mode imaging. The absolute incidence of recurrent carotid disease was 28% (69 of 248), with a 13% (33 of 248) incidence of hemodynamically significant restenosis and a 15% (36 of 248) incidence of hemodynamically insignificant disease. Life table analysis of the data projected a 32% incidence of hemodynamically significant restenosis after 7 years and a 40% incidence of hemodynamically insignificant recurrence. These data demonstrate a progressively increasing rate of restenosis.

The incidence of ipsilateral neurologic events was 8% (24 of 310); 12 occurred in association with noninvasively evident recurrent disease (12 of 69, 17%), whereas 11 occurred in noninvasively determined normal arteries (11 of 179, 6%). Noninvasive follow-up was not available in 1 patient. Of the 12 events associated with recurrent disease, 5 occurred in association with hemodynamically significant restenosis (5 of 33, 15%), whereas 7 occurred in association with hemodynamically insignificant disease (7 of 36, 19%). Carotid endarterectomy is a durable operative procedure with 92% (286 of 310) of arteries remaining asymptomatic over the period of clinical follow-up. However, absolute and life table projections of the incidence of asymptomatic restenosis are high, and this factor should be considered in the selection of patients for carotid endarterectomy, particularly in the absence of lateralizing symptoms. (Stroke 1987; 18:1031-1036)

Recurrence following carotid endarterectomy has been described previously. The incidence of restenosis, however, remains variable, dependent on the methods of diagnosis and the inclusion of asymptomatic as well as symptomatic recurrence. Stoney and String reported a 1.9% incidence of recurrent disease based on recurrent symptoms, whereas Nicholls et al and O'Donnell and Callow have documented recurrence rates of 12–22% based on the results of noninvasive diagnostic techniques. The implications of these data are significant and relevant to the determination of operative indications in symptomatic and asymptomatic patients.

The technologic improvements in noninvasive diagnostic methods have provided safe and practical means of following patients after carotid endarterectomy. The purpose of this report is to determine the incidence of restenosis in patients undergoing carotid endarterectomy for symptomatic and asymptomatic lesions, using ocuoplethysmography and ultrasonography. Data were assessed using life table analysis for a 5–7-year period of clinical follow-up.

Subjects and Methods

Between January 1976 and December 1984, 265 patients underwent 310 carotid endarterectomies. The annual number of procedures increased from 17 in 1976 to 83 in 1984. Postoperatively, these patients were followed at 6–12 month intervals. The results of noninvasive examination were available for 248 procedures in 214 patients; for the remainder, clinical follow-up was obtained by letter or telephone communication.

The noninvasive techniques employed included ocular pneumoephysmography (OPG-G), spectrum analysis, and real-time B-mode ultrasonography, which was used from 1979 until the present. Spectrum analysis was introduced in 1980. Prior to these dates, OPG-G was the noninvasive modality used.

The OPG-G (Electrodiagnostic Instruments, Burbank, Calif.) was considered abnormal if the difference between ophthalmic artery pressures was ≥5 mm Hg or if the ophthalmic artery:brachial artery systolic pressure index was <0.66. A 5-MHz continuous-wave Doppler velocimeter (Model D-10, Medasonics, Mountain View, Calif.) and a real-time spectrum analyzer (Angioscan II, Unigon, Inc., Mt. Vernon, N.Y.) were employed for spectral analysis, and the studies were interpreted relative to the peak systolic frequency. Frequencies of <5 kHz were considered normal and those of >8 kHz consistent with a hemodynamically significant stenosis. Frequencies between 5 and 8 kHz were considered significant only if the OPG-G was also positive. Real-time B-mode ultrasonography

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Images were interpreted only for the presence or absence of disease. The hemodynamic significance of any disease was based on the results of spectrum analysis or OPG-G.

Our criteria for the diagnosis of hemodynamically significant (>50% by diameter) carotid restenosis were defined as 1) positive OPG-G in the absence of additional studies, 2) peak systolic frequency of ≥8 kHz, 3) peak systolic frequency of >5 kHz and a positive OPG-G, or 4) B-mode ultrasonography indicating recurrent stenosis and a positive OPG-G or a peak systolic frequency of >8 kHz.

The presence of hemodynamically insignificant carotid restenosis (<50% by diameter) was defined as 1) peak systolic frequency between 5 and 8 kHz and a normal OPG-G, or 2) B-mode ultrasonography indicating recurrent stenosis and a normal OPG-G and a peak systolic frequency of <8 kHz.

Patients were grouped according to the operative indication; the incidences of recurrent stenosis, symptomatic recurrence, and periparative and late mortality were evaluated to the date of last follow-up, as well as by the life table method.15,16 Recurrent stenoses were separated further into hemodynamically significant and insignificant restenoses, and symptomatic recurrences as ipsilateral or contralateral to the operated side.

Results

Of the 265 patients, 30 were women who underwent 35 carotid endarterectomies, and 235 were men who underwent 275 operations. Forty-five patients had staged bilateral carotid endarterectomies. Seventy-three patients had a history of diabetes mellitus, 161 of hypertension, and 168 of tobacco use; their ages ranged from 31 to 86 years. Seventy-seven of the 310 operations were performed for asymptomatic disease, whereas 138 were performed following a history of transient ischemic attack (TIA), and 58 following a cerebrovascular accident (CVA).

There were 44 (17%) deaths during the period of follow-up; 3 (1%) of these deaths were in the perioperative period. The cumulative life table mortality (Table 1) was 6% after 1 year, 20% after 3 years, 33% after 5 years, and 48% after 7 years. Two perioperative deaths were secondary to myocardial infarction, and 1 patient died of unknown causes. Of the 41 late deaths, 3 (7%) died following CVA, 10 (24%) of myocardial infarction, 13 (32%) of causes unrelated to atherosclerosis, and 15 (37%) of undetermined causes.

On the basis of serial noninvasive examinations available following 248 procedures, 69 (28%) of the arteries had evidence of restenosis at the date of last follow-up; 33 (13%) had hemodynamically significant and 36 (15%) hemodynamically insignificant restenosis. Using the life table technique, the projected or cumulative recurrence rates at 1, 3, 5, and 7 years were 8, 17, 19, and 32%, respectively, for hemodynamically significant disease (Table 2, Figure 1) and 8, 13, 27, and 40%, respectively, for hemodynamically insignificant disease (Table 2, Figure 2). Serial follow-up was
available for 63 of the 77 arteries asymptomatic at the time of operation; the cumulative recurrence rate after 5 years was 40% for all evidence of disease and 25% for hemodynamically significant disease (Table 3, Figure 3). For those patients who were symptomatic prior to endarterectomy (172 of 196 arteries available for follow-up), the cumulative recurrence rate after 6 years was 48% for all evidence of disease and 26% for hemodynamically significant disease (Table 4, Figure 4).

During the period of follow-up, 286 of 310 operated sides (92%) remained asymptomatic. Ipsilateral neurologic events (TIA or CVA) occurred following 24 procedures (8%), of which 7 were perioperative. Four events were associated with a previously asymptomatic lesion (19 of 196, 10%) (p>0.05). Noninvasive follow-up was not available for 1 patient. The cumulative rate of ipsilateral symptomatic recurrence (Table 5, Figure 5) was 5% after 1 year, 7% after 3 years, and 22% after 5 and 7 years. Twelve of the ipsilateral neurologic events were associated with recurrent stenosis (12 of 69, 17%), whereas 11 were associated with arteries having normal noninvasive studies (11 of 179, 6%); this difference was significant (p<0.05). Of the 33 hemodynamically significant restenoses, 5 (15%) were associated with ipsilateral neurologic events, whereas 7 (19%) of the 36 hemodynamically insignificant restenoses were associated with ipsilateral events (p>0.05). Contralateral neurologic events (TIA or CVA) occurred following 10 of 220 (4.5%) unilateral procedures (Table 5).

In addition to the 7 perioperative central neurologic events, there were 16 (5%) peripheral nerve deficits; 8 involved the mandibular branch of the facial nerve, 6 the hypoglossal nerve, and 2 the recurrent laryngeal nerve. There were 9 repeat operations (2.9%) for recurrent disease. Five of the patients had experienced TIAs, and 4 were asymptomatic with stenoses of >75% (by diameter).

**Discussion**

Conclusions drawn from previous reports examining the incidence of recurrent disease following carotid endarterectomy have varied widely. Stoney and Stringer reported a 1.9% incidence of symptomatic recurrence, whereas Nicholls et al observed a 22% incidence of hemodynamically significant recurrent stenosis. This variation not only reflects differences in the definition of recurrent disease but also in the methods of diagnosis.

Cossman et al reviewed 361 carotid endarterectomies in 251 patients, reporting a 3.6% incidence of early restenosis (within 2 years of surgery), which they attributed to myointimal proliferation. Reevaluation was prompted by recurrent symptoms in 5 patients, by a new bruit in 1, and was incidental in 1. Hertzer et al reported a 1% incidence of restenosis in 1,250 patients. The majority (87%) experienced neurologic symptoms associated with recurrent stenosis.

Arteriography yields a greater incidence of recurrent disease. Blaisdell et al followed 100 patients over 5 years. Follow-up arteriography, 10–60 days after sur-
surgery, was available in 95 patients and demonstrated 1 occlusion (1%). After 5 years, arteriographic follow-up was available in 15 patients, with a 13% incidence of recurrent stenosis. Edwards et al reported arteriographic correlation in 30 patients (43 carotid endarterectomies) 5 or more years after carotid endarterectomy; 3 patients had significant restenosis and 6 had stenoses of <25%, yielding a 21% incidence of recurrent disease. Schutz et al reported angiographic evaluation following 59 carotid endarterectomies; 6 of the 59 (10%) were occluded.

The use of noninvasive diagnostic techniques following carotid endarterectomy has been reported by Kremen et al and Cantelmo et al. Kremen and associates, using OPG-G, observed a 9.8% incidence of recurrent stenosis following 173 endarterectomies; only 2% were symptomatic. Cantelmo et al combined ultrasonic arteriography with oculoplethysmography, reporting a 12% incidence of restenosis; 62% were asymptomatic, and 25% of the stenoses were hemodynamically insignificant.

Previous studies reporting the incidence of symptomatic recurrence, or of recurrent stenosis at the time of death or last follow-up, weight each operation equally, regardless of the length of follow-up. For example, in the current series the incidence of hemodynamically significant recurrent stenosis was 13% for 248 arteries followed 1–7 years. If the life table method is employed, however, recurrence is reported relative to the patient population at risk during a given interval of observation. It is therefore possible to use all accumulated data and, at the same time, to weight the data in relation to the duration of follow-up. Thus, in our series the 13% incidence of hemodynamically significant restenosis yields a cumulative recurrence of 32% after 7 years. The 22% incidence of recurrent stenosis reported by Nicholls et al yields a cumulative incidence of approximately 40% after 4 years.

While the incidence of hemodynamically significant restenosis, 13% of 248 arteries, is comparable with that in many studies, the use of real-time B-mode imaging has permitted the identification of lesser, hemodynamically insignificant, degrees of restenosis. By reporting a recurrence rate of 15% for hemodynamically insignificant disease, the total recurrence rate in this study has more than doubled. O'Donnell and Cal- low also employed a combination of Doppler ultrasonography and real-time B-mode imaging and reported a 27% recurrence rate, with a 12% incidence of hemodynamically significant restenosis and a 15% incidence of hemodynamically insignificant restenosis.

The incidence of recurrent stenosis appears to be unrelated to the operative indication. Because there were fewer operations performed for asymptomatic indications, the data are compared at 5 years. The cumulative incidence of all recurrent stenosis was 40% following those operations for asymptomatic indications, with a 25% incidence of hemodynamically significant recurrence. The incidence of all recurrence following operations for symptomatic indications was 41% and cumulative incidence of hemodynamically significant restenosis 16%.

Despite this seemingly significant incidence of recurrent stenosis following carotid endarterectomy, the

Table 4. Recurrent Stenosis Associated With Symptomatic Operative Indication

<table>
<thead>
<tr>
<th>Interval (months)</th>
<th>At risk</th>
<th>Recurrence</th>
<th>Removed</th>
<th>Interval recurrence</th>
<th>Recurrence - free</th>
</tr>
</thead>
<tbody>
<tr>
<td>0-12</td>
<td>172</td>
<td>24</td>
<td>47</td>
<td>16%</td>
<td>84%</td>
</tr>
<tr>
<td>12-24</td>
<td>101</td>
<td>5</td>
<td>22</td>
<td>6%</td>
<td>97%</td>
</tr>
<tr>
<td>24-36</td>
<td>74</td>
<td>4</td>
<td>11</td>
<td>6%</td>
<td>75%</td>
</tr>
<tr>
<td>36-48</td>
<td>59</td>
<td>6</td>
<td>18</td>
<td>12%</td>
<td>66%</td>
</tr>
<tr>
<td>48-60</td>
<td>35</td>
<td>3</td>
<td>10</td>
<td>10%</td>
<td>90%</td>
</tr>
<tr>
<td>60-72</td>
<td>22</td>
<td>2</td>
<td>8</td>
<td>11%</td>
<td>89%</td>
</tr>
</tbody>
</table>

The use of noninvasive diagnostic techniques following carotid endarterectomy has been reported by Kremen et al and Cantelmo et al. Kremen and associates, using OPG-G, observed a 9.8% incidence of recurrent stenosis following 173 endarterectomies; only 2% were symptomatic. Cantelmo et al combined ultrasonic arteriography with oculoplethysmography, reporting a 12% incidence of restenosis; 62% were asymptomatic, and 25% of the stenoses were hemodynamically insignificant.

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The incidence of recurrent stenosis appears to be unrelated to the operative indication. Because there were fewer operations performed for asymptomatic indications, the data are compared at 5 years. The cumulative incidence of all recurrent stenosis was 40% following those operations for asymptomatic indications, with a 25% incidence of hemodynamically significant recurrence. The incidence of all recurrence following operations for symptomatic indications was 41% and cumulative incidence of hemodynamically significant restenosis 16%.

Despite this seemingly significant incidence of recurrent stenosis following carotid endarterectomy, the
incidence of associated symptomatic recurrence was low and apparently unrelated to the degree of restenosis. Only 5 (15%) of the 33 hemodynamically significant recurrent stenoses were associated with ipsilateral neurologic events, as were 7 (19%) of the 36 hemodynamically insignificant recurrences. These data are not dissimilar from those reported by Kremen et al and O'Donnell and Callow. O'Donnell and Callow reported recurrent symptoms in 3 (18%) of 17 patients with hemodynamically significant recurrence, and O'Donnell and Callow observed symptomatic recurrence associated with 4 (8%) of 49 significant restenoses. Cantelmo et al, conversely, reported a 48% incidence of symptomatic recurrence. Based on the ultrasonic characteristics and morphology of the recurrent plaques, the low incidence of recurrent symptoms is not surprising. O'Donnell and Callow reported that the majority of recurrent lesions had a smooth surface, without ulceration or irregularity; the plaque was weakly echo-reflective and homogeneous, suggestive of a high lipid content, and without evidence of plaque hemorrhage. The 4 recurrent stenoses in that series that were associated with symptomatic recurrence showed echo characteristics of plaque hemorrhage and/or debris.

While the ultrasonic morphology of the majority of recurrent stenoses is benign, the incidence of symptomatic recurrence is significantly increased if there is noninvasive evidence of recurrent stenosis. Of the 24 ipsilateral neurologic events, 12 occurred among the 69 arteries (17%) with recurrent disease, whereas 11 events were associated with normal noninvasive examinations (6% of 179 arteries). Consequently, we recommend routine postoperative noninvasive evaluation following carotid endarterectomy. Although this may alert the clinician to the greater risk of neurologic complications, the overall incidence of these symptoms is reassuringly low and suggests the possibility of control by medical therapy including antiplatelet medications.

As the use of noninvasive techniques has increased the reported incidence of recurrent stenosis, greater consideration must be given to this complication in selecting patients for endarterectomy. The volume of carotid endarterectomies has tripled nationally during the period 1970-1980, with asymptomatic lesions accounting for an estimated 45% of cases. Clagett et al have noted that there is a disproportionate number of women with recurrent stenosis, that the mean age at endarterectomy was significantly lower in patients with recurrence, and that 95% of patients with recurrent disease continued to smoke following initial endarterectomy. Although we can be assured that symptomatic recurrences are much less common than recurrent stenosis, perhaps a reconsideration of operative indications in asymptomatic patients with these risk factors will become increasingly appropriate.

References

Table 5. Recurrent Symptoms Following Carotid Endarterectomy

<table>
<thead>
<tr>
<th>Interval (months)</th>
<th>At risk</th>
<th>Ipsilateral</th>
<th>Removed</th>
<th>Interval symptoms</th>
<th>Symptom-free</th>
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<tr>
<td>0-12</td>
<td>310</td>
<td>12</td>
<td>136</td>
<td>5%</td>
<td>95%</td>
</tr>
<tr>
<td>12-24</td>
<td>162</td>
<td>2</td>
<td>51</td>
<td>1%</td>
<td>94%</td>
</tr>
<tr>
<td>24-36</td>
<td>109</td>
<td>1</td>
<td>22</td>
<td>1%</td>
<td>93%</td>
</tr>
<tr>
<td>36-48</td>
<td>86</td>
<td>4</td>
<td>29</td>
<td>6%</td>
<td>88%</td>
</tr>
<tr>
<td>48-60</td>
<td>53</td>
<td>5</td>
<td>12</td>
<td>11%</td>
<td>78%</td>
</tr>
<tr>
<td>60-72</td>
<td>36</td>
<td>0</td>
<td>14</td>
<td>0%</td>
<td>78%</td>
</tr>
<tr>
<td>72-84</td>
<td>22</td>
<td>0</td>
<td>11</td>
<td>0%</td>
<td>78%</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>At risk</th>
<th>Contralateral</th>
<th>Removed</th>
<th>Interval symptoms</th>
<th>Symptom-free</th>
</tr>
</thead>
<tbody>
<tr>
<td>220</td>
<td>2</td>
<td>104</td>
<td>1%</td>
<td>99%</td>
</tr>
<tr>
<td>114</td>
<td>5</td>
<td>36</td>
<td>5%</td>
<td>94%</td>
</tr>
<tr>
<td>73</td>
<td>1</td>
<td>17</td>
<td>2%</td>
<td>92%</td>
</tr>
<tr>
<td>55</td>
<td>2</td>
<td>18</td>
<td>4%</td>
<td>88%</td>
</tr>
<tr>
<td>35</td>
<td>0</td>
<td>11</td>
<td>0%</td>
<td>88%</td>
</tr>
<tr>
<td>24</td>
<td>0</td>
<td>7</td>
<td>0%</td>
<td>88%</td>
</tr>
</tbody>
</table>

Ipsilateral 0% | Contralateral 0%

Key Words • endarterectomy • carotid artery • real-time B-mode ultrasonography
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