Restenosis and Occlusion After Carotid Surgery Assessed by Duplex Scanning and Digital Subtraction Angiography

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SUMMARY  In a study of 140 patients operated upon with 143 carotid endarterectomies (mean follow-up time 5.2 ± 2.3 years, range 1 month — 9.3 years), vessel morphology was examined with duplex scanning in 113 patients and with digital subtraction angiography (DSA) in 82 patients. The operative mortality was 1.4%; persisting stroke morbidity 3.6% and the combined operative mortality/morbidity 5%. During the follow-up time a further 20 patients (14.5%) died, 13 had new strokes and 14 new TIAs. By life table analysis, the annual rate of stroke including the operative period was 2.7% (1.7% on the operated side and 1.0% on the non-operated side). Fourteen new occlusions (12%) of the operated carotid artery was found and restenosis (>50%) in 13 patients (11.2%). Progression of the atherosclerotic disease in the contralateral non-operated carotid artery was found in 41 patients (37%) including 3 new occlusions. Agreement DSA/ duplex was 88% on the operated side and 92% on the non-operated side. New strokes or TIAs on the operated side were more common in patients with occlusions or restenosis (p < 0.05), whereas no symptoms were referable to occlusions on the non-operated side. Risk factor analysis revealed an increased risk of atherothrombotic progression on the non-operated side in smokers and those with two or more risk factors. The risk of restenosis in the operated carotid artery was higher in females (p < 0.025).

MORPHOLOGICAL AND HAEMODYNAMIC CHANGES in extracranial arteries following endarterectomy have not been extensively investigated, since serial angiography examinations involve a certain risk. 1,2 The rate of restenosis > 50% of diameter reduction/occlusion has previously been investigated predominantly in patients with recurrent neurological symptoms and is reported to amount to 1—5%.3,4 Using continuous wave Doppler, the incidence of restenosis > 50% and occlusion has been reported to be 36% after a mean observation time of 6 years.4 A combination of 2-D image and pulsed Doppler, so-called duplex, offers the advantage of providing both anatomical and haemodynamic information and makes possible the detection of stenosis less than 50%.7,8 The validity of this method has also been demonstrated in patients after endarterectomy in comparison with postoperative angiogram.9 With this technique, the incidence of restenosis > 50%/occlusion has been reported to be 19%10 after a mean observation time of 16 months.

A new semi-invasive method, digital subtraction angiography (DSA), has gained wide use during recent years and is still under evaluation although hitherto the reported results are less accurate compared to conventional angiography.11-13

The aim of the present study was to evaluate the frequency of restenosis or occlusion after carotid endarterectomy (CE), the possible correlation between morphological changes and recurrent symptoms and the possible influence of vascular risk factors on these events.

There are few published investigations on the natural course of asymptomatic carotid artery lesions.14

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The contralateral non-operated artery was therefore studied as well in order to elucidate this problem.

Materials and Methods

Patients

At the University Hospital, Linköping, Sweden, 143 carotid endarterectomies were performed in 140 patients during the period 1974–82. One hundred and thirty-seven patients had unilateral operation and three bilateral. There were 111 males and 29 females with a mean age 61 ± 7.7 years. Neurological investigation including angiography and selection of candidates for surgery was done at the Department of Neurology. Fifty-nine patients (42%) had transient ischemic attacks (TIA) and 74 (53%) minor stroke; all selected to carotid lesions on the operated side. Seven patients had asymptomatic stenosis with a high degree lesion on the contralateral side. In the latter category, the operation was done in order to improve intracranial haemodynamics. The ratio left/right CE was 76/67.

All patients had angiography, the majority both selective common carotid angiography and arcus arch angiography. Plaques with stenosis <15% diameter reduction were found in 18 patients, stenosis 16–49% in 30 patients, stenosis 50–75% in 28 patients, and stenosis 76–99% in 64 patients. On the contralateral side, high grade lesions were noted in 16 vessels; stenosis 50–75% in 9 vessels, stenosis 76–99% in 5 vessels and in 2 vessels occlusion was found.

Established vascular risk factors were the following: treated arterial hypertension in 81 patients (58%), diabetes mellitus in 11 (8%) and smoking in 84 patients (60%), angina pectoris in 26 patients (19%) and previous myocardial infarction in 8 patients (6%). Peripheral vascular disease was present in 11 (8%) and hyperlipidemia in 29 patients (21%). One hundred and thirteen patients were treated with anticoagulant drugs (AC) before, and approximately 2–3 months after operation. Fifteen received antiplatelet drugs and the remaining patients were without antithrombotic therapy.

The operations, performed by three vascular surgeons, were conventional endarterectomies. Intraluminal shunt was used in 106 patients.

After thrombendarterectomy all patients were reexamined by a neurologist within one week, after three months and thereafter yearly. At follow-up investigation in 1983–84, 118 patients, representing 121 CE, were available. The examination included neurological status, filling in of a special questionnaire, duplex scanning of the carotid vessels and periorbital Doppler examination. All medical records from the Departments of Surgery and Neurology were available including those of patients who died. When a patient died at another hospital, the death certificate and a copy of the medical record was requested. The mean observation time between operation and examination was 5.2 ± 2.3 (SD) years, (range 1 month–9.3 years). Only 8 patients, of whom 4 had died, were observed less than 2 years. All patients were advised to perform DSA, but 20 refused.

Duplex Scanning

Duplex scanning was performed in 113 patients. The duplex scanner (ATL Mark 500) was equipped with a combined 7.5 MHz short focus transducer used for two-dimensional echo image and a 5 MHz short focus variable single-gate pulsed Doppler with Fast Fourier spectral analysis in the same scan head, as described earlier.

The duplex findings were classified as follows: (1) normal: a narrow spectral flow curve throughout systole and no visible plaques; (2) stenosis <15%: slight spectral broadening in the decelerating phase of systole and/or small wall irregularities; (3) stenosis 16–49%: spectral broadening throughout systole, velocity up to 1.2 m/sec; (4) stenosis 50–75%: velocity exceeding 1.2 m/s; (5) stenosis 76–99%. Subgrouping into these two last categories was done using the following equation: y = 45.8 ± 7.19 peak systolic velocity (m/sec) + 4.8 late diastolic velocity (m/sec) + 7.2 the result of periorbital Doppler (coded as normal = 0 and abnormal = 1); (6) occlusion: no signal detected in the imaged vessel and usually low diastolic flow close to zero in common carotid artery.

Digital Subtraction Angiography

DSA was performed in 82 patients with a Technicare DR 960. For each imaging sequence, 40 ml bolus of iodinated contrast media was injected into the central venous system. A routine DSA study included two oblique views of the carotid arteries and, in case of vessel superimposition, additional projections were performed. The stenosis was measured as the greatest percentage reduction of the lumen diameter seen in any projection. DSA could not be carried out because of contrast allergy in 5 patients, increased creatinine level in two patients and technical problems in a further two patients. In two patients, the images were uninterpretable due to motion artifacts. Twenty patients did not accept the investigation, and in two symptomatic patients, conventional multiplane arteriography was performed instead of DSA.

DSA results were classified into the following categories: (1) normal, (2) stenosis 1–49%, (3) stenosis 50–75%, (4) stenosis 76–99% and (5) occlusion.

Statistical Methods

The Chi-square test and life table analyses were used for statistical evaluation.

Results

Clinical Events

The longitudinal course of clinical events is presented in table 1.

Early Perioperative Period

During the operation and in the week following the operation, 6 patients had TIA/RIND and 7 patients had a stroke; in the latter group two patients died within 5 weeks after the operation. Thus the peri-operative mortality was 1.4%, persisting morbidity 3.6% and combined mortality-morbidity 5%.
TABLE 1  The Longitudinal Course of Clinical Events  

<table>
<thead>
<tr>
<th></th>
<th>Operated side</th>
<th>Non-operated side</th>
</tr>
</thead>
<tbody>
<tr>
<td>Perioperatively</td>
<td></td>
<td></td>
</tr>
<tr>
<td>n = 140</td>
<td>6 TIA</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>7 stroke</td>
<td></td>
</tr>
<tr>
<td></td>
<td>(2 deaths)</td>
<td></td>
</tr>
<tr>
<td>Late follow-up</td>
<td></td>
<td></td>
</tr>
<tr>
<td>dead</td>
<td>1 stroke</td>
<td>2 stroke (1 VB)</td>
</tr>
<tr>
<td>n = 20 (+ 2 periop)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Not examined</td>
<td>1 TIA</td>
<td>1 TIA</td>
</tr>
<tr>
<td>n = 5</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Follow-up examinations</td>
<td>10 TIA</td>
<td>4 TIA (1 VB)</td>
</tr>
<tr>
<td>n = 113</td>
<td>5 stroke</td>
<td>5 stroke (1 VB)</td>
</tr>
<tr>
<td>n = 140 (143 CE)</td>
<td>(VB = vertebrobasilar).</td>
<td></td>
</tr>
</tbody>
</table>

Recurrent Symptoms

During the follow-up period (mean 5.2 ± 2.3 years, range 1 month - 9.3 years) of the remaining 138 patients, a further 20 patients died (14.5%), three of whom had experienced stroke; one on the operated side, one from the contralateral side and one from the vertebral-basilar territory. The latter patient died due to brainstem infarction, but the other patients died from causes other than neurological — myocardial infarction (13), neoplasm (1) and from other causes (5). Of the 118 surviving patients, 5 could not participate in the study, one of whom suffered from sequelae after subarachnoid haemorrhage and another patient had had TIA from the operated side and from the vertebral-basilar system. The remaining three patients were asymptomatic.

Thus 113 patients were able to attend the complete follow-up examination. Among these patients, 10 (8.9%) had experienced stroke and 14 (13.2%) TIA. In 5 patients with stroke (4.3%) and 10 patients with TIA (8.9%), the lesion was referable to the operated side. Four strokes (3.6%) and 3 TIA (2.7%) were referable to the contralateral non-operated side. One patient had stroke (0.9%) and one TIA (0.9%) related to the vertebral-basilar territory. Eighty nine patients remained asymptomatic.

Total Peri- and Postoperative Period

Using the life table (fig. 1), at 9 years 23.2% of the patients had experienced new strokes, 11.1% being referable to operated vessels. The annual stroke rate was 1.7% on the operated side and 1.0% on the non-operated side, a total of 2.7% on all sides. If perioperative strokes were excluded, the annual incidence of stroke was 0.7% on the operated side and unchanged on the non-operated side.

Morphological Findings

Operated Side

Twenty seven (24%) were found to have either a high grade stenosis (>50%) or an occlusion diagnosed by at least one method. In 13 patients (11.5%), a restenosis >50% was detected and in 14 patients (12.5%) there was an occlusion. The risk of restenosis was higher in females (p < 0.025, chi square 5.24).

The presence of restenosis/occlusion was significantly commoner in the vessels with high grade (>50%) preoperative stenosis (p < 0.025, chi square 5.47). Twenty two of 70 vessels with preoperative high grade stenosis developed late restenosis/occlusion compared to 5 of 46 vessels with preoperative low-grade (<50%) stenosis. Investigation by duplex scanning was performed in 113 patients. The results are given in figure 2. The results of the DSA performed on 82 patients are given in figure 3. DSA showed a smaller number of restenoses, only 3 stenoses >50% of which one >75%. The difference between duplex and DSA, however, was often only 10–20% (table 2). The duplex results agreed with DSA in 72 of 82 vessels (88%).

The Correlation Between Clinical and Morphological Findings (Fig 2 & 3)

In the group with restenosis >50%, 3 patients had new neurological symptoms, one of them TIA + minor stroke and another patient TIA alone, 6 and 3 years...
respectively, after the operation. The third patient with stenosis >75% had stroke 7 years postoperatively.

Fourteen of the examined patients had an occlusion of the operated artery. Of these, 4 had late symptoms (3 TIA, one stroke) (fig 2).

In 86 patients in whom the vessels operated on were patent and without restenosis at the follow-up, late recurrent symptoms had appeared in only 8 patients (7%). Late recurrent symptoms were thus commoner in patients with stenosed or occluded arteries ($p < 0.05$, chi square 3.88) (fig 2).

**Non-operated Side**

One hundred and ten vessels were examined by duplex scanning. The results are presented in figure 4. Compared with angiographic findings before operation, a clear progression of atherosclerotic disease was noted in 38 patients (34.5%) when estimating progress in all stenosis >15% lumen diameter reduction (table 3). With DSA, 79 non-operated vessels were examined. Two symptomatic vessels were examined by aortocervical angiography. DSA classified 9 vessels as stenosis 50–75%, 5 as stenosis 76–99% and 5 as an occlusion. Agreement DSA-duplex on the non-operated side was 73/79 (92%), which is slightly better than on the operated side. Using both methods, a total of 41 vessels progressed from a category of lesser degree of lumen diameter reduction to a category of greater diameter reduction, compared to preoperative angiography.

**Risk Factors**

We found no correlation between risk factors, the number of neurological events and postoperative vessel morphology on the operated side. There was, however, a relationship between the number of risk factors and progression of atherosclerotic disease on the non-operated side, where 27 of 41 patients had at least two or more risk factors, a significant difference ($p < 0.05$, chi square 3.88) (fig 2).

**TABLE 3 As in Table 2**

<table>
<thead>
<tr>
<th>Duplex after</th>
<th>Normal</th>
<th>1-15%</th>
<th>16-49%</th>
<th>50-75%</th>
<th>76-99%</th>
<th>100%</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Angio before</td>
<td>6T</td>
<td>4T</td>
<td>24T</td>
<td>5ss</td>
<td>1</td>
<td>43</td>
<td></td>
</tr>
<tr>
<td>Normal</td>
<td>5</td>
<td>8</td>
<td>1</td>
<td>3</td>
<td>9</td>
<td>40</td>
<td></td>
</tr>
<tr>
<td>1-15%</td>
<td>15</td>
<td>1</td>
<td>4</td>
<td>4T</td>
<td>9</td>
<td>5</td>
<td></td>
</tr>
<tr>
<td>16-49%</td>
<td>2</td>
<td>9</td>
<td>1</td>
<td>3</td>
<td>4</td>
<td>40</td>
<td></td>
</tr>
<tr>
<td>50-75%</td>
<td>1</td>
<td>4</td>
<td>1</td>
<td></td>
<td>9</td>
<td>5</td>
<td></td>
</tr>
<tr>
<td>76-99%</td>
<td>1</td>
<td>4</td>
<td>1</td>
<td>5</td>
<td>2</td>
<td>2</td>
<td></td>
</tr>
<tr>
<td>100%</td>
<td>1</td>
<td>4</td>
<td>1</td>
<td>5</td>
<td>2</td>
<td>2</td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>7</td>
<td>45</td>
<td>22</td>
<td>22</td>
<td>9</td>
<td>5</td>
<td>110</td>
</tr>
</tbody>
</table>

T = TIA; S = Stroke.
chi square 4.29) from the group which did not progress. In the latter group, 30 of 69 patients had a combination of two or more risk factors. As a single risk factor, smoking was related (p < 0.05, chi square 3.8, one-tailed test) to atherosclerotic disease progression: 31 of 41 patients with progression were smokers as opposed to 38 of 69 patients in whom the atherosclerotic lesions were stable. Furthermore, 10 of 41 patients with progression had a history of myocardial infarction either prior to operation or during the follow-up, compared to only 6 of the 69 patients without progression (p < 0.05, chi square 3.91). Hyperlipidemia was insignificant.

Discussion

The clinical results are in accordance with several other studies and show a concentration of mortality and morbidity during the operative period. If the strokes during the operation and the following month are excluded, new strokes on all sides occurred at a rate of 1.7% per year, which is about the same rate as has been reported during long-term follow-up after CE in other studies. Approximately a half of the new strokes appeared in the territory of the operated carotid artery during the perioperative period, and at that time no strokes occurred on the side not operated on. Thereafter no difference in stroke frequency between the operated and non-operated side was observed. For this reason it is probable that these late strokes were related to the natural progression of the atherosclerotic process. On the operated side, there was a stronger relation between the grade of restenosis or occlusion and the appearance of a new stroke. Most previous studies of the postoperative pathology have been evaluated only in patients with recurrent symptoms. However, Zierler 1982, using ultrasonic duplex examination, found in 76 patients (89 CE) that 19% of the operated vessels had a severe restenosis within 16 months. Only one occlusion was found. That result can be compared with the present rate of 23% restenosis or occlusion during a long follow-up time after the operation of mean 62 months.

Totally, 14 occlusions (12%) were found in 116 operated and examined vessels. About the same amount was found by Norrving et al 1981, who performed angiography in the common carotid artery within 2 weeks after the operation in 81 CE patients and found 7 early occlusions. With ultrasound technique, 10 occlusions (16%) were found in the same investigation at follow-up after 72 months in 64 examined operated vessels. Comparable results are reported by Schutz, 1970, who with angiography found 6 occlusions (12%) in 50 patients. Recently, also Padayachee, 1983, using continuous wave Doppler, found occlusion of the operated internal carotid artery in 7 of 54 CE patients (13%), all associated with a stroke within the first postoperative week.

In our study, no risk factor could be found to predict the rate of restenosis or occlusion on the operated side, except that high-grade restenosis/occlusion were significantly commoner in vessels with high-grade preoperative stenosis and that proportionately more females developed recurrent stenosis. Possible explanations are that females have smaller arteries or differing platelet function than males.

In order to detect early restenosis or occlusion, a perioperative Doppler investigation may be performed after closure of the arteriotomy but before skin closure. The finding of a lack of improvement or a deterioration in the Doppler spectrum may be useful in selecting patients for operative angiography. An early detected severe restenosis or occlusion in an operated patient is an indication for immediate revision.

The results presented in this study do not allow unequivocal conclusions to be drawn. As shown in figures 2 and 4, late neurological symptoms were seen both in low and high grade stenotic vessels, whereas normal vessels were asymptomatic.

If the results of two methods used in the study (the duplex ultrasound and the DSA technique) are compared, good agreement is seen in the detection of occlusions on both sides and restenosis in the non-operated carotid vessels. On the operated side, the duplex technique more often showed stenosis 50–75% than did DSA. Two alternative explanations alone or in combination are possible; duplex tended to slightly overestimate the degree of stenosis because of postoperative remodelling of bulb geometry; DSA tended to underestimate the severity of lesions. This has been shown in several studies in comparison with angiography.

To date, there is no way of fortelling which vessels might develop late symptoms and morphological lesions after carotid endarterectomy in patients with atherosclerotic vessel disease. The duplex ultrasound technique would seem to be the most appropriate method for the serial follow-up of the postoperative course in these "at risk" patients.

Acknowledgments

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Familial Hyperlipidemia in Stroke in the Young

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SUMMARY Serum cholesterol, low density lipoproteins (LDL), very low density lipoproteins (VLDL) and chylomicron levels were studied in 25 young patients (age 40 years or less) of non-embolic ischemic stroke of unknown aetiology. Fifteen patients were males and 10 were females. The prevalence of hyperlipidemia was found to be 60%. Fredrickson's type IIb hyperlipoproteinemia was the commonest (32%) abnormal pattern observed, followed by type IIa (12%), type IV (12%) and type V (4%). Family studies were carried out in all the 25 index patients (15 hyperlipidemic and 10 normolipidemic). Familial hyperlipidemia (i.e. 2 or more hyperlipidemic members in the same family) was found in 9 of the 15 hyperlipidemic index patients and in none of the normolipidemic index patients. The common pattern was found to be that of familial combined hyperlipidemia. The study indicates that screening the family members of hyperlipidemic young patients of non-embolic ischemic stroke may delineate a group of high risk individuals for possible primary prevention before they develop the disease.

Since Cerebral Stroke is often crippling, and the impact of treatment on the prognosis is limited, the potential to control the disease lies in its primary prevention.1-3 This implies reliable and comprehensive information on the factors related to the risk of stroke. Hyperlipidemia has been considered as one of the important risk factors in the causation of atherothrombotic stroke.4-2 The task of identifying the individuals with high lipid levels in the general population sounds cumbersome. A desirable and feasible alternative approach, however, could be to screen the first degree relatives of hyperlipidemic young patients of atherothrombotic stroke for familial hyperlipidemia, thus delineating a group of high risk individuals for possible primary prevention before they develop the stroke. Since the relative contribution of genetic factors in the causation of any trait may vary among different populations, a pilot study has been carried out to identify the importance of familial hyperlipidemia in patients of ischemic stroke in Haryana (North India).

Material and Methods
Selection of the Index Patients
This study was conducted in the Department of Neurology at Medical College and Hospital, Rohtak (Haryana). Twenty-five patients (15 males and 10 females), of the age of 40 years or less, suffering from cerebral infarction (nonembolic ischemic stroke) of unknown aetiology (based on the criteria of Walker et al, 198110) were taken for the study as index patients. Diagnosis was made on the basis of history, physical

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