Prognostic Significance of Severity of Carotid Atheroma in Early Manifestations of Cerebrovascular Disease


SUMMARY Two hundred and fifteen patients with transient ischaemic attacks, reversible ischaemic neurological deficit, or completed stroke were studied angiographically. The appearances of the carotid bifurcation were classified as normal, irregular, stenosed or occluded and the possible prognostic significance of the angiographic categories sought in a follow up study. Over a mean follow up period of 4.1 years 12% of patients were found to have died, and 10% had had a stroke. Fourteen percent had TIAs and 5.1% had sustained a myocardial infarction. Mortality and stroke risk were greatest with carotid occlusion which was least often followed by TIAs. Strokes, but not TIAs, were less frequent in the presence of normal angiograms.

CAROTID ATEROMA is detected angiographically in 50–60% of patients investigated for transient ischaemic attacks and mild strokes. While there is evidence that hypertension has an adverse effect on the prognosis increasing the risk of stroke during follow up, there is little direct evidence on whether the severity of the angiographic changes has predictive value. The present study considers this point relating the outcome of prolonged follow up to the angiographic findings at the time of presentation with transient ischaemic attacks, or with recovering strokes.

Method

Two hundred and fifteen patients (154 males and 61 females) referred to one of us (JM) for investigation of symptoms due to cerebrovascular disease within the carotid territory, had had carotid or arch angiography with categorization of the severity of atheromatous changes at the carotid bifurcation.

The clinical presentation had been in the form of a transient ischaemic attack (TIA, recovery within 24 hours) in 119 patients, or with a reversible ischaemic neurological deficit (RIND, recovery within 1 month) in 32 cases. In 64 patients the deficit, though eventually recovering sufficiently for the patient to return home, was persistent (completed stroke). When patients had had more than one type of episode they were classified according to their longest attack.

A note was made of whether the patient had cervical bruits, and of whether they had had one or more previous cerebrovascular episodes. For the purposes of this study the angiographic findings were classified into one of four groups. If there was no evidence of atheromatous disease at the carotid bifurcation, the angiogram was classified as 'normal'. If wall changes were minor with little or no encroachment at the lumen (less than 20% narrowing) they were said to show 'irregularity'. Greater degrees of encroachment on the lumen were classified as 'stenosis'. Total obstruction formed the fourth 'occluded' group.

Follow up information was obtained from clinic notes supplemented by a postal survey. Mortality and cardiovascular morbidity were noted together with details of any subsequent manifestations of cerebrovascular disease. The nature and outcome of any vascular surgery was studied, and medical treatment documented.

Results

The angiographic appearances of the carotid bifurcation appropriate to the symptoms were normal in 42 cases. Irregularity of the vessel wall was present in 71 cases and 58 had a stenosis with narrowing of the lumen. In 44 cases the carotid artery was occluded.

Of the total group 51 per cent had a blood pressure with either a systolic reading over 150 mm Hg and/or a phase IV diastolic of over 90 mm Hg. Cervical bruits were heard in 26 per cent and 77 per cent admitted to smoking regularly at the time of presentation.

Normal angiograms were more frequently found in those patients presenting with TIAs, and carotid occlusion was most often encountered among those with completed strokes (table 1). Thus 22% of TIA patients had normal X-ray appearances at the bifurcation compared with 3% of stroke victims (Chi square 10.3 p < .001). 12.5% of TIA cases showed carotid occlusion compared with 37.5% of the stroke patients (Chi square 15.3 p < .001). Patients with reversible ischaemic neurological deficit showed an intermediate position as far as carotid occlusion was concerned (seen in 16%) but had the highest incidence of normal angiography (44%).

Patients with normal angiograms were least often hypertensive (table 2). There was no difference in the
The proportion of smokers in the different angiographic groups. Bruits were not unexpectedly found most commonly in those with angiographic stenosis but they were also recorded by the clinician in 7–10 per cent of those with little or no evidence of vessel wall disease.

Follow up: The follow up period varied from a few months to 17 years (mean 4.1 years). Twenty-seven patients were untraceable from hospital notes or by post, 6 each from the groups with normal or occluded carotid arteries, 2 from the group with stenosis and 13 from the largest ‘irregular’ group.

Of the 188 who were traced (87.5%) 26 were dead, 8 from ischaemic heart disease and six with fatal strokes. Three had died within 48 hours of surgery and 5 had malignancies. There were three deaths from pneumonia (developing in one instance after infarction of small bowel). One patient had a fatal cerebral haemorrhage while on anticoagulants.

Strokes had occurred in 22 patients (including the 6 that were fatal). In 5 instances strokes occurred in relationship to therapy, twice to angiography, twice at the time of endarterectomy and once after an extracranial-intracranial bypass procedure. Further TIs were experienced by 31 patients and 12 had had acute myocardial infarcts. There were 111 patients who had had no further problems referable to the cerebral or coronary circulations.

The relationship between the angiographic appearances and the clinical outcome is shown in table 3. The incidence of TIA, stroke and myocardial infarction is expressed as a percentage of those in each group for whom follow up information is available. Mortality is expressed as the overall mortality including all causes of death. With increasing severity of atheromatous change as judged by the angiographic appearances there is evidence of a decreasing risk of TIA, but an increasing risk of stroke during follow up. Thus 1 in 4 of the normal angiogram group had further TIAs, but only 1 in 20 of those with an occluded carotid (Chi square for trend in all 4 groups 5.11, for direct comparison of the normal and occluded categories 5.3). Strokes occurred in none of the normal group but in 21% of those with occlusion (Chi square for trend in all groups 9.0, for direct comparison 7.6). The incidence of myocardial infarction, and the overall mortality, was also greatest in the follow up of those with carotid occlusion although these differences were not statistically significant.

The possibility that the relationship of angiographic findings to outcome might have been a reflection of different therapeutic management was considered further. Sixty-one patients had had an endarterectomy for disease at the carotid bifurcation. In 41 the vessel was stenosed, in 12 ulcerated (irregular group). In 8 patients the vessel operated upon was contralateral to a symptomatic carotid occlusion. Of these operations 2 resulted in death and 2 in a completed stroke. All 4 victims of operative mortality or morbidity had had

### Table 1: Nature of Presenting Clinical Events

<table>
<thead>
<tr>
<th>Angiographic Appearance</th>
<th>Number of Events</th>
<th>TIA (%)</th>
<th>RIND (%)</th>
<th>Stroke (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal (42)</td>
<td>16</td>
<td>26</td>
<td>26</td>
<td>14</td>
</tr>
<tr>
<td>Irregular (71)</td>
<td>25</td>
<td>46</td>
<td>42</td>
<td>9</td>
</tr>
<tr>
<td>Stenosis (58)</td>
<td>12</td>
<td>46</td>
<td>36</td>
<td>4</td>
</tr>
<tr>
<td>Occlusion (44)</td>
<td>11</td>
<td>33</td>
<td>15</td>
<td>5</td>
</tr>
<tr>
<td>Total (215)</td>
<td>64</td>
<td>151</td>
<td>119</td>
<td>32</td>
</tr>
</tbody>
</table>

### Table 2: Clinical Features of Patients Studied Related to Angiographic Appearances

<table>
<thead>
<tr>
<th>Angiographic Appearance</th>
<th>Number</th>
<th>M/F</th>
<th>Mean Age</th>
<th>Elevated BP (%)</th>
<th>Smoking (%)</th>
<th>Neck Bruit (%)</th>
<th>Period of Follow up Years (Mean)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal</td>
<td>42</td>
<td>2:1</td>
<td>49.2</td>
<td>24</td>
<td>76</td>
<td>7</td>
<td>5.8</td>
</tr>
<tr>
<td>Irregular</td>
<td>71</td>
<td>4:1</td>
<td>57.7</td>
<td>57</td>
<td>75</td>
<td>10</td>
<td>3.8</td>
</tr>
<tr>
<td>Stenosis</td>
<td>58</td>
<td>1.8:1</td>
<td>56.3</td>
<td>69</td>
<td>74</td>
<td>50</td>
<td>3.8</td>
</tr>
<tr>
<td>Occlusion</td>
<td>44</td>
<td>3:1</td>
<td>53.3</td>
<td>43</td>
<td>82</td>
<td>39</td>
<td>3.6</td>
</tr>
</tbody>
</table>

* *≥ 150 syst and/or ≥ 90 diastolic pressure (mm Hg)

### Table 3: Overall Incidence of TIA, Stroke (CVA), Myocardial Infarction (MI) and Death (All Causes) Related to Angiographic Findings

<table>
<thead>
<tr>
<th>Angiographic Group</th>
<th>No Followed</th>
<th>TIA (%)</th>
<th>CVA (%)</th>
<th>MI (%)</th>
<th>Deaths (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal</td>
<td>42</td>
<td>36</td>
<td>25</td>
<td>0</td>
<td>8</td>
</tr>
<tr>
<td>Irregularity</td>
<td>71</td>
<td>58</td>
<td>19</td>
<td>12</td>
<td>2</td>
</tr>
<tr>
<td>Stenosis</td>
<td>58</td>
<td>56</td>
<td>16</td>
<td>12.5</td>
<td>3.5</td>
</tr>
<tr>
<td>Occluded</td>
<td>44</td>
<td>38</td>
<td>5</td>
<td>21</td>
<td>16</td>
</tr>
<tr>
<td>Chi square</td>
<td>5.11</td>
<td>9.0</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Prior strokes, no such complications being seen when the patients had presented with TIAs. One patient with TIAs and an inaccessible stenosis had an EC-IC bypass operation and died of operative complications. Nine operated patients had TIAs, and 10 major strokes during follow up.

Of 22 patients known to have received aspirin as their primary treatment 4 had subsequent TIAs and 2 completed strokes. Of 91 who were given warfarin 15 had later TIAs and 6 completed strokes. One patient died of a cerebral haemorrhage. Forty patients received other forms of medical treatment, e.g. dipyridamole, hypotensive agents, venesection. Of these 3 had further TIAs and 4 strokes.

The risks of further TIAs and strokes show little variation among the different therapeutic regimes (table 4) making it unlikely that treatment has distorted the prognostic influence of the angiographic findings. The observations on treatment are of course uncontrolled and do not provide a true comparison of the effectiveness of carotid endarterectomy and antithrombotic measures.

The results of the follow up study in the 119 patients who presented with episodes resolving within 24 hours are separately set out in table 5. As in the overall group normal angiograms were associated with a reduced stroke risk and carotid occlusion with a reduced incidence of further TIAs. As the follow up period was longest in the group with normal angiograms (table 2) the adverse prognosis with the more severe angiographic findings may have been somewhat underestimated.

Discussion

The natural history of cerebrovascular disease is very variable, and incompletely documented despite some excellent studies such as those by Marquardson and Hutchinson and Acheson. Any features that could help in giving individual patients prognostic advice would clearly be valuable. The present study suggests that the angiographic appearances, reflecting the severity of atheromatous disease in the neck vessels, can be useful in predicting the outcome over a 3 to 5 year follow up period. The risk of a subsequent stroke was greatest if the carotid artery had been found to be occluded, and these patients also had the highest overall mortality. Patients with normal angiograms had the lowest mortality and had least strokes but many had further TIAs as did patients with minor angiographic abnormalities. The low stroke risk in those with normal angiograms contrasts with the higher estimate obtained by Marshall and Wilkinson. The increased chance of detecting potential cardiac sources of embolism with the recent advent of such techniques as echo cardiography may have played a role in altering the spectrum of cases included in this subgroup.

With the advent of non-invasive visualisation of the carotid vessels by Doppler angiography and by intravenous digitalised angiography, it will be possible to assess the severity of atheroma in a larger number of patients presenting with the early features of cerebrovascular disease. The prognostic significance of the present findings may therefore be of value in a wider spectrum of patients than those currently subjected to angiography.

Of patients with TIAs 22% had normal angiograms and no overt cardiac abnormality, a finding in keeping with that of de Bono and Warlow. The aetiology of such TIAs remains of great interest especially as this study suggests the prognosis may differ. These findings are therefore also relevant to the comparisons of outcome made in controlled trials of antithrombotic regimes in TIA patients. It may be necessary to analyse the results of such trials in a way that allows for differences according to the angiographic appearances.

Acknowledgement

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References

Prognostic significance of severity of carotid atheroma in early manifestations of cerebrovascular disease.
M J Harrison and J Marshall

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