Visual Disturbance and Carotid Artery Disease

500 Symptomatic Patients Studied by Non-Invasive Carotid Artery Testing Including B-Mode Ultrasonography

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SUMMARY Non-invasive carotid artery testing was performed on 500 consecutive patients with visual disturbances not related to local ophthalmic pathology to determine the extent of carotid artery disease, particularly in patients with symptoms not typical of amaurosis fugax. Three hundred eighty-six patients (77.2%) had an abnormal study. However, the incidence of hemodynamically significant lesions was only 16%. The patients could be divided into three groups: 1) Patients with symptoms that could be explained on an ocular basis, including amaurosis fugax, had a 79% incidence of ipsilateral carotid plaques. 2) Patients with symptoms which could not be easily explained on an ocular basis, such as bilateral blurred vision, bilateral visual loss (both transient and permanent), and homonymous hemianopsia had an incidence of carotid artery plaques similar to patients with amaurosis fugax. 3) Patients with unilateral blurred vision and bilateral scintillations had a lower incidence (57%) of carotid plaques than the other groups. Younger symptomatic patients had less carotid plaques than the overall series. Twenty-one percent of patients under age 50 had the Doppler finding of early systolic flutter turbulence, which is usually of mitral valve origin.

Women predominated in the under 50 age group by about 2:1. In view of the prevalence of carotid plaques in the population of patients with visual symptoms other than amaurosis fugax, evaluation of these patients with non-invasive testing is indicated to determine which of these patients has hemodynamically significant obstruction to flow at the carotid artery bifurcation.

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had symptoms as described in the bilateral group, above, but clearly unilateral. Gradual Visual Loss, Unilateral — These 39 patients had progressive, unilateral visual failure. Gradual Visual Loss, Bilateral — Ten patients had symptoms analogous to the unilateral group. Homonymous Hemianopia — 33 patients with transient or permanent bilateral homonymous visual field disturbance, hemianopic or quadrantic, excluding "positive" symptoms. Acute Permanent Visual Loss, Unilateral — These 22 patients noted an acute onset of visual loss similar to that described in the amaurosis fugax group, but with permanent residua. Transient Loss of Vision — These 18 patients had transient total visual loss or "blackouts of vision," often with an onset similar to that described in amaurosis fugax, but bilateral. Excluded were patients who reported faint or impending faint, or any other disturbance of consciousness. Ischemic Optic Neuropathy — These 15 patients were referred by an ophthalmologist who had noted bright plaques in the retinal arteries, ischemic optic atrophy, or ocular neovascularization on a suspected ischemic basis during ophthalmological examination. Permanent Visual Loss, Bilateral — These 2 patients had sudden onset of bilateral visual disturbance with residua. Two Visual Symptoms — Twenty-one patients had two of the above listed symptoms on different occasions, and have been included in both appropriate groups, giving a total of 521. No patient had more than two visual symptoms.

Non-Invasive Test Methodology

Ophthalmic artery pressure was measured by pneumo-oculoplethysmography (Life Sciences PVR), with a normal mean value taken to be 75% ± 5% SD of the brachial artery pressure. Supraorbital Doppler analysis was performed using a 9.0 MHz bidirectional Doppler (Parks 908), employing superficial temporal artery compression to determine the extent of collateral flow from the external to the internal carotid circulation. Carotid pulse wave form analysis was performed with the 9 mHz bidirectional Doppler device (Parks 908) and a 4 mHz Duplex Doppler (Sonomed). Patterns of turbulence were identified either aural-ly or by spectral analysis of Doppler frequencies. In combination, these three techniques (oculoplethysmography, supraorbital Doppler analysis and carotid Doppler flow studies) have shown a 95% correlation with angiographic demonstration of hemodynamically obstructive lesions.

To determine the presence of non-obstructive lesions at the carotid bifurcation, and to better define obstructive ones, real-time B-Mode ultrasonography was performed using a small-parts scanner at 7.5 MHz (High Stoy). This technique has been shown to demonstrate lesions not seen by angiography, when the lesion does not distort the origin of the internal or external carotid artery.

A hemodynamically significant lesion was diagnosed when an apparently obstructive plaque seen on B-Scan was associated with high frequency turbulence on Doppler flow analysis (with or without broadening of spectral frequencies) and either a reduction in ophthalmic artery pressure or a reversal of supraorbital Doppler flow ipsilaterally. High frequency turbulence indicates a narrowing of the lumen of the carotid artery severe enough to force a small stream of red blood cells through the lumen at a high velocity, resulting in a narrowed Doppler systolic wave form with a large proportion of high frequency signals. A non-obstructive lesion was diagnosed when a plaque was noted on B-scan in patients in whom normal ophthalmic artery pressure, normal supraorbital flow and normal carotid Doppler pulse wave form or low frequency turbulence were found.

Early Systolic Flutter Turbulence on direct carotid artery flow analysis was also noted in several patients. This finding is not related to pathology at the carotid bifurcation, and has been shown to correlate highly with dysfunction of the mitral valve. It is most commonly observed in patients with mitral valve prolapse (p < 0.001). A biphasic systole can be found in both mitral and aortic valve lesions, but we have noted the auscultative finding of Early Systolic Flutter Turbulence only with mitral valve lesions.

All patients were studied with the complete non-invasive test battery bilaterally, regardless of their symptoms. Statistical analysis employed the Chi-Square method.

Results

Overall Group

Table 1 lists the findings in the entire series of patients with respect to age and sex distribution. There were nearly twice as many women as men in the youngest age group, with 22 of 245 men (8.9%) and 41 of 255 women (16.5%) below age 50 (p < 0.02). Normal studies were found in 114 patients (22.8%), with a significantly higher (p < 0.01) percentage in the youngest age group.

Bilateral carotid disease was present in 293 patients (58.6%). Eighty patients (16%) had at least one hemodynamically significant lesion, with all but 6 of these occurring in patients with bilateral disease.

Early Systolic Flutter Turbulence (suggesting mitral valve disorders) occurred with approximately equal frequency among men and women, with 28 of the 31 patients (90%) being age 65 or younger. Women again dominated the youngest age group, with 10 of 41 women (24.4%) and 3 of 22 men (13.6%) below age 50 having Early Systolic Flutter Turbulence.

Table 2 correlates the symptoms of all the patients in the series with the extent of atherosclerotic plaque at the carotid artery bifurcation.

1) Amaurosis Fugax

One hundred seventy one patients complained of symptoms typical of amaurosis fugax. A carotid lesion ipsilateral to the affected eye was present in 35 (79%). This is similar to the incidence of 76% reported by Heyman et al. The lesion was hemodynamically significant in 37 (21.6%). There was a significantly
VISUAL DISTURBANCE AND CAROTID ARTERY DISEASE/Gaul et al

TABLE 1 Correlation of Age and Sex Distribution and Associated Conditions with Carotid Findings

<table>
<thead>
<tr>
<th>Age range</th>
<th>Total</th>
<th>Normal</th>
<th>Bilateral disease</th>
<th>Unilateral disease</th>
<th>Hemodynamic lesions</th>
<th>Diabetes</th>
<th>Hypertension</th>
<th>ESFT</th>
</tr>
</thead>
<tbody>
<tr>
<td>Males</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>50 yrs</td>
<td>22</td>
<td>14</td>
<td>7</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>3</td>
</tr>
<tr>
<td>50-65 yrs</td>
<td>102</td>
<td>30</td>
<td>48</td>
<td>24</td>
<td>12</td>
<td>10</td>
<td>15</td>
<td>10</td>
</tr>
<tr>
<td>65 yrs</td>
<td>121</td>
<td>9</td>
<td>84</td>
<td>28</td>
<td>29</td>
<td>13</td>
<td>10</td>
<td>2</td>
</tr>
<tr>
<td>All males</td>
<td>245</td>
<td>53</td>
<td>139</td>
<td>53</td>
<td>42</td>
<td>24</td>
<td>26</td>
<td>15</td>
</tr>
<tr>
<td>Females</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>50 yrs</td>
<td>41</td>
<td>29</td>
<td>6</td>
<td>6</td>
<td>1</td>
<td>1</td>
<td>5</td>
<td>10</td>
</tr>
<tr>
<td>50-65 yrs</td>
<td>82</td>
<td>20</td>
<td>51</td>
<td>11</td>
<td>12</td>
<td>8</td>
<td>11</td>
<td>5</td>
</tr>
<tr>
<td>65 yrs</td>
<td>132</td>
<td>12</td>
<td>97</td>
<td>23</td>
<td>25</td>
<td>7</td>
<td>20</td>
<td>1</td>
</tr>
<tr>
<td>All females</td>
<td>255</td>
<td>61</td>
<td>154</td>
<td>40</td>
<td>38</td>
<td>16</td>
<td>36</td>
<td>16</td>
</tr>
<tr>
<td>Total</td>
<td>500</td>
<td>144</td>
<td>293</td>
<td>93</td>
<td>80</td>
<td>40</td>
<td>62</td>
<td>31</td>
</tr>
</tbody>
</table>

The extent of unilateral and bilateral carotid artery disease is demonstrated for each age group in patients presenting with visual disturbances. The number of males and females in each group is indicated. The number of patients with associated conditions which can also be responsible for ischemic symptoms (diabetes, hypertension and mitral valve disease (ESFT) is shown.

Increased incidence of carotid lesions on the side of the symptoms as compared to a random distribution (p < 0.01). Among 23 patients with bilateral lesions in which only one was hemodynamically obstructive, 19 (83%) had the symptom on the side of the hemodynamic lesion (p < 0.02), indicating that a hemodynamic lesion is more likely to give rise to ischemic symptoms than a non-obstructive lesion in a given patient when all other factors are equal.

Fifteen of 16 patients (94%) with hypertension had an ipsilateral carotid lesion. Only seven of 12 diabetics (58%) had ipsilateral carotid disease and 5 (42%) had normal studies bilaterally. The diabetics with amaurosis fugax were younger than the rest of the group. Five patients had both hypertension and diabetes. The difference between hypertensives and diabetics was statistically significant (p < 0.05). This finding is similar to previous reports implicating local small arterial thrombosis as a greater source of ischemia in diabetics than carotid artery disease.20

TABLE 2 Correlation of Visual Symptoms with Carotid Disease

<table>
<thead>
<tr>
<th>Category</th>
<th>Total patients</th>
<th>Total ipsilateral lesions (%A)</th>
<th>Ipsilateral (B) hemodynamic lesion</th>
<th>Bilateral lesion</th>
</tr>
</thead>
<tbody>
<tr>
<td>1) Amaurosis fugax</td>
<td>171</td>
<td>78.9%</td>
<td>21.6%</td>
<td>64.3%</td>
</tr>
<tr>
<td>2a) Blurred vision bilateral</td>
<td>70</td>
<td>81.4% (A)</td>
<td>12.9%</td>
<td>62.9%</td>
</tr>
<tr>
<td>2b) Blurred vision unilateral</td>
<td>58</td>
<td>56.9%</td>
<td>3.4%</td>
<td>48.3%</td>
</tr>
<tr>
<td>3a) Positive symptoms bilateral</td>
<td>50</td>
<td>58.0% (A)</td>
<td>4.0% (B)</td>
<td>38.0%</td>
</tr>
<tr>
<td>3b) Positive symptoms unilateral</td>
<td>33</td>
<td>75.8%</td>
<td>0</td>
<td>72.7%</td>
</tr>
<tr>
<td>4a) Gradual visual loss unilateral</td>
<td>39</td>
<td>74.4%</td>
<td>10.3%</td>
<td>56.4%</td>
</tr>
<tr>
<td>5a) Permanent visual loss unilateral</td>
<td>22</td>
<td>95.5%</td>
<td>22.7%</td>
<td>77.3%</td>
</tr>
<tr>
<td>6) Homonymous hemianopia</td>
<td>33</td>
<td>63.6%</td>
<td>0</td>
<td>48.5%</td>
</tr>
<tr>
<td>7) Transient visual loss bilateral</td>
<td>158</td>
<td>77.8% (A)</td>
<td>16.7% (B)</td>
<td>61.1%</td>
</tr>
<tr>
<td>8) Ischemic retinopathy</td>
<td>15</td>
<td>66.7%</td>
<td>6.7%</td>
<td>60.0%</td>
</tr>
<tr>
<td>4b) Gradual visual loss bilateral</td>
<td>10</td>
<td>90.0% (A)</td>
<td>20.0% (B)</td>
<td>60.0%</td>
</tr>
<tr>
<td>5b) Permanent visual loss bilateral</td>
<td>2</td>
<td>100.0% (A)</td>
<td>0 (B)</td>
<td>100.0%</td>
</tr>
<tr>
<td>Two visual symptoms</td>
<td>21</td>
<td>81.0% (A)</td>
<td>14.3% (B)</td>
<td>57.1%</td>
</tr>
</tbody>
</table>

The category of visual symptoms is numbered corresponding to the text of the Result Section. The number of patients with each visual symptom is tabulated in the second column Total Patients. The third column (ipsilateral disease) indicates the percent of patients with a carotid lesion ipsilateral to the visual disturbance. The percentage of hemodynamically obstructive lesions is shown in the fourth column. The percentage of patients with bilateral carotid disease in each symptom group follows (bilateral disease). Twenty-one patients complained of more than one visual symptom.

A) When patients complained of bilateral symptoms, the percentage of patients with a carotid lesion on either side is shown in the ipsilateral lesion column.

B) When patients complained of bilateral symptoms, the percentage of patients with a hemodynamic lesion on either side is shown in the hemodynamic lesion column.
Four patients with amaurosis fugax had glaucoma and all 4 had bilateral nonobstructive plaques. One patient with associated temporal arteritis had a normal carotid study.

All 16 patients with signs or symptoms of transient or permanent cerebral ischemia from the hemisphere ipsilateral to the eye with amaurosis fugax had disease in the appropriate carotid distribution.

2) Non-Specific Blurred Vision
   a) Fifty-seven of 70 patients (81.4%) complaining of bilateral blurred vision had carotid lesions, and 44 (63%) had bilateral disease. Nine carotid lesions were hemodynamically significant. Ten patients with bilateral blurred vision had either hypertension, diabetes, or both. Five patients had glaucoma and two had temporal arteritis.
   b) Fifty-eight patients complained of unilateral blurred vision that was not clearly amaurosis fugax. Thirty-three (56.9%) had carotid lesions ipsilateral to the symptoms, of which only 2 were hemodynamically significant. Seven patients had diabetes or hypertension. Three patients had glaucoma. Patients with unilateral non-specific blurred vision had a lower incidence of ipsilateral carotid lesions than patients with typical amaurosis fugax ($p < 0.01$).

3) Positive Visual Symptoms
   a) Twenty-one of 50 patients (42%) complaining of bilateral positive visual symptoms had normal studies. There were only two hemodynamically significant lesions. Five of the 8 patients (62.5%) who reported scintillations in homonymous bilateral fields had normal carotid studies.
   b) Twenty-five of 33 (76%) of patients complaining of unilateral positive visual symptoms had carotid lesions ipsilateral to the symptom, similar to the incidence in patients with typical amaurosis fugax.

4) Gradual Visual Loss
   a) Twenty-nine of 39 patients (74%) complaining of gradual unilateral visual loss had ipsilateral carotid lesions of which 5 lesions were hemodynamic. There were 6 hypertensives and 7 diabetics.
   b) Ten patients complained of bilateral gradual visual loss. Only one had a normal carotid study. Six had bilateral disease. Two lesions were hemodynamically significant.

5) Acute Permanent Visual Loss
   a) Twenty-one of 22 patients (95.5%) complaining of acute permanent unilateral visual loss had ipsilateral carotid lesions. Five of these lesions (22.7%) were hemodynamic. This major symptom category had the highest percentage of carotid atheroma in the entire series of 500 patients. There were 2 diabetics and 6 hypertensives.
   b) Two patients had acute onset of bilateral visual loss. Both had bilateral nonobstructive carotid lesions.

6) Homonymous Hemianopia
   Twenty-one of 33 patients (64%) presenting with signs of homonymous hemianopia had carotid lesions ipsilateral to the appropriate cerebral hemisphere (contralateral to symptoms). None of these lesions were hemodynamically significant. Eleven of 17 patients (65%) with associated hemimotor/sensory syndromes ipsilateral to the homonymous field disturbance had a lesion in the appropriate carotid.

7) Transient Bilateral Loss of Vision
   Eighteen patients complained of bilateral simultaneous transient loss of vision. Four (22%) had normal carotid studies. Eleven (61%) had bilateral carotid lesions, of which three were hemodynamically significant.

8) Ischemic Optic Neuropathy
   Ten of 15 patients (67%) referred by an ophthalmologist with a diagnosis of ischemic retinopathy had ipsilateral carotid lesions. The subgroup of 7 patients without associated conditions related to cerebrovascular disease had a much lower percentage (2 of 7, 29%) of ipsilateral carotid lesions. Age does not appear to account for this difference, which is statistically significant ($p < 0.01$).

Early Systolic Flutter Turbulence
   Early systolic flutter turbulence occurred in 31 cases (6% of the entire series), consistent with a reported incidence of mitral valve prolapse in the general population of 5–6%, but was found in 21.6% of patients with visual disturbance below age 50. While 9 patients of the 171 with amaurosis fugax had early systolic flutter turbulence (5%), 8 of the 50 patients with positive bilateral symptoms had early systolic flutter turbulence (16%) ($p < 0.02$). Five of 58 patients (9%) with unilateral blurred vision had early systolic flutter turbulence. These latter five patients were all in the under 50 year age group, and all 5 had normal carotid studies.

Discussion
   There is a strikingly high incidence of carotid artery disease in this population of 500 patients with visual disturbance and no known ophthalmologic disorder to account for their symptoms. 386 patients (77.2%) had evidence of atherosclerotic plaque at the carotid bifurcation. This should be compared with the unselected autopsy series of Fisher et al. who reported an overall incidence of disease at the carotid bifurcation to be 39.3% in cases with an age range quite similar to this series (under 50 years, 12%; 59–69 years, 36%; over 70 years, 52%). Kollarits, et al. reviewed a series of 100 consecutive carotid arteriograms performed in hospital patients at least 60 years old and found an incidence of carotid atheromatous disease of only 24%. Embolism of atheroma from the carotid bifurca-
tion to the retinal circulation probably accounts for a large proportion of monocular visual symptoms, including amaurosis fugax, monocular scintillating scotomas and unilateral acute permanent visual loss. In Fisher’s series, only 17 patients (9.5%) with carotid lesions had evidence of cerebral infarction due to probable embolism in spite of the much greater prevalence of plaque. Amaurosis fugax was associated with hemispheric symptoms in 16 of 171 patients (9.4%) and all 16 had ipsilateral carotid disease. Transient ischemic attacks, particularly ocular, appear to be a much more frequent occurrence with carotid artery lesions than cerebral infarction. Pessin has suggested that an embolus of sufficient size to temporarily obstruct the central retinal artery may be too small to cause clinically evident cerebral dysfunction.

Several studies have indicated that hemodynamically significant carotid stenosis poses an increased risk for cerebral hemispheric symptoms and stroke. This is not the case for ocular stroke. In this series, 22 patients had permanent visual loss, while 171 patients had amaurosis fugax. Thus, 22 of 193 patients (11.4%) with a definite retinal ischemic event had an ocular stroke, similar to the incidence of 11.8% reported by Marshall and Meadows. Permanent visual loss occurred in 5 of 42 patients (11.9%) with an ocular ischemic event ipsilateral to a hemodynamic carotid lesion, the same percentage as patients with amaurosis fugax. There was an increased incidence of permanent visual loss in hypertensives (6/22, 27.2%) (p < 0.02), but not in diabetics.

In the younger age group 14 of 22 men (63.6%) and 29 of 41 women (70.7%) had normal carotid studies. In our series, early systolic flutter turbulence originating from the mitral valve was present in 21.6% of the patients with visual disturbance who were under age 50. The frequency was twice as high in women as in men (p < 0.01). There is a relationship between mitral valve prolapse and cerebral ischemia, particularly in younger patients and in those without other risk factors for stroke. This suggests that dysfunction at the mitral valve, with possible embolic phenomena, is related to the increased incidence of visual disturbances in these younger patients, particularly women.

Patients with unilateral positive symptomatology have an incidence of ipsilateral carotid disease almost exactly that of the amaurosis fugax group. Dyll et al have reported symptoms of “bright lights” preceding episodes of amaurosis fugax suggesting a common etiology for these symptoms.

The highest percentage of normal carotid studies and lowest incidence of bilateral carotid disease occurred in patients with bilateral positive symptoms (significant p < 0.01 compared to amaurosis fugax). Only 10 of the 50 patients in this group had headaches. Patients with the unclear clinical syndrome of migraine were probably less likely to be referred for their visual syndromes. The patients with bilateral positive symptoms had the highest incidence of early systolic flutter turbulence (16%), significantly (p < 0.02) more frequent than in the amaurosis fugax group (5%). The incidence of carotid disease and hemodynamic lesions in the group of patients with non-specific unilateral blurred vision was also lower than patients with amaurosis fugax (p < 0.01). Migraine may account for many of the symptoms in these patients.

Patients with bilateral blurred vision had an incidence of carotid artery disease much like the amaurosis fugax group, though they had significantly fewer hemodynamic lesions than patients with amaurosis fugax (p < 0.02). Troost has noted that “blurred vision” and “transient loss of vision” are frequently accompanied by complaints of dizziness and vertigo, and that they can occur in the situation of transient brainstem ischemia. Atherosclerotic disease in the carotid bifurcation may indicate there is disease in the vertebrobasilar system as well and reduced flow in the carotid circulation may also influence vertebrobasilar disease. This may account for the high incidence of carotid disease in patients whose visual symptoms cannot be easily explained on an ocular basis.

There are clinical differences between diabetics and hypertensives with visual complaints. The diabetics are younger, with 68% being under age 65, as compared to 45% in the hypertensives (p < 0.05). Diabetics also have a higher proportion of normal carotid studies, 33%, compared to 13% in hypertensives (p < 0.02). This may be accounted for by the age difference, but diabetics may be more prone to pathology other than carotid disease, such as small vessel disease, platelet dysfunction or biochemical abnormalities.

Since 114 patients (22.8%) in the series had completely normal non-invasive carotid studies, there remains a significant proportion of people whose visual disturbances are not due to disease at the carotid bifurcation, especially in the younger age groups. These patients probably have their symptoms on the basis of local vascular disease or emboli of cardiac origin. One case of amaurosis fugax with ophthalmic artery stenosis and a normal carotid bifurcation has been documented. Mitral valve prolapse may play a role, especially in younger patients.

There is a dramatic prevalence of carotid disease in the population of patients with visual complaints. It is not possible to predict, on the basis of clinical presentation, which patient with visual disturbance will have a hemodynamically significant carotid lesion, and thus a higher risk of stroke. However, the incidence of hemodynamic stenosis in these patients is only 16%. In view of the small but significant proportion of complications associated with carotid angiography, non-invasive carotid testing with B-mode imaging in conjunction with spectral analysis of the Doppler shift signal and ocular plethysmography provides an appropriate method for evaluating the carotid artery bifurcation in these patients.

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References


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