Color Doppler Imaging of Orbital Arteries for Detection of Carotid Occlusive Disease

Han-Hwa Hu, MD; Wen-Yung Sheng, MPH; May-Yung Yen, MD;
Shiau-Ting Lai, MD; Michael Mu-Huo Teng, MD

Background and Purpose: Distal to a hemodynamically significant stenosis, the Doppler effect becomes dampened. Thus, measuring the flow profile in the ophthalmic artery and the central retinal artery with color Doppler imaging may provide hemodynamic information about the carotid circulation.

Methods: To validate the flow profile measurement with color Doppler imaging in the ophthalmic and central retinal arteries and to determine the sensitivity and specificity of this examination in the detection of hemodynamically significant carotid stenosis, we compared color Doppler imaging examinations with ocular pneumoplethysmography and ophthalmodynamometry examinations in 66 patients with atherothrombotic ischemic cerebrovascular disease. The degree of carotid stenosis in these patients was determined by a duplex scan with color Doppler imaging, and 57 patients underwent angiography to verify the stenosis.

Results: The flow velocities (systolic peak velocity and end-diastolic velocity) and pulsatility indices (A/B ratio and resistance index) in the ophthalmic and central retinal arteries decreased as the degree of carotid stenosis increased. There is a statistically significant difference in the mean of systolic peak velocity and the mean of end-diastolic velocity of the ophthalmic and central retinal arteries among groups with various degrees of carotid stenosis (P<.02). Using the flow velocities of the ophthalmic and central retinal arteries to diagnose carotid stenosis (≥75% stenosis and occlusion), 8 cm/s for systolic peak velocity in the central retinal artery and 29 cm/s for systolic peak velocity plus flow direction reversal in the ophthalmic artery gave the maximum accuracy (sensitivities, 84% and 85.7% and specificities, 89.6% and 81.7%, respectively). The systolic peak velocity in the central retinal artery varied directly with the systolic pressure of the ophthalmic and central retinal arteries.

Conclusions: The flow velocity and pulsatility in orbital arteries examined by color Doppler imaging provide further hemodynamic information; this test can be used to complement current sonographic examination of carotid disease. (Stroke 1993;24:1196-1203)

KEY WORDS • carotid artery diseases • ophthalmic artery • retinal artery • ultrasonics

Extracranial occlusive disease of the internal carotid artery is an important cause of stroke and is amenable to surgical intervention.1,2 Cerebral angiography is the established method of visualizing the cervical carotid artery, yet under even the best conditions it carries a small but definite risk. The need to access the carotid circulationatraumatically and repeatedly has led to the development of noninvasive vascular methods that provide hemodynamic or morphological information about the extracranial circulation. Direct noninvasive tests such as ultrasonic diagnosis of carotid disease with duplex sonography have proved to be an accurate and effective means of detecting and assessing carotid disease,3,4 but there remains the difficulty of detecting lesions in high bifurcation,5 those in distal parts of internal carotid artery, and those at the petrous and cavernous portions of the internal carotid artery.6 Furthermore, calcified plaques in the artery prevent ultrasound penetration.7 Indirect noninvasive tests such as ocular pneumoplethysmography (OPG-Gee) and ophthalmodynamometry (ODM), because of their valuable principle of pressure measurement, are also currently widely used to evaluate the hemodynamic significance of a carotid artery lesion. The arterial pressure of the ophthalmic artery and the central retinal artery measured by OPG-Gee and ODM, respectively, reflects the distal internal carotid artery pressure8-11; measurement of a decreased pressure reflects a stenotic inflow artery, including the petrous and cavernous portions of the internal carotid artery. OPG-Gee and duplex scan examinations are considered complementary methods to increase the accuracy of diagnosis.12,13

Color-coded Doppler imaging (CDI) is a relatively new technique that displays both anatomic and velocity data on blood flow in a color-encoded, real-time format. It is a useful adjunct to conventional duplex sonography for carotid artery examination14,15 and has proved to be a simple, reproducible, and noninvasive method of detecting the flow profile in orbital arteries.16-18

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From the Departments of Neurology (H.-H.H., W.-Y.S.), Ophthalmology (M.-Y.Y.), Surgery (S.-T.L.), and Radiology (M.M.-H.T.), Taipei Veterans General Hospital, Yang-Ming Medical College, Taipei, Taiwan, Republic of China.

Correspondence to Han-Hwa Hu, MD, Department of Neurology, Taipei Veterans General Hospital, Taipei, Taiwan, 11217, Republic of China.
TABLE 1. Systolic Peak Velocities and End-Diastolic Velocities of Orbital Arteries With Varied Degrees of Carotid Stenosis

<table>
<thead>
<tr>
<th>Orbital artery</th>
<th>Degree of carotid stenosis</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>&lt;50% (n=84)</td>
</tr>
<tr>
<td>Central retinal artery</td>
<td></td>
</tr>
<tr>
<td>Peak systolic velocity</td>
<td>11.64±3.04</td>
</tr>
<tr>
<td>End-diastolic velocity</td>
<td>3.46±1.41</td>
</tr>
<tr>
<td>Short posterior ciliary artery</td>
<td></td>
</tr>
<tr>
<td>Peak systolic velocity</td>
<td>16.60±6.41</td>
</tr>
<tr>
<td>End-diastolic velocity</td>
<td>4.97±2.97</td>
</tr>
<tr>
<td>Ophthalmic artery</td>
<td></td>
</tr>
<tr>
<td>Peak systolic velocity</td>
<td>41.69±14.38</td>
</tr>
<tr>
<td>End-diastolic velocity</td>
<td>11.05±6.35</td>
</tr>
</tbody>
</table>

n, Number of cases. *n=16; †n=7; ‡cases with reverse flow were excluded, n=13.

Distal to a hemodynamically significant stenosis, the blood pressure is known to decrease and the Doppler effect becomes dampened, causing diminished flow velocity and decreased pulsatility.19 The objectives of our study were to validate in the ophthalmic and central retinal arteries flow profile measurements obtained by CDI by comparing them with the blood pressure measurements in these arteries obtained by OPG-Gee and ODM and to determine the sensitivity and specificity of this examination in the detection of hemodynamically significant carotid stenosis by measuring the flow velocities and pulsatility of these ocular arteries.

**Subjects and Methods**

Sixty-six patients (59 men and 7 women, 49 to 78 [mean, 63±12.1] years of age) with transient ischemic attack or minor stroke were included in this study. Thirty-nine patients (59.1%) had hypertension, 14 (21.2%) had heart disease (ie, myocardial infarction, angina, or cardiomegaly), 9 (13.6%) had diabetes, and 29 (43.9%) were smokers.

All 66 patients underwent extracranial carotid artery examination performed by duplex scan with CDI (5 MHz for Doppler and 7.5 MHz for B-scan imaging; HP SONOS 1000, Hewlett Packard, Calif). Fifty-seven patients also underwent carotid angiographic examination for comparison. To ensure uniform interpretation, all angiograms were reevaluated by a neuroradiologist who was unaware of the results of noninvasive studies. The methods of calculating the percentage of diameter reduction in angiograms20 and luminal area reduction for duplex scans5 have been reported elsewhere. In this study, we defined hemodynamically significant carotid disease as a greater than 50% reduction of the diameter of the carotid artery determined by angiography, which corresponds to an approximately 75% reduction in luminal area by sonography.5,21

After sonographic examination of the extracranial carotid artery, patients were scheduled to receive OPG-Gee, ODM, and CDI examinations of the eyes. These three tests were performed on the same day. The method of CDI examination for the eyes has been described elsewhere.16-18 All examinations were performed with the HP SONOS 1000 transducer used for direct sonography for the carotid artery. This system enabled detection of amplitude, phase, and frequency shift, resulting in a real-time gray scale/color-flow imaging. Color assignment depends on direction of flow and is selectable by the operator. Flow toward the transducer was selected as red and that away from the transducer as blue, resulting in normal antegrade arterial flow appearing red and normal venous flow appearing blue. The color saturation in the imaging represents the average frequency (first-moment average) from a spectral analysis performed at each sample site. These frequencies can be converted to velocities by solution of the Doppler equation for velocity.

TABLE 2. Pulsatility Indices of Orbital Arteries With Varied Degrees of Carotid Stenosis

<table>
<thead>
<tr>
<th>Orbital artery</th>
<th>Degree of carotid stenosis</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>&lt;50% (n=84)</td>
</tr>
<tr>
<td>Central retinal artery</td>
<td></td>
</tr>
<tr>
<td>A/B ratio</td>
<td>3.41±1.51</td>
</tr>
<tr>
<td>Resistance index</td>
<td>0.68±0.08</td>
</tr>
<tr>
<td>Short posterior ciliary artery</td>
<td>3.73±2.75</td>
</tr>
<tr>
<td>Resistance index</td>
<td>0.69±0.10</td>
</tr>
<tr>
<td>Ophthalmic artery</td>
<td></td>
</tr>
<tr>
<td>A/B ratio</td>
<td>4.09±1.29</td>
</tr>
<tr>
<td>Resistance index</td>
<td>0.74±0.09</td>
</tr>
</tbody>
</table>

n, Number of cases. A/B ratio=systolic velocity/diastolic velocity. Resistance index=(systolic−diastolic)/systolic.

*n=16; †n=7; ‡cases with reverse flow were excluded, n=13.
Fig 1. Panel A, Transverse (axial) scan through globe shows central retinal artery (arrow). B, Doppler spectrum within central retinal artery can be demonstrated. C, Transverse (axial) scan through globe shows short posterior ciliary artery (arrow). D, Doppler spectrum within short posterior ciliary artery can be demonstrated. E, Transverse (axial) scan through globe shows ophthalmic artery (arrow). F, Doppler spectrum within ophthalmic artery can be demonstrated. G indicates globe; LAT, lateral; and ON, optic nerve.
The patients were supine with both eyes closed during examination; coupling jelly was placed directly on the closed eyelids. The estimated in situ spatial peak temporal average intensity with a power setting of −10 dB was 6.4 mW/cm² in the color imaging mode and 8.5 to 39 mW/cm² during pulsed Doppler examination. The spatial peak temporal average intensity in the pulsed Doppler examination exceeded the limit of 17 mW/cm² suggested by current Food and Drug Administration guidelines for ophthalmic application but was lower than those given in the ultrasound safety guidelines of the American Institute for Ultrasound in Medicine.

Transverse (axial) scans through the eye and orbit were performed. Color-encoded central retinal artery blood flow was identified within the B-scan gray scale image of the optic nerve (Fig 1A), whereas short posterior ciliary artery flow was depicted just adjacent to the optic nerve within the retrobulbar space (Fig 1C). The ophthalmic artery was typically identified as a larger-caliber, pulsatile vessel adjacent to the optic nerve (Fig 1E). Doppler frequency shifts within the ophthalmic artery, central retinal artery, and short posterior ciliary artery were measured to determine the systolic peak velocity and end-diastolic velocity (Fig 1B, 1D, and 1F) and then to calculate the pulsatility indices, such as the A/B ratio and resistance index.

Velocity measurements are dependent on and vary with the angle of Doppler insonation. We determined these angles by aligning the angle cursor with color pixels that identified blood flow within the particular vessel.

ODM was performed in the manner described by Hollenhorst,10,11 Both systolic and diastolic retinal artery pressure were obtained using the Bailliart ophthalmodynamometer. No patient had glaucoma. Examinations were performed by a neuro-ophthalmologist, using the following criteria for abnormality: (1) an asymmetry of at least 15% in systolic pressure, (2) an asymmetry of at least 50% in diastolic pressure, and (3) an absolute systolic pressure ≤ 40 mm Hg or an absolute diastolic pressure ≤ 10 mm Hg. OPG-Gee was performed with the Gee ocular pneumoplethysmography four-channel instrument according to the technique previously described by Gee.24 Criteria for abnormality were (1) an asymmetry of ≥ 5 mm Hg in the ophthalmic systolic pressure or (2) a ratio of ophthalmic systolic pressure to brachial systolic pressure falling below a regression line developed by Gee et al.24

For tests of statistical significance, analysis of variance was used for four group comparisons. Doppler values are reported as mean±SD. The kappa statistic was used to measure the agreement between two kinds of diagnostic methods: κ=1.0 indicates perfect agree-

**Table 3. Validity of Each Indirect Noninvasive Test in Diagnosis of Hemodynamically Significant Carotid Stenosis**

<table>
<thead>
<tr>
<th>Diagnostic method</th>
<th>Sensitivity</th>
<th>Specificity</th>
<th>Accuracy</th>
<th>Predictive values</th>
<th>Likelihood ratio</th>
<th>Likelihood ratio</th>
<th>k</th>
</tr>
</thead>
<tbody>
<tr>
<td>OPG</td>
<td>55.5</td>
<td>94.8</td>
<td>88.6</td>
<td>66.7</td>
<td>91.9</td>
<td>10.7</td>
<td>0.52</td>
</tr>
<tr>
<td>ODM</td>
<td>75.0</td>
<td>75.0</td>
<td>75.0</td>
<td>50.0</td>
<td>90.0</td>
<td>3.0</td>
<td>0.43</td>
</tr>
<tr>
<td>CRA ≤8</td>
<td>84.0</td>
<td>89.6</td>
<td>88.5</td>
<td>65.6</td>
<td>96.0</td>
<td>8.1</td>
<td>0.66</td>
</tr>
<tr>
<td>OA ≤29 or flow reversal</td>
<td>85.7</td>
<td>80.9</td>
<td>81.7</td>
<td>47.4</td>
<td>96.9</td>
<td>4.5</td>
<td>0.51</td>
</tr>
</tbody>
</table>

*Hemodynamically significant carotid stenosis is defined as a >75% reduction in luminal area and occlusion. OPG indicates ocular pneumoplethysmography; ODM, ophthalmodynamometry; CRA, central retinal artery; and OA, ophthalmic artery.*
Results

All 66 patients underwent duplex scan with CDI examinations of the neck carotid artery, and 57 also underwent carotid angiographic examination for comparison (intra-arterial digital subtraction angiography [DSA] in 42 and conventional angiography in 15). The agreement between the findings of angiography and sonography regarding the degree of carotid stenosis at bifurcation was excellent (κ = 0.91), and the overall accuracy of sonography in the diagnosis of carotid stenosis was 96% in this study. The degree of carotid stenosis at bifurcation was classified as <50% stenosis (84 arteries), 50% to 74% stenosis (23 arteries), 75% to 99% stenosis (17 arteries), and total occlusion (8 arteries).

All 66 patients completed the CDI examination of the orbital arteries. The velocities of the ophthalmic artery and the central retinal artery were all detected successfully, but we failed to detect short posterior ciliary artery velocities in 2 subjects; OPG-Gee results could not be obtained from 3 patients because of intolerance of the ocular cups. The ODM test failed in 13 patients chiefly due to intolerance of the procedure and difficulty in identifying the retinal artery in the case of cataract. Thus, only 53 patients underwent successful ODM examination. The flow velocities (systolic peak velocity and end-diastolic velocity) of the orbital arteries are shown in Table 1; both the systolic peak velocity and end-diastolic velocity in the orbital arteries decreased as the degree of carotid stenosis increased. There is a statistically significant difference in the mean of systolic peak velocity and the mean of end-diastolic velocity of the ophthalmic and central retinal arteries among groups with varied degrees of carotid stenosis. This difference remained significant after adjustment for hypertension and diabetes. The pulsatility indices (A/B ratio and resistance index) of the orbital arteries appear in Table 2; both the pulsatility indices decreased as the degree of carotid stenosis became more severe. Using the flow velocities of the ophthalmic artery and the central retinal artery for the diagnosis of hemodynamically significant carotid stenosis (≥75% stenosis and occlusion), the sensitivities and specificities altered as the diagnostic cutoff threshold values of velocity were varied. The diagnostic accuracy of the flow velocity measurement was determined from receiver operating characteristic curves (plots of the various sensitivities and specificities that alter as the diagnostic cutoff threshold of the measurement is varied). As illustrated in Figs 2 and 3, when the systolic peak velocity threshold level increased, the sensitivity (i.e., the ability to detect carotid stenosis when it was present) increased but the specificity (i.e., the ability to identify correctly the disease of carotid stenosis) decreased. From the receiver operating characteristic curves, 8 cm/s for systolic peak velocity in the central retinal artery and 29 cm/s for systolic peak velocity in the ophthalmic artery gave the maximum accuracy; the sensitivities were 84% and 85.7% and the specificities 89.6% and 81.7%, respectively.

Table 3 shows the diagnostic accuracy of each indirect noninvasive test in the diagnosis of carotid artery disease. The overall accuracy is similar but slightly superior for OPG and the systolic peak velocity in the central retinal artery. The agreement between the direct sonographic diagnosis of carotid disease and each indirect method is moderately good; it is best for the peak systolic velocity in the central retinal artery (κ = 0.66, Table 3).

The systolic peak velocities in the central retinal artery varied directly with ophthalmic systolic pressure (r = .33, P = .0002) and systolic pressure of the central retinal artery (r = .42, P = .001), but there was no linear relationship between the systolic peak velocities in the ophthalmic artery and systolic pressure in the ophthalmic artery and the central retinal artery.

Discussion

Our results confirmed the assumptions that there is a dampening of the Doppler effect following a severe arterial inflow stenosis, lower flow velocities, and lower pulsatility in the central retinal artery (Tables 1 and 2). The systolic peak velocities in the central retinal artery varied directly with systolic pressure of the ophthalmic artery and the central retinal artery, but these Doppler effects in the ophthalmic artery were not observed consistently. Lower flow velocities in the central retinal artery were also reported by Ho et al17 in patients with severe internal carotid artery stenosis or occlusion with ocular ischemic syndrome, but the pulsatility values increased compared with those in the control group; in our present study the pulsatility values decreased. No patient in our group had ocular ischemic syndrome, and the distinction of findings of pulsatility in the central retinal artery between patients in our group (without the syndrome) and the group of Ho et al (with the syndrome) may provide some clue to understanding its pathophysiology and perhaps forming the basis for rational treatment.

The accuracy, sensitivity, and specificity in the present study in detecting severe carotid disease for OPG-Gee and ODM were similar to those reported elsewhere.25-27 The flow velocities of the ophthalmic, central retinal, and short posterior ciliary arteries detected in the groups with nonstenotic carotid arteries were similar to those in the normal control subjects reported elsewhere.16,17 The present study also indicates that measuring the blood flow velocities in the ophthalmic and central retinal arteries and determining the flow direction in the ophthalmic artery were valid means of identifying patients with carotid stenosis. The accuracy of CDI in the diagnosis of hemodynamically significant carotid stenosis with these measurements is comparable to, if not better than, that of OPG-Gee and ODM.

The ophthalmic artery, with its branches, is an accessible brain artery that also reflects hemodynamic alterations due to cerebrovascular disease.28,29 Reversal of the flow direction of the ophthalmic artery indicates that it plays the role of a collateral circuit from external to intracerebral circulation; it has been suggested that ophthalmic collateral is likely to be indicative of the inadequacy of collateral circulation through the circle of Willis and a poor prognosis.29-31 In addition, the ophthalmic collateral may serve as a channel for embolization from the stump of the internal carotid artery32 or from the external carotid artery and the common carotid artery.33 Thus, delineating the direction of flow in
the ophthalmic artery is important in the assessment of patients with cerebrovascular disease and may enhance our understanding of the pathogenesis of stroke in some cases.

Many false-negative results were reported in all indirect noninvasive studies for assessing hemodynamically significant stenosis of the internal carotid artery.\textsuperscript{10,27} In the present study, there were also four false-negative results in using the criteria of systolic peak velocity in the central retinal artery and three false-negative by the criteria of the velocity in the ophthalmic artery. Because the variation of the flow velocities in the ophthalmic artery was prominent, the accuracy of diagnosis was relatively less. Thus, we were most concerned with the false-positive results in central retinal artery examinations, and there were 11 such results. When checking the angiographic findings (two of the patients underwent conventional carotid angiography and five intra-arterial DSA), two subjects had siphon stenoses proximal to the origin of the ophthalmic artery (confirmed in one by conventional angiography and in the other by intra-arterial DSA); in four others, the findings failed to delineate the distal internal carotid artery and siphon due to the quality of the DSA; and one patient had a very tortuous common carotid artery. All of these conditions may influence the hemodynamics in the orbital arteries and account for the false-positive results.

Although direct carotid sonographic examination with duplex is accurate in the diagnosis of carotid stenosis at the bifurcation, additional CDI testing may provide further information on the hemodynamics of the internal carotid artery and orbital arteries, including (1) the velocities and pulsatility indices of the orbital arteries, which may reflect the hemodynamics of proximal carotid stenosis as well as the distal resistance of the orbital arteries; (2) the flow direction of ophthalmic artery (reversal of flow direction is likely to be indicative of inadequacy of collateral circulation and a poor prognosis); and (3) the possibility of a hemodynamically significant lesion distal to the bifurcation of the carotid artery. In two patients with siphon stenosis the CDI examination was abnormal, but only a small, nonstenotic lesion was detected by conventional duplex scan. This additional hemodynamic information may be helpful in the selection of patients for endarterectomy or extracranial-intracranial bypass in the treatment of ocular ischemic syndrome.\textsuperscript{34,35}

Examination of the orbital arteries with CDI is a technically simple, reproducible, noninvasive method. We completed examinations of the ophthalmic, central retinal, and short posterior ciliary arteries and the central retinal vein within 10 minutes for one eye. If the purpose of the examination is to study the hemodynamics of carotid artery disease, from our experience less than 5 minutes is required to learn the flow direction of the ophthalmic artery and the flow velocities in the ophthalmic and central retinal arteries of one eye. The possibilities for CDI in future research include the differential diagnosis of amaurosis fugax, central retinal artery or central vein occlusive disease, anterior ischemic optic neuropathy, carotid-cavernous fistula, and occlusion of the superior ophthalmic vein and evaluation of the influences of systemic diseases such as diabetes, hypertension, and arteritis.

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