Limitations of Quantitative Oculoplethysmography and of Directional Doppler Ultrasonography in Cerebrovascular Diagnosis: Assessment of an Air-Filled OPG System

MYRON D. GINSBERG, M.D., STEVEN A. GREENWOOD, AND HERBERT I. GOLDBERG, M.D.

SUMMARY 500 consecutive patients were evaluated for extracranial disease of the internal carotid arteries by an automated, air-filled, digital oculoplethysmographic system (OPG) of the Kartchner type (Zira) and by supraorbital (SO) and supratrochlear (ST) directional Doppler ultrasonography. Cerebral arteriograms were performed in 58 patients (110 vessels), and OPG timing criteria for detecting hemodynamically significant carotid artery stenosis (60% or greater diameter reduction) were ascertained. Optimal criteria were a delay of one ocular pulse, relative to the other, of greater than 12 msec; and a delay of an ocular pulse, relative to the earlier ear (external carotid) pulse, of greater than 36 msec. These criteria correctly identified 73% of vessels with 0 to 59% stenosis and 76% of vessels with 60 to 100% stenosis. However, in 26% of the vessels, OPG was either inconclusive or inaccurate. Correct diagnosis of bilateral hemodynamically significant carotid artery stenoses was made by OPG in 6 of 9 affected patients. SO Doppler was normal in 70% of vessels with 0-59% stenosis, and abnormal in 75% of vessels with 60-100% stenosis. Corresponding percentages for ST Doppler were 95% and 44%. Abnormal Doppler responses to compression of contralateral facial branches were predictive of intracranial cross-collateralization in only 25% of patients. These results suggest that both quantitative OPG in its present form and directional Doppler studies have serious limitations as non-invasive diagnostic methods.

OCULOPLETHYSMOGRAPHY (OPG) and directional Doppler ultrasonography are useful techniques in the diagnosis of hemodynamically significant stenosis of the extracranial portion of the internal carotid arteries (ICA).1-12 In a previous study which examined the diagnostic effectiveness of OPG and directional Doppler, we made use of an analog OPG device with fluid-filled eye cups.2 The detection of pulse delays by that system required the operator to inspect waveform tracings visually and analyze the relative position and deflection of a derived, superimposed "differential" waveform. These procedures were not amenable to quantitation, and differences of interpretation among observers were possible. In cases of bilateral hemodynamically significant ICA stenosis, reliable detection of both stenoses required the recognition of delays between an ear pulse and each of the ocular pulses. With the analog system, this could not always be accurately accomplished.

For these reasons, we have assessed the diagnostic capabilities of a quantitative OPG system having air-filled cups, which employs digital microprocessor circuitry and yields direct digital data concerning the presence or absence of pulse delays, obviating the need for interpretation of waveform tracings. It was anticipated that this instrument might provide more accurate diagnosis of extracranial ICA stenoses, particularly in cases of bilateral disease. The present study assesses the strengths and limitations of quantitative OPG and compares it with directional Doppler ultrasonography of periorbital vessels and with carotid phonoangiography.

Methods

The test battery included 1) oculoplethysmography (OPG); 2) directional Doppler ultrasonography; and 3) carotid phonoangiography (CPA).

In performing OPG, an automated, digital, air-filled system was employed (Zira International, Inc., Model OPG 100-A, Tucson, AZ). The corneas were first anesthetized topically with proparacaine hydrochloride, 0.5%. Transparent air-filled cups were held against the cornea of each eye by a slight suction. Light opacity sensors were placed on both earlobes for recording external carotid artery (ECA) pulses. Pulse data were registered on 3 channels of the instrument. One channel displayed the elapsed time between the rising portion of the pulsatile waveforms from the right and left eye; a second channel indicated delays of one ear pulse relative to the other. An additional light-emitting diode indicated for each of these channels whether the delayed pulse was the left or the right. The third channel displayed the duration of the delay between the earlier ear pulse and the earlier ocular
pulse and indicated which of the 2 occurred later. All data were displayed in milliseconds of elapsed time. Eight successive noise-free pulses were automatically averaged, and the average value held in the display for transcription. A minimum of 6 cycles of 8 such pulses were recorded for each patient, of which 3 were obtained with the left and right eye cups and the left and right ear sensors reversed, in order to detect sources of technical artifact. In addition to the digital data, an analog tracing of both eye pulses, one ear pulse, and a differential signal (equivalent to twice the difference in amplitude between the 2 eye pulses) was made and preserved in the chart record but was not analyzed further in the present study.

In directional Doppler ultrasonography, use was made of a Parks Model 806C instrument (Parks Electronics, Beaveron, OR). The direction of resting flow was first determined in the supratrochlear (ST) and supraorbital (SO) arteries. Next, a series of ipsilateral and contralateral external carotid artery branch compression maneuvers was performed, according to the schema of Ackerman (unpublished), while recording from the ST and SO arteries. These compression maneuvers are outlined in our earlier publication. An abnormal directional Doppler examination consisted of a reversal of resting flow and/or an abnormal response to external carotid artery branch compressions.

Carotid phonoangiography (CPA) consisted of the recording of bruits from 3 sites overlying each carotid artery. The tracings were displayed on an oscilloscope and permanently recorded on Polaroid film. The amplitude of bruits was estimated semi-quantitatively as small, moderate, and large, as described previously. For the last 200 examinations of this series, the CPA device (Medical Electronic Devices, Tucson, AZ) was modified by the addition of a commercial audioequalizer (Shure Model SR 107), which provided a 15 dB boost in the 63-500 Hz range and 15 dB of attenuation at frequencies of 2000 Hz and above.

Patients. The patient population consisted of 500 consecutive patients studied in the Neurovascular Laboratory of the Hospital of the University of Pennsylvania. Out-patients and in-patients were equally represented. Indications for study included transient ischemic attack, completed stroke, asymptomatic carotid bruits, anticipated or completed carotid endarterectomy, and various neurological symptoms such as syncope and dizziness. Cerebral arteriograms were performed in 58 of these patients. The study consisted most commonly of selective catheterization of one or both common carotid arteries; less often, a single- or double-view aortic arch injection was performed. One hundred ten vessels were satisfactorily visualized. Arteriograms were reviewed by one of us (H.I.G.) without knowing the results of the non-invasive studies; the percentage of stenosis was calculated as the ratio of the smallest diameter of the stenotic segment divided by the diameter of the normal vessel distal to the stenosis.

### Results

Carotid Phonoangiography. Carotid artery bruits were not a reliable indicator of ICA or common carotid artery (CCA) stenosis as determined on cerebral arteriograms (table 1). Bruits were recorded from vessels both with and without hemodynamically significant degrees of stenosis. Bruits of moderate or large amplitude were heard even over two occluded ICA's, presumably owing to an associated ECA stenosis of 77% in one case and a 44% CCA stenosis in the other.

Oculoplethysmography

Eye-to-Eye Interval. Accepting diameter narrowing of 60% or greater as signifying a hemodynamically significant degree of stenosis, we analyzed the extent to which the duration of delay of one ocular pulse relative to the other (the "eye-to-eye delay") correlated with stenosis of this degree. Various timing criteria were assessed (table 2). An eye-to-eye delay of 12 msec or less was recorded in 27 of 31 patients (87%) with 0-59% stenosis; and delays greater than 12 msec were seen in 15 of 23 patients (65%) with stenosis of 60-100%. Only one patient, in whom one eye was absent, could not be assessed. The overall diagnostic accuracy of the 12 msec criterion for eye-to-eye delay was 76%. As table 2 indicates, 90% of vessels with 60% stenosis or greater had eye-to-eye delays exceeding 4 msec; but the use of this criterion would have led to a false-positive diagnosis in 55% of vessels with less than 60% stenosis (table 2).

It is possible that false-negative results with the eye-

### Table 1. Correlation of Carotid Bruits by Phonoangiography and Stenosis by Arteriography

<table>
<thead>
<tr>
<th>Percent Stenosis of Internal or Common Carotid Artery by Arteriography</th>
<th>Bruits by Phonoangiography</th>
</tr>
</thead>
<tbody>
<tr>
<td>0%</td>
<td>33 (89%)</td>
</tr>
<tr>
<td>1–59%</td>
<td>25 (63%)</td>
</tr>
<tr>
<td>60–99%</td>
<td>4 (17%)</td>
</tr>
<tr>
<td>100%</td>
<td>4 (50%)</td>
</tr>
</tbody>
</table>

### Table 2. Effectiveness of Alternative Ocular-Pulse-to-Ocular-Pulse Interval Criteria in Predicting Hemodynamically Significant* Carotid Artery Stenosis

<table>
<thead>
<tr>
<th>Ocular-Pulse-to-Ocular-Pulse Interval</th>
<th>TN+</th>
<th>TP</th>
<th>FP</th>
<th>FN</th>
<th>Inconclusive</th>
<th>Accuracy</th>
</tr>
</thead>
<tbody>
<tr>
<td>&gt; 4 msec</td>
<td>14</td>
<td>21</td>
<td>17</td>
<td>2</td>
<td>1</td>
<td>64%</td>
</tr>
<tr>
<td>&gt; 10 msec</td>
<td>25</td>
<td>16</td>
<td>6</td>
<td>7</td>
<td>1</td>
<td>75%</td>
</tr>
<tr>
<td>&gt; 12 msec</td>
<td>27</td>
<td>15</td>
<td>4</td>
<td>8</td>
<td>1</td>
<td>76%</td>
</tr>
<tr>
<td>&gt; 14 msec</td>
<td>28</td>
<td>14</td>
<td>3</td>
<td>9</td>
<td>1</td>
<td>76%</td>
</tr>
</tbody>
</table>

* Diameter narrowing of 60% or greater.
† TN = true negatives; TP = true positives; FP = false positives; FN = false negatives.
‡ Patient with absent right eye.

Accuracy = (TN + TP + FP + FN + Inconclusive Cases) / (TN + TP + FP + FN)
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Earlier-Ear-to-Eye Interval. The interval between the earlier ear pulse and the earlier of the 2 ocular pulses could be read directly from the OPG instrument. The earlier-ear-to-eye interval for the eye with the later-arriving ocular pulse was calculated simply as the sum of the eye-to-eye delay (read from instrument channel 2) and the earlier-ear-to-earlier-eye delay (read from instrument channel 3). Earlier-ear-to-eye intervals are correlated with ipsilateral stenosis in figure 1 for the 77 instances for which interpretable ocular pulse data were present. In the remaining 33 vessels, ipsilateral earlier-ear-to-eye intervals could not be interpreted, either because of inconsistency of readings or because the earlier ear pulse was delayed with respect to the earlier ocular pulse. Figure 1 shows the tendency of the earlier-ear-to-eye interval to increase with increasing degree of vascular stenosis. Table 3 presents the diagnostic validity of various interval criteria. An earlier-ear-to-eye interval of greater than 36 msec was optimal in detecting stenosis of 60% or greater, yielding an overall diagnostic accuracy of 55%.

Combined Criteria. We next examined the ability of the 2 criteria employed in combination (an eye-to-eye delay of greater than 12 msec, or an earlier-ear-to-eye delay of greater than 36 msec, or both) to diagnose hemodynamically significant stenosis. The results are shown in table 4. The OPG information from 13 vessels was inconclusive owing to ambiguous earlier-ear-to-earlier-eye intervals in 12 cases and an absent eye in one case. The overall diagnostic accuracy of the OPG criteria in combination was 74%.

Of the 9 false-positive studies obtained with the combined OPG criteria, 5 represented vessels with 44–53% stenosis; in 2 of these patients and one additional patient, tandem ICA-ICA or ICA-CCA stenoses were present. One false-positive result was accounted for by a hypoplastic ophthalmic artery fed by ECA branches. Five of the 7 false-negative results with the combined OPG criteria were in patients having contralateral ICA or CCA stenoses of 47% or greater.

Among the 9 patients studied by OPG in whom bilateral extracranial stenoses were present (defined as an ICA or CCA stenosis of at least 60% on one side and at least 50% on the other), the use of the combined OPG criteria presented above led to the accurate detection of bilateral disease in 6 cases. In another 6 patients having at least 60% ICA or CCA stenosis on one side but only 40–49% stenosis contralaterally, none showed OPG abnormalities on the less stenotic side.

Ear-to-Ear Interval. The OPG instrument yielded consistent data on the interval between the two ear pulses.

### Table 3. Effectiveness of Alternative Earlier-Ear-Pulse-to-Ocular-Pulse Interval Criteria in Predicting Hemodynamically Significant Carotid Artery Stenosis

<table>
<thead>
<tr>
<th>Earlier-Ear-to-Eye Criterion</th>
<th>TN*</th>
<th>TP*</th>
<th>FP*</th>
<th>FN*</th>
<th>Inconclusive*</th>
<th>Accuracy*</th>
</tr>
</thead>
<tbody>
<tr>
<td>&gt;30 msec</td>
<td>34</td>
<td>21</td>
<td>16</td>
<td>6</td>
<td>33</td>
<td>50%</td>
</tr>
<tr>
<td>&gt;36 msec</td>
<td>42</td>
<td>18</td>
<td>8</td>
<td>9</td>
<td>33</td>
<td>55%</td>
</tr>
<tr>
<td>&gt;40 msec</td>
<td>43</td>
<td>16</td>
<td>7</td>
<td>11</td>
<td>33</td>
<td>54%</td>
</tr>
</tbody>
</table>

*See table 2 for definitions.

*Inconsistent value*, or delay of earlier ear pulse with respect to earlier ocular pulse. One patient with absent eye.

### Table 4. Combined OPG Criteria in Predicting Hemodynamically Significant Carotid Artery Stenosis

<table>
<thead>
<tr>
<th>Percent Stenosis</th>
<th>Criteria Negative</th>
<th>Positive</th>
<th>Inconclusive</th>
</tr>
</thead>
<tbody>
<tr>
<td>0 — 59%</td>
<td>56 (73%)</td>
<td>9 (12%)</td>
<td>12 (16%)</td>
</tr>
<tr>
<td>60 — 100%</td>
<td>7 (21%)</td>
<td>25 (76%)</td>
<td>1 (3%)</td>
</tr>
</tbody>
</table>

*Eye-to-eye delay > 12 msec and/or earlier-ear-to-eye delay > 36 msec.
*Diameter narrowing of 60% or greater.

*See text.
pulses in only 28 of the 58 patients (48%). In 8 of these patients, an ear-to-ear delay of greater than 30 msec was observed. This delay corresponded to an ECA stenosis of 63–100% in 4 instances and to a CCA occlusion in one case. The remaining 3 patients with greater than 30 msec delay had non-stenotic ECAs and CCAs. Conversely, another 4 patients had ear-to-ear delays of less than 25 msec despite 71–100% stenotic lesions of the ECA or CCA. Thus, the correspondence between ear-to-ear delay and ECA stenosis was, at best, minimal.

Doppler Studies

Table 5 presents the ability of SO and ST Doppler to diagnose ipsilateral ICA or CCA stenosis of 60% or greater. False-positive results were obtained in 30% of SO studies but in only 5% of ST studies. Of the 23 false-positive SO studies, 8 corresponded to non-stenotic vessels; 12 to vessels with 17–48% stenosis; and only 3 to vessels with 50–60% stenosis. In 3 of the 4 false-positive ST studies, the SO examination was also abnormal.

In 5 of the 8 false-negative SO studies, there was an ipsilateral ECA stenosis of 53–70%, which may have accounted for the failure to observe SO flow reversal. Similarly, ECA stenosis exceeding 50% was observed in 39% of the false-negative ST Doppler studies. Figure 2 shows the arteriographic findings in a patient with false-negative Doppler studies.

In analyzing the Doppler results of this series, we assessed the diagnostic value of abnormal SO and ST Doppler responses to compression of contralateral external carotid artery branches on the face. Nine patients of our series exhibited diminution or reversal of SO or ST flow in response to contralateral ECA branch compression maneuvers. In 8 of these cases, an ICA or CCA stenosis exceeding 60% was present ipsilateral to the side of the Doppler examination. However, if contralateral compression maneuvers had been omitted, a reversal of resting SO or ST flow and an abnormal response to ipsilateral ECA branch compressions would have still permitted at least 7 of these stenoses to be accurately diagnosed. It is of note that, of the 9 patients with abnormal Doppler responses to contralateral ECA branch compressions, cerebral arteriograms showed evidence of interhemispheric cross-collateralization in only 2 patients. Conversely, 9 patients of the entire series exhibited arteriographic evidence of interhemispheric collateralization; but only 2 of these also had abnormal Doppler responses to contralateral ECA branch compressions. In each of these two patients, the lesion was a complete occlusion of the common carotid artery. Thus, our data suggest that performing contralateral ECA branch compressions as part of the Doppler examination does not appreciably enhance its diagnostic accuracy and cannot be used reliably to predict intracranial cross-collateralization.

Discussion

Quantitative OPG offers 2 numerical means of assessing carotid artery stenosis. The first is the interval between the arrival times of the 2 ocular pulses. In individual patients of this series, the eye-to-eye pulse interval was consistent and reproducible on successive runs. However, it was only rarely equal exactly to zero (5 of the 58 patients studied); thus, this interval was used only to draw inferences concerning the carotid system ipsilateral to the delayed eye pulse. In order to obtain a reference point by which both ocular pulses could be assessed, we made use of a second criterion, the interval from the earlier-arriving ear pulse to each ocular pulse (table 3). The data obtained, however, indicate that the ear pulse is an inadequate reference point. In a high percentage of instances, there was marked inconsistency among successive runs in the same patient, or else the earlier ocular pulse appeared paradoxically to precede the earlier ear pulse. Furthermore, the present study confirmed our earlier observation that a unilateral ear pulse delay is invalid as a criterion of external carotid artery stenosis, as had been suggested by Kartchner and colleagues (T.M.C. Ocular Pulse Manual, unpublished). Consistent ear-to-eye pulse interval data were registered in fewer than one-half of our patients, and an excessive incidence of false-positive and false-negative results was obtained. These observations strongly suggest that the ear pulse is untrustworthy as an external carotid reference pulse and should be replaced in future versions of OPG by a more consistent reference from which individual ocular pulse arrival times can be measured. An electrocardiographic reference point might be suitable for this purpose.

In the present study, the optimal criteria for detecting hemodynamically significant carotid artery stenosis by quantitative OPG were found to be an eye-to-eye pulse delay exceeding 12 msec and an earlier-ear-to-eye pulse delay exceeding 36 msec. An abnormal study was defined as one in which one or both of these diagnostic criteria were satisfied (table 4). Of the studies which yielded conclusive data, the OPG was normal in 86% of vessels with 0–59% stenosis and abnormal in 78% of vessels with stenosis of 60% or greater. The overall diagnostic accuracy in these patients was 84% — comparable to the accuracy reported by Kartchner and co-workers, and by others. Unfortunately, despite the fact that patients tolerated the air-filled ocular cups of this study better than the fluid-filled system used previously, the inconclusive data obtained with the digital instrument thwarted diagnosis in fully 12% of arteriographically visualized vessels in this study (table 4). If these inconclusive studies are taken into account, the overall accuracy of OPG obtained with the combined criteria

**Table 5. SO and ST Doppler in Predicting Hemodynamically Significant* Carotid Artery Stenosis**

<table>
<thead>
<tr>
<th></th>
<th>TN*</th>
<th>TP*</th>
<th>FP*</th>
<th>FN*</th>
<th>Accuracy*</th>
</tr>
</thead>
<tbody>
<tr>
<td>SO Doppler</td>
<td>54</td>
<td>24</td>
<td>23</td>
<td>8</td>
<td>72%</td>
</tr>
<tr>
<td>ST Doppler</td>
<td>74</td>
<td>14</td>
<td>4</td>
<td>18</td>
<td>80%</td>
</tr>
</tbody>
</table>

*See table 2 for definitions*
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FIGURE 2. Right carotid arteriogram of patient having a 14.3 msec delay of the right ocular pulse compared to the left, and a moderate-amplitude right bifurcational bruit, but normal SO and ST Doppler studies. The right ICA contains a 65% stenosis of its intracavernous portion (smaller arrow) as well as a 58% stenosis of the petrosal (precavernous) segment (larger arrow). In addition, there is a 69% stenosis of the origin of the right ECA (open arrowhead). The combined ICA and ECA stenoses may have accounted for the false-negative Doppler studies.

falls to 74%. By contrast, in our previous study employing the waveform OPG instrument,² we reported a 93% diagnostic accuracy in those patients who tolerated the procedure; with correction for the 6% of patients in that study who were intolerant of the fluid-filled cups, the accuracy fell to 88%. A comparison of the 2 series suggests, therefore, that the fluid-filled, waveform OPG device may be somewhat superior.

The ability to quantitate earlier-ear-to-eye pulse intervals bilaterally with the digital OPG device made us hopeful of detecting bilateral carotid stenoses with greater accuracy than was possible using the waveform OPG instrument. In the present study, bilateral extracranial stenoses were accurately detected in 67% of affected patients. By contrast, in the previously reported study, the waveform OPG device led to accurate diagnosis of bilateral disease in only 45% of affected patients.³

All of the published references to digital air-filled OPG are in the form of brief reports which contain no details regarding method or diagnostic criteria employed.¹⁷⁻²⁰ An overall diagnostic accuracy of 78–85% has been reported for stenoses of 40% or greater,¹⁸⁻¹⁹ and an overall accuracy of 92–94% for stenoses exceeding 75–80%.¹⁷⁻¹⁸ Atrial fibrillation has been reported to produce misleading OPG results.¹⁷ Pearce and co-workers found quantitative OPG to be a useful technique for continuous monitoring of carotid hemodynamics in carotid endarterectomy.²⁰

The high incidence of false-positive SO Doppler studies in the present series exceeds that reported in an earlier investigation from our laboratory² but is consistent with other reported series, in which false-positive rates ranged from 17 to 31%.⁶⁻¹² These results support the view that SO Doppler employed alone has major limitations as a screening test for carotid artery stenosis. ST Doppler, while much more specific for hemodynamically significant stenosis (false-positive rate only 5%), was a relatively insensitive test (true-positive rate only 44% with stenosis of 60% or greater — table 5). Even with complete carotid occlusion, ST Doppler remained normal or only suggestively abnormal in 3 of 8 cases; in 2 of these,
however, coexistent external or common carotid artery stenoses may have prevented ST flow reversal. Since we observed only one instance of an abnormal Doppler response to contralateral external carotid compression maneuvers occurring in the absence of an abnormal response to ipsilateral compressions, omission of the former maneuvers would seem warranted in an attempt to simplify the Doppler examination. Barnes and colleagues similarly noted contralateral facial branches to be a source of collateral in only 1 of 61 abnormal ST Doppler examinations. Those authors, however, observed several instances of abnormal responses to contralateral common carotid artery compression, suggestive of intracranial cross-collateralization. We did not perform common carotid compression, though the addition of this maneuver to the Doppler examination appears warranted in view of its low risk if performed properly. As expected, there was no correlation in our study between Doppler evidence of extracranial cross-collateralization and arteriographic signs of intracranial cross-collateralization.

Ackerman has cogently summarized the state-of-the-art in non-invasive diagnosis of carotid disease. We concur with his conclusion that no “best test” currently exists, and that each has its characteristic strengths and limitations in the screening for, and detection of, stenotic or occlusive disease of the carotid arteries. Quantitative OPG is a promising technique, but the present results indicate that additional improvements in the method are still needed.

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Limitations of quantitative oculoplethysmography and of directional Doppler ultrasonography in cerebrovascular diagnosis: assessment of an air-filled OPG system.
M D Ginsberg, S A Greenwood and H I Goldberg

doi: 10.1161/01.STR.12.1.27

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