Indirect Assessment of Carotid Occlusive Disease by Ocular Pneumoplethysmography

500 mm Hg Vacuum Pressure Measurements and Ocular Pulse Timing

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SUMMARY The interpretation and diagnostic value of the ophthalmic artery pressure measurement and ocular pulse timing modes of the 500 mm Hg vacuum OPG-Gee ocular pneumoplethysmograph were evaluated in 65 patients who underwent aortic arch and cerebral arteriography. Data analysis revealed the OPG-Gee differential tracing which electronically compares and amplifies differences between the right and left eye pulse waveforms to be of little value. In predicting the presence of a ≥50 percent diameter unilateral stenosis, an eye-eye pulse interval of ≥15 msec was 82 percent accurate, a ≥5 mm Hg ophthalmic artery pressure difference was 77 percent accurate and when combined these two criteria were 84 percent accurate. Neither of the criteria intended to detect bilateral carotid lesions, eye-ear pulse interval nor ophthalmic/brachial pressure index, were reliable. Ocular pulse timing was found to be highly specific but insensitive to hemodynamically significant carotid disease. OPG-Gee pressure determinations were more sensitive but lacked specificity. In combination, these criteria allowed identification of unilateral hemodynamically significant lesions with a sensitivity of 83 percent and a specificity of 86 percent. If used to detect more severe degrees of arteriographic stenosis, 60 and 70 percent diameter reduction, the overall diagnostic accuracy of these techniques was not improved. These results do not justify the use of the OPG-Gee instrument as a single noninvasive test for carotid arterial disease.

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for several years, a review of the pertinent medical literature has revealed few reports concerning its use.6,7

This study was undertaken to establish optimal criteria useful in interpretation of the 500 mm Hg vacuum OPG-Gee pressure and time delay tracings, and to evaluate the accuracy of these measurements in detecting hemodynamically significant carotid stenoses or occlusions when compared to cerebrovascular angiography.

Methods and Materials

The records of all patients referred to the University of Illinois and West Side Veterans Administration peripheral vascular laboratories for cerebrovascular examinations were evaluated for inclusion in this study. Criteria for acceptance were concurrent OPG-Gee testing and technically adequate complete cerebrovascular arteriography.

Noninvasive Techniques

OPG-Gee tests were performed by several trained vascular laboratory technicians utilizing the Gee-OPG model IV. The instrument is a binocular, air-filled device similar to that initially developed by Gee. The inclusion of a fourth channel on the chart recorder allowed the addition of the differential and pulse timing test modes. Prior to testing, cerebrovascular and ophthalmologic histories were elicited, bruits noted, and right and left brachial systolic blood pressures recorded. The examination is contraindicated in patients with conjunctivitis, acute or chronic untreated glaucoma, a history of spontaneous retinal detachment, recent eye trauma or surgery, and allergy to local anesthetic or epoxy materials. If no contraindication to testing existed, the patients' conjunctiva were anesthetized, photocells were applied to the ear lobes with double-stick clear tape and standard ECG electrodes were attached. With the patient supine, the ocular suction cups were placed on the patient's lateral sclera and approximately 75 mm Hg vacuum applied to hold them in place. The test was then performed by increasing the scleral vacuum to 500 mm Hg which was then decreased to the baseline vacuum over 30 seconds while simultaneously recording the volume changes in each ocular globe, vacuum pressure and ECG on the chart recorder at a paper speed of 10 mm/sec. The supine brachial pressure was again recorded from the extremity previously noted to have the higher pressure. The instrument was then switched to the differential mode, and right and left ocular pulse waveforms were recorded simultaneously with the differential line at a chart speed of 100 mm/sec. The differential line represents an electronic subtraction of the right and left ocular signals. The line is expected to be flat if each ocular pulse waveform is equal in amplitude and time of arrival in reference to the R wave of the ECG tracing. The test was concluded by switching the instrument to the pulse timing mode which simultaneously records both eye and ear pulse waveforms and ECG at a chart speed of 100 mm/sec.

The OPG-Gee pressure tracings were analyzed with the plastic overlay ruler supplied by the manufacturer, which describes the relationship between the applied vacuum pressure and the corresponding ophthalmic artery systolic pressure (OSP). The OSP values for the right and left eye tracings were read from the overlay scale and recorded. The vertical deviation of the differential line was then noted. According to the manufacturer, if a significant timing delay exists between the two ocular pulse waveforms, there should be a vertical deflection of the differential line. The deflection should be upward if the left ocular pulse waveform is delayed and downward if the right is delayed. The direction of the differential line deflection and its peak amplitude from the horizontal were recorded. The pulse timing tracings were then examined by drawing a vertical line from the ECG R wave and measuring, in mm, the distance from the vertical line to the point of initial deflection of the eye and ear pulse waveforms (1 mm = 10 msec). The resultant R wave — eye pulse intervals and R wave — ear pulse intervals were then recorded and compared.

Arteriography

Arteriograms were performed within several days of noninvasive testing. They were by standard Seldinger technique, and consisted of flush aortic arch and biplanar, selective carotid injections with intracranial views. All radiographs were reviewed by one of the authors (JAS) without knowledge of the noninvasive test results. When a stenosis was noted, the transverse diameter of the narrowest portion of the lesion in either plane was measured and compared to the diameter of the normal appearing vessel just cephalad to the lesion. The percentage of diameter stenosis was then calculated. Since a reduction in ophthalmic artery pressure and flow may result from a significant stenosis in any portion of the proximal arterial system, all vessels from the ascending aorta to the ophthalmic artery were carefully inspected.

Data Analysis

An arteriographic lesion of ≥50 percent diameter reduction was considered hemodynamically significant. All arteriographic and noninvasive tracing measurements were recorded to the nearest 0.5 mm. The means and variances of the OPG-Gee differential and pulse timing data were calculated. Statistical analysis of the effect of a significant arteriographic stenosis on the magnitude of eye-eye pulse delay, eye-ear pulse delay and differential line deflection was performed by using the unpaired Student's t test and Welch's modified t test. A five percent confidence level was accepted as statistically significant. To define the optimal criteria useful in interpreting the OPG-Gee pressure measurements, the ophthalmic systolic pressures (OSP) were compared to each other and the brachial systolic pressures (BSP) using multiple decision thresholds by constructing receiver operator characteristic curves (ROC). The optimal criteria for interpretation of the pulse timing data were similarly established.
by use of ROC analysis. To assess the reliability of both OPG-Gee pressure and pulse timing measurements in detecting the presence of hemodynamically significant carotid occlusive disease, decision matrix analysis was employed. Finally, to determine the effect of advanced disease on the results of the decision matrix analysis, the data was evaluated against angiographic standards of 60 and 70 percent reduction in luminal diameter.

**Results**

**Arteriography**

The arteriographic results of the 65 patients are summarized in table 1. Of the 130 carotid arterial systems measured, there were 34 arteries with a $\geq 50\%$ diameter arterial stenosis. Thirty-one lesions, including all occlusions were at the level of the extracranial internal carotid artery. The remaining three lesions were at the level of the carotid siphon. If the arteriographic results are expressed per patient: 35 patients demonstrated normal arteries or insignificant stenoses; 24 patients had a unilateral, significant stenosis or occlusion; and six patients had significant disease bilaterally.

**Ocular Pulse Timing**

Statistical analysis of the differential and pulse timing data revealed a highly significant difference ($p < 0.001$) between the mean eye-eye pulse delay in the group of patients without a $\geq 50\%$ diameter arterial stenosis (4.6 msec $\pm$ 4.8), and the patient group with a unilateral significant stenosis or occlusion (19.2 msec $\pm$ 16.3). Analysis of the mean eye-ear pulse intervals revealed no difference between eye-ear pulse timing in carotid arterial systems with and without significant angiographic lesions (22.5 msec $\pm$ 27.0 and 13.0 msec $\pm$ 25.0, respectively), (fig. 1). The mean vertical deflection of the differential line, (fig. 2), was also not statistically different when comparing patients without significant carotid occlusive disease (2.7 mm $\pm$ 4.2) and those with unilateral significant angiographic lesions (3.8 mm $\pm$ 3.3). Inspection of the plotted data in figures 1 and 2 does not reveal any discriminant threshold which might serve as a useful criteria in interpreting the OPG-Gee differential line or eye-ear pulse intervals.

When plotted, the eye-eye pulse interval afforded a sufficient degree of data separation to warrant further analysis. To define the best discriminant criteria for the detection of unilateral, $\geq 50\%$ diameter carotid stenoses by eye-eye pulse timing, a ROC curve was constructed using decision thresholds of 0, 5, 10, 15 and 20 msec delays. The optimal compromise between the true positive and false positive rates was noted when an eye-eye pulse delay of 15 msec was considered normal. Employing these criteria (>15 msec eye-eye delay for a positive test) decision matrix analysis yielded a diagnostic specificity and sensitivity of 95 percent and 57 percent respectively, and an accuracy of 82 percent for ocular pulse timing. The positive predictive value for this test was 86 percent and the negative predictive value was 80 percent (table 2).

**Ophthalmic Artery Pressure**

Multiple criteria for pressure tracing interpretation were evaluated by ROC curves. In addition to Gee’s recommended criteria of $\geq 5$ mm Hg OSP difference and a .66 OSP/BSP index, OSP differences of 4–10 mm Hg and OSP/BSP indices of .60–.70 were analyzed separately and in combination. ROC analysis revealed a $\geq 5$ mm Hg OSP difference to be the optimal criteria useful in the detection of a unilateral, $\geq 50\%$ diameter carotid stenosis. When applied in this patient population, a $\geq 5$ mm Hg OSP difference was 70 percent sensitive, 81 percent specific and 77 percent accurate. The positive and negative predictive values using this criterion were 72 percent and 85 percent, respectively. An OSP/BSP index of .66 was the best discriminant value for bilateral disease, in that it correctly identified four of the six patients with bilateral lesions; however, if both the OSP difference and OSP/
Grahic lesion in 71 percent of the patients with unilateral deflection correctly identified the side of the arteriographic standards of disease (table 3), the balance between the test specificity and sensitivity was shifted, however, overall accuracy was only slightly altered.

Severe Disease

If the six patients with bilateral disease were excluded from the analysis, and the OPG-Gee pressure and time delay tests combined with a positive test defined as the presence of a ≥5 mm Hg OSP difference and/or a >15 msec eye-eye delay, the best overall results were obtained: sensitivity 83 percent, specificity 85.7 percent, accuracy 84 percent, positive predictive value 80 percent, and negative predictive value 88 percent (table 2).

The second objective of this study was to assess the diagnostic reliability of the 500 mm Hg vacuum OPG-Gee pressure and pulse timing test modes. Our results reveal that OPG-Gee ophthalmic artery pressure measurements was also analyzed by the ROC method. This analysis confirmed that Gee’s originally recommended criteria of a 5 mm Hg or greater OSP difference and an OSP/BSP index of .66 afford optimal results.

Diagnostic Efficacy

The effect of selecting different OSP differences and OSP/BSP indices in the interpretation of OPG-Gee pressure measurements was also analyzed by the ROC. The results indicate that the eye-eye delay is a more specific indicator of the absence of carotid stenosis or occlusion than ophthalmic artery pressure measurement (table 2), but much less sensitive to the presence of hemodynamically significant lesions. If the results of our pulse timing analysis are compared to those reported by Baker in his evaluation of OPG-Gee pulse timing, using the same >15 msec eye-eye delay, different results are noted. Baker reported a sensitivity of 85 percent, specificity of 100 percent and accuracy of 94 percent in his study.
of the chronopulse automated OPG-Gee pulse timing technique in detecting the presence of a ≥60 percent arteriographic stenosis. Our data employing the same 60 percent standard of disease (table 3) revealed a lower sensitivity (72 percent), specificity (90 percent), and accuracy (85 percent). These different results might be explained by slight differences in data analysis, but are more likely due to a significantly higher incidence of disease in our patient population. In Baker's study, 46 percent of the patients examined had normal arteriograms; whereas, only 29 of 130 arteries (22 percent) in our study were normal. As one might expect, if a relatively insensitive technique, such as pulse timing, is applied to a population with a much higher incidence of disease inferior results are obtained.

Our results of OPG-Gee pressure measurements (table 2) are consistent with some of the varied results reported in the literature. In a collective review of ten studies concerning the 300 mm Hg vacuum OPG-Gee and other pressure OPG instruments, Summer reported a median sensitivity of 88 percent (range 28–97%) and specificity of 94 percent (range 39–100%). Once again however, our results are lower than those published by Baker et al, in an evaluation of 500 mm Hg vacuum OPG-Gee pressure measurements, in which he noted a sensitivity of 75 percent, specificity of 91 percent and test accuracy of 87 percent. These varied results may be influenced by Baker's use of slightly different criteria to interpret the test, but more importantly, reflect differences between the patient populations studied. In Baker's report, 42 percent of the arteries studied were abnormal, compared to a 77.5 percent incidence of abnormal arteriograms in the present investigation. This higher incidence of carotid stenosis in our study, compared to other reports, may afford a more realistic assessment of the clinical application of the OPG-Gee technique, since the test is commonly used to evaluate patients with cerebral symptoms who are suspected of having carotid arterial disease.

Combining the pressure and time delay criteria afforded the best overall results (table 2). This combined approach in which the test was called positive when either the pressure or time delay criteria was positive, and negative only if both were negative, yielded an increased sensitivity but decreased specificity when used to detect patients with unilateral disease. Improved results with combined testing methods have also been noted by other investigators of additional indirect noninvasive cerebrovascular tests used in conjunction with OPG testing.

The analysis of OPG-Gee testing in relation to advancing severity of disease (table 3) reveals that the accuracy of each technique does not improve when used to detect progressively stricter definitions of arteriographic disease. These data do however, illustrate the dynamic relationship between test sensitivity (ability to detect presence of disease) and specificity (ability to recognize the absence of disease). If the angiographic definition of disease is strict, such as 70 percent diameter stenosis (91% cross-sectional area reduction), the apparent sensitivity of the test increases with a decrease in the apparent specificity when compared to a 50 percent angiographic standard. The opposite occurs, sensitivity is decreased and specificity increased, if a more lax definition of disease is employed. These measures are independent of the numbers of true-negative and true-positive results in the total population and are more meaningful than the overall accuracy. The choice of angiographic stenosis for a positive test is arbitrary and depends on the purpose of the test and clinical implications of false positive and false negative studies. The degree of arterial stenosis considered positive for noninvasive carotid testing has varied in the literature from 40 to 75 percent diameter reduction. The use of these various arterio-

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<tr>
<th>Criteria for positive test</th>
<th>Sensitivity (%)</th>
<th>Specificity (%)</th>
<th>Accuracy (%)</th>
<th>PPV*</th>
<th>NPV†</th>
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<td>≥5 mm Hg OSP difference</td>
<td>70</td>
<td>81</td>
<td>77</td>
<td>72</td>
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<tr>
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<td>68</td>
<td>69</td>
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<td>57</td>
<td>95</td>
<td>82</td>
<td>86</td>
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<tr>
<td>≥5 mm Hg OSP and/or &gt;15 msec eye–eye delay</td>
<td>83</td>
<td>86</td>
<td>84</td>
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<td>88</td>
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*Positive predictive value. †Negative predictive value. 1≥50% arteriographic standard.

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<tr>
<th>Criteria for positive test</th>
<th>Arteriographic Standard*</th>
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<tr>
<td></td>
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<tr>
<td>≥5 mm Hg OSP</td>
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<td>&gt;15 msec eye–eye delay</td>
<td>57</td>
</tr>
<tr>
<td>≥5 mm Hg OSP&gt;15 msec eye–eye delay</td>
<td>83</td>
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*Percent diameter stenosis.
graphic "standards" undoubtedly represents manipulation of data to achieve the highest accuracy with the technique in question. The fact remains that both in-vivo and in-vitro data, relating poststenotic pressure and flow to percent stenosis, has shown that hemodynamic alterations occur when the arterial cross-sectional area is reduced by 75 percent (50 percent or greater reduction in diameter) at physiologic flow rates.

The results of the present study indicate a significant incidence of false negative and false positive OPG-Gee examinations. A major factor contributing to these diagnostic errors undoubtedly involves the use of a physiologic test, such as ophthalmic artery pressure measurement or ocular pulse timing, to detect an anatomical lesion, arteriographic stenosis. Although it is well established that the radius of the residual vessel lumen determines the hemodynamic significance of an arterial stenosis, calculation of area reduction of an isolated angiographic stenosis of the internal carotid artery and subsequent hemodynamic alterations in the cerebral circulation may not be directly related. Other factors such as length of stenosis, flow rate, vessel wall compliance, collateral pathways, luminal surface geometry and subcritical lesions in series all play a role in producing a pressure gradient across arterial stenoses; and may account for false negative and false positive OPG-Gee results. In addition, biplanar angiography may underestimate the true anatomical extent of carotid disease in some cases and is open to interpretive errors itself. Finally, since the OPG-Gee instrument measures arterial pressure and pulse wave delays indirectly by the systolic filling of the ocular globes, accuracy may be further reduced by errors inherent to the method such as different elastic properties of the distal ocular vessels, pressure induced changes in the compliance of the eye or asymmetry of eye cup placement.

Comments

Based on our analysis, the pulse timing feature of the OPG-Gee allows an acceptable level of diagnostic specificity in identifying patients without significant carotid occlusive disease; and therefore, might be useful in excluding carotid lesions as an etiology of cerebral bruits or non-specific cerebral symptoms. However, the sensitivity of pulse timing, 57 percent, is poor and insufficient to recommend its use as a screening test or method of selecting patients for angiography.

The pressure measurements are much more sensitive compared to pulse timing but lack specificity. The overall accuracy of pulse timing, 82 percent, and pressure measurement, 77 percent, in this patient group were similar; yet as we and other authors have noted, accuracy remains limited as an index of diagnostic performance since it is strongly affected by the prevalence of disease in the population tested and must be interpreted with caution. Combining the pressure and pulse timing modes increase test sensitivity at the expense of specificity. This approach may be advantage when one is testing a population with a high incidence of disease, such as patients with cerebral symptoms, coronary artery disease, diabetes or atherosclerosis involving other major vessels.

The available evidence seems to support several conclusions. The diagnostic reliability of the 500 mm Hg vacuum ocular pneumoplethysmogram (Gee-OPG model IV) is not sufficient to recommend its use as a single noninvasive method to detect hemodynamically significant carotid disease. The inability to detect bilateral carotid disease remains an apparent major shortcoming of the device. Further study will be necessary to develop accurate secondary interpretive criteria useful in identification of bilateral lesions. In fact, the exclusion of the six patients with significant bilateral disease from our evaluation of the combined use of the unilateral pressure and pulse timing criteria, realistically decreases the diagnostic value of OPG-Gee testing more than the results of the decision matrix analysis indicate. And finally, although OPG-Gee testing allows objective, indirect hemodynamic evaluation of the carotid circulation; it certainly cannot replace arteriography as the primary diagnostic modality in cerebral arterial disease.

References

Indirect assessment of carotid occlusive disease by ocular pneumoplethysmography. 500 mm Hg vacuum pressure measurements and ocular pulse timing.
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