THE RECENT ACCELERATED ADVANCES in noninvasive vascular technology have resulted in the development of a wide variety of techniques intended to identify atherosclerotic disease in the carotid arteries. Several methods use the first major branch of the internal carotid artery, the ophthalmic artery, to indirectly evaluate internal carotid artery blood pressure and flow. These methods include two types of oculopletysmography to detect phasic changes in the volume of the eye produced by pulsatile blood flow. One method, oculopletysmography introduced by Gee (OPG-Gee), indirectly measures ophthalmic artery pressure by monitoring the pressure at which systolic ocular pulsations reappear following occlusion of ophthalmic artery inflow by application of 300 mm Hg vacuum capacity and also by the addition of 500 mm Hg vacuum pressure. 5 As experience with OPG-Gee has accumulated, several modifications have been suggested. Since these techniques are sensitive to a decrease in ophthalmic artery pressure or flow, they are theoretically capable of identifying proximal, hemodynamically significant carotid lesions or complete occlusions. Previous studies have demonstrated that significant effects on post-stenotic pressure and flow occur distal to lesions which reduce the cross-sectional area of the arterial lumen by 75 percent or more (50 percent diameter reduction). 3 4 Gee has reported an accuracy of 92 percent in identifying patients with 75 percent diameter carotid stenoses with the 300 mm Hg suction instrument. 5 As experience with OPG-Gee has accumulated, several limitations of the test have been identified: 1) subsequent studies have reported varied results with the test, 2) the ocular pulse could not be obliterated by 300 mm Hg vacuum in many patients due to systemic hypertension, and 3) the test was unable to accurately detect the presence of bilateral carotid stenoses. Due to these limitations, the original OPG-Gee instrument has been modified in several respects, by the introduction of 500 mm Hg vacuum capacity and also by the addition of differential and pulse timing modes to allow adjunctive testing, similar to the time delay technique employed in the OPG-Kartchner instrument. Although the newer OPG-Gee instrument has been commercially available.
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 arteriography.

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 intracerebral 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 ≥50 percent reduction in transverse diameter. 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 ≥50% diameter arterial stenosis (4.6 msec ± 4.8), and the patient group with a unilateral significant stenosis or occlusion (19.2 msec ± 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 arteriographic lesions (22.5 msec ± 27.0 and 13.0 msec ± 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 ± 4.2) and those with unilateraly significant arteriographic lesions (3.8 mm ± 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, ≥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 ≥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 ≥5 mm Hg OSP difference to be the optimal criteria useful in the detection of a unilateral, ≥50% diameter carotid stenosis. When applied in this patient population, a ≥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 disease, 82 percent of the patients tested without a significant stenosis also demonstrated vertical differential line deviations (fig. 2). This marked overlap severely limits the diagnostic efficacy of this test mode. It may be that the instrument is too sensitive to slight differences in the ocular pulse waveforms which, when amplified, result in differential line deflections which are of no clinical significance. A similar overlap in the eye-ear pulse intervals measured in carotid arterial systems with and without hemodynamically significant stenoses (fig. 1) substantially detracts from its value as a diagnostic criterion to identify patients with bilateral disease. By considering a bilateral eye-ear pulse delay of 30 msec or greater as indicating bilateral disease, as suggested by Archie et al, only three of six patients with \( \geq 50 \) percent bilateral stenoses were identified by the OPG-Gee pulse timing mode. However, 10 percent of the remaining 59 patients in our sample also manifested bilateral eye-ear delays \( \geq 30 \) msec. This inability to detect bilateral lesions demonstrated by the present study could not be accounted for by the presence of significant external carotid stenoses.

The optimal eye-eye delay, determined by ROC analysis, for discriminating negative from positive results was 15 msec. The pulse timing mode of the OPG-Gee instrument is technically restricted in that increments of less than 5 msec cannot be accurately gauged on the tracing without sophisticated calipers, which were not employed in this evaluation. However, it is interesting to note that an identical eye-eye delay criteria of 15 msec was likewise established by Baker et al, in his evaluation of the chronopulse, an automated ocular pulse arrival time recorder attachment to the OPG-Gee, which electronically averages the pulse timing of 10 cardiac cycles.

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 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 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 measurement and the ancillary pulse timing feature provide information of comparable diagnostic accuracy (77 percent and 82 percent, respectively). 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 \( \geq 15 \) 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.
TABLE 3

Comparison of OPG-Gee Results Using Various Interpretive Criteria

<table>
<thead>
<tr>
<th>Criteria for positive test</th>
<th>Sensitivity (%)</th>
<th>Specificity (%)</th>
<th>Accuracy (%)</th>
<th>PPV*</th>
<th>NPV†</th>
</tr>
</thead>
<tbody>
<tr>
<td>≥5 mm Hg OSP difference</td>
<td>70</td>
<td>81</td>
<td>77</td>
<td>72</td>
<td>85</td>
</tr>
<tr>
<td>≥5 mm Hg OSP or 0.66 OSP/BSP</td>
<td>70</td>
<td>68</td>
<td>69</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>&gt;15 msec eye-eye delay</td>
<td>57</td>
<td>95</td>
<td>82</td>
<td>86</td>
<td>80</td>
</tr>
<tr>
<td>≥5 mm Hg OSP and/or &gt;15 msec eye-eye delay</td>
<td>83</td>
<td>86</td>
<td>84</td>
<td>80</td>
<td>88</td>
</tr>
</tbody>
</table>

*Positive predictive value.
†Negative predictive value.
≥50% arteriographic standard.

TABLE 2

Comparison of OPG-Gee Results in Relation to Degree of Stenosis

<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>≥5 mm Hg OSP</td>
<td>50%</td>
<td>70</td>
<td>81</td>
<td>77</td>
<td>70</td>
<td>82</td>
<td>77</td>
<td>70</td>
<td>82</td>
<td>77</td>
</tr>
<tr>
<td>&gt;15 msec eye-eye delay</td>
<td>50%</td>
<td>57</td>
<td>95</td>
<td>82</td>
<td>57</td>
<td>90</td>
<td>85</td>
<td>57</td>
<td>84</td>
<td>81</td>
</tr>
<tr>
<td>≥5 mm Hg OSP or 0.66 OSP/BSP</td>
<td>50%</td>
<td>83</td>
<td>86</td>
<td>84</td>
<td>83</td>
<td>86</td>
<td>84</td>
<td>78</td>
<td>78</td>
<td>76</td>
</tr>
</tbody>
</table>

*Percent diameter stenosis.

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, Sumner 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.11-14

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-
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 ophthamalic 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 cervical 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 increased test sensitivity at the expense of specificity. This approach may be advanta-

References

Indirect assessment of carotid occlusive disease by ocular pneumoplethysmography. 500 mm Hg vacuum pressure measurements and ocular pulse timing.
J A Schwartz, P Flanigan, J J Schuler, T J Ryan and J J Castronuovo

Stroke. 1984;15:521-526
doi: 10.1161/01.STR.15.3.521

The online version of this article, along with updated information and services, is located on the World Wide Web at:
http://stroke.ahajournals.org/content/15/3/521