The Impact of Cardiac Index on Cerebral Hemodynamics

Madhumita Saha, MD; Murali R. Muppala, MD; John E. Castaldo, MD; William Gee, MD; James F. Reed III, PhD; D. Lynn Morris, MD

Background and Purpose: Current noninvasive testing allows accurate assessment of cerebrovascular hemodynamics. The cardiovascular influence on the noninvasive assessment of cerebrovascular studies has not been defined. This study was designed to determine the effect of cardiac index (CI) on cerebral blood flow velocities, ocular pulse amplitude, ophthalmic systolic pressure, and ocular blood flow (OBF) as currently estimated by noninvasive laboratories.

Methods: Based on a retrospective study of 181 patients, we prospectively evaluated 45 patients undergoing right heart catheterization for hemodynamic monitoring to correlate the relation between CI, transcranial Doppler sonography, and ophthalmic pneumoplethysmography. Patients with hemodynamic instability, severe carotid stenoses, massive cerebral infarct, or sepsis were ineligible for the study. Simultaneous recordings of systemic blood pressure, ophthalmic systolic pressure, heart rate, ocular pulse amplitude, middle cerebral artery blood flow velocities, and cardiac output were obtained on all patients. OBF was calculated from the heart rate and ocular pulse amplitude.

Results: The relation between OBF and CI is expressed by the equation CI=2.36+0.61×OBF (r=.47, P=.0010). The middle cerebral artery peak systolic velocities and CI had a correlation of .36 (P=.0181). The equation, derived from the linear relation between OBF and CI, was then validated on a sample of 15 patients. With the apparent linear relation between OBF and CI, we used the derived equation to predict CI from OBF. The OBF determination predicted CI within 30% in all patients and within 20% in 53.3% of the patients.

Conclusions: We demonstrated that OBF and middle cerebral artery systolic velocity decrease with diminishing CI. Our findings suggest that CI may be potentially estimated in selected patients by noninvasive assessment of OBF using ophthalmic pneumoplethysmography. (Stroke. 1993;24:1686-1690.)

Key Words • cardiac catheterization • hemodynamics • ophthalmic pneumoplethysmography • ultrasonics

Cerebral hemodynamics of the stroke-prone patient may be accurately assessed noninvasively using transcranial Doppler sonography (TCD)1-4 and ophthalmic pneumoplethysmography (OPG-Gee).5-9 Cardiovascular function influences cerebrovascular hemodynamics and thus the results of these tests, but simultaneous assessment of cerebral and cardiac physiology has never been studied.

Technological advancements have made available various noninvasive methods to assess the adequacy of the intracerebral circulation. OPG-Gee testing noninvasively measures ophthalmic systolic pressure (OSP) and ocular blood flow (OBF) and may be used to assess the ocular hemodynamics of patients with severe carotid stenosis. TCD is a relatively new and innovative test used to assess blood flow velocities of the basal intracranial vessels, including those that compose the circle of Willis. Normal values for both tests have been generated from a population of patients with presumed normal cardiovascular function. Since these tests are often obtained on patients who are at risk for stroke and have significant cardiac disease, determining the impact of cardiac function on these tests would appear to be of considerable clinical importance.

The influence of cardiac function on the noninvasive assessment of cerebral hemodynamics remains unclear to date. In an attempt to determine the relation between cardiac function and OBF, a retrospective study was conducted at our institution on a random series of 181 patients who underwent nonnonsimultaneous testing with OPG and right heart catheterization.10 The results of this retrospective study prompted us to prospectively evaluate the impact of cardiac function on cerebral hemodynamics to define the relation. To accomplish this, we simultaneously recorded OPG and TCD and measured cardiac index (CI) in a select patient population undergoing right heart catheterization.

Subjects and Methods

The retrospective series consisted of patients referred to the vascular laboratory for OPG testing who also underwent right heart catheterization. From January 1, 1987, to May 31, 1987, 181 patients underwent both tests nonsimultaneously, but usually performed within...
TABLE 1. Inclusion Criteria for the Prospective Series

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<td>1. Hemodynamic stability (see text for definition)</td>
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<td>2. Absence of clinical shock with cardiac index between 2.0 and 4.5 L/min per square meter</td>
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<td>3. Radiographic confirmation of adequate positioning of pulmonary artery catheter</td>
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<td>4. Adequate oxygenation (PO2 &gt; 60 mm Hg)</td>
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<td>5. Adequate pH (7.3 &lt; pH &lt; 7.5)</td>
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<td>6. Hemoglobin concentration &gt; 8.0 g/dL</td>
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the week. There were no inclusion or exclusion criteria for this arm of the study.

The prospective series consisted of 45 patients in whom all physiological data were collected essentially simultaneously (within 10 minutes). Our patient population included 17 pre- and 28 post—open heart surgery patients undergoing elective right heart catheterization, between the ages of 39 and 93 years, who were capable of giving informed consent to participate in the study. This select group was composed of hemodynamically stable patients, as determined by the attending cardiologist. All patients had measured CI between 2.0 and 4.5 L/min per square meter. Mean arterial blood pressure recordings for the group ranged between 49 and 114 mm Hg (mean, 83 mm Hg), and heart rates were between 58 and 124 beats per minute, in sinus rhythm, at the time of data collection without wide variation for an individual patient. None of these patients required vasoactive medications or mechanical assist devices to maintain hemodynamic stability. Inclusion criteria required adequate ventilation with PO2 greater than 60 mm Hg and a pH between 7.3 and 7.5. All patients had a Pco2 between 30 and 46 mm Hg (mean, 39 mm Hg). Patients with severe carotid stenoses (75% or more cross-sectional area reduction) were excluded from the study as determined by concordantly negative OPG and duplex ultrasound, which has been shown to have a negative predictive value of 98.6% at our institution. Other inclusion and exclusion criteria for the prospective arm of the study are listed in Tables 1 and 2.

Right heart catheterization was performed from either the subclavian, internal jugular, or femoral vein approach. A 7F or 8F balloon flotation pulmonary artery catheter (Swan-Ganz catheter, American Edwards, Baxter) was inserted percutaneously and advanced to the main pulmonary artery. Cardiac output (CO) was measured using the pulmonary artery flota-

TABLE 2. Exclusion Criteria for the Prospective Series

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<td>1. Intervventional measures to maintain hemodynamic stability (medical and/or mechanical)</td>
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<td>2. Febrile</td>
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<td>3. Hemodynamically significant carotid stenosis as measured by noninvasive tests (see text)</td>
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<td>4. Recent major neurological insult</td>
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<td>5. Retinal detachment within past 6 months</td>
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<td>6. Ocular surgery within past 6 months</td>
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<td>7. Uncontrolled glaucoma</td>
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<td>8. General anesthesia within 24 hours of study</td>
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tion catheter by the thermodilution method. The value was the mean of at least three determinations falling within a 10% range. This was the rate-limiting step in simultaneous data collection. The average of these three values of CO was used for analysis. CI was calculated from CO using the formula

\[
\text{CI} \left[ \frac{\text{L/min}}{\text{m}^2} \right] = \frac{\text{CO (L/min)}}{\text{Body Surface Area (m}^2)\text{.}}
\]

An Electro-Diagnostic Instruments model LP-3 OPG-Gee and a Medsonics Transpect portable TCD unit were used. Bilateral simultaneous OSP and maximum ocular pulse amplitude (OPA) were obtained with the OPG instrument. The heart rate (HR) was documented on an electrocardiographic channel concomitantly, using the same instrument. Immediately after the test, a brachial blood pressure was obtained with a cuff and stethoscope. Ophthalmobrachial systolic pressure (OBSP) indexes were calculated from the brachial and ophthalmic systolic pressures (BSP and OSP, respectively) using the following formula:

\[
\text{OBSP} = \text{OSP} - 0.43 \times \text{BSP}
\]

Ocular blood flow in our study was estimated using a mathematical formula from the HR and maximum OPA data generated by OPG-Gee testing. The ocular pulse wave channels of the OPG are volume-calibrated, such that a 1.0-mm³ volume change results in a 10-mm pen deflection. The ratio of the total surface area of the eye to the surface area of the eye covered by the eyecup is 14.9. To express flow in its usual terms of milliliters, cubic millimeters are converted with the factor mL/1000 mm³. These three fixed factors are associated with the two variable factors, heart rate (HR/min) and maximum ocular pulse amplitude in millimeters (OPA mm), with the following formula for calculating the OBF:

\[
\text{OBF} = \left( \frac{\text{HR}}{\text{min}} \times (\text{OPA mm}) \times (\text{mm}^3/10 \text{ mm}) \right) \\
\times (\text{mL}/1000 \text{ mm}^3) \times 14.9
\]

By rearranging the equation and by canceling elements common to the numerator and denominator, the formula for calculating the OBF is simplified to the following formula:

\[
\text{OBF} = \text{HR} \times \text{OPA} \times 0.00149
\]

During the 10-minute data collection window, TCD recordings of the intracranial internal carotid artery (ICA) and the middle cerebral artery (MCA) were obtained using standard techniques. MCA and intracranial ICA systolic and diastolic blood flow velocities (Vs and Vd, respectively) were recorded from a trans-temporal approach using a 2-MHz hand-held probe, a fast-Fourier system, and a Sony video printer. In two patients, in whom no transcranial window could be found, transorbital recording of intracranial ICA was performed. MCA and ICA mean blood flow velocities (Vm) were calculated from the Vs and Vd using the following formula:

\[
\text{Vm} = \text{Vd} + (\text{Vs} - \text{Vd})/3
\]

At the completion of the prospective study comprising 45 patients, an equation relating CI and OBF was generated. This equation was applied to 15 additional patients (with selection based on the same eligibility criteria) in a validation study in which OBF and CI were
simultaneously measured to determine the accuracy of noninvasively estimated CI using OBF.

Data were entered into a database and screened for accuracy and consistency. After validating the data, analysis was completed using srs.

Pearson's product-moment correlation analysis was used to assess the relation between continuous variables. Because of the number of statistical tests being performed, the usual $\alpha=0.05$ was adjusted to 0.025 (Bonferroni adjustment) to reduce the probability of detecting spurious correlations.

**Results**

In the retrospective series of nonsimultaneous data collection, the relation of OBF to CI was defined by the linear equation $CI=1.99+0.59 \times OBF$, with $r=.43$ and $P<.001$ (Fig 1). In the prospective series of simultaneous data, the relation of OBF to CI was defined by the linear equation $CI=2.36+0.61 \times OBF$, with $r=.47$ ($P=.0010$) (Fig 2). OBF and BSP were also linearly related to CI ($r=.48$, $P=.0009$ [Fig 3] and $r=.42$, $P=.0042$, respectively). No significant correlation was observed between CI and OBSP.

Of the TCD-generated data, MCA systolic velocity was correlated with CI ($r=.36$, $P=.0181$) (Fig 4). No significant relations were found between intracranial ICA flow velocities and CI, or between MCA mean or diastolic flow velocities and CI.

In view of the association between OBF and CI, an additional 15 patients underwent simultaneous evaluation to validate the relation (Fig 5). This figure depicts the effectiveness of OBF in predicting CI. Eight of the predicted CI values, as calculated from the OBF measurement, fell within 20% of the thermodilution CI determination. None fell beyond 30%, as predicted.

**Discussion**

The net driving force of the cerebral circulation is defined as the cerebral perfusion pressure (CPP), which represents the difference between arterial pressure forcing blood into the cerebral circulation and the venous back-pressure. Under normal physiological conditions, venous pressure is negligible, and therefore CPP is usually equal to the mean systemic arterial pressure.

Since the cerebral circulation is autoregulated, changes in CPP do not necessarily equate to changes in cerebral blood flow.

The systolic blood pressure of the ophthalmic artery is virtually identical to that of the carotid siphon and main-stem MCA, as shown in simultaneous measurements of the intraoperative stump pressures and OPG pressures in patients undergoing carotid endarterectomy.

Hence, under normal physiological conditions where venous pressure is negligible and intracranial pressure is normal, regional CPP would be expected to be correlated with OSP as measured by the OPG-Gee.

In our study OSP was linearly related to CI, as shown in Fig 3.
Fig 4. Plot depicts relation between cardiac index (CI) and middle cerebral artery (MCA) peak systolic blood flow velocity in a prospective series. CI (in liters per minute per square meter) was calculated by thermodilution method and peak systolic blood flow velocity (in centimeters per second) determined in a prospective series of 43 patients undergoing simultaneous testing.

Since animal studies have shown that the bulk of OBF is to the choroid, a nonautoregulated vascular bed, changes in CI might be expected to directly affect this parameter. Our study supports this hypothesis with the linear relations demonstrated between CI and OBF (Figs 1 and 2).

The two equations generated by the retrospective and the prospective series statistically had equivalent slopes and differed only in their intercepts (1.99 and 2.36, respectively), giving added strength to this linear relation. That the mathematical formulas differ only in the intercepts between the two groups likely reflects the nature of the data acquisition. The retrospective series represented nonsimultaneous tests acquired over 1 week, while the prospective series was a select group of hemodynamically stable patients with specific inclusion and exclusion criteria and data collected as rapidly as physically possible within a 10-minute time frame. OBSP, an index of OSP and BSP, was not affected by falling CI, although such a fall in CI during cardiogenic shock might potentially affect OSP and produce false-positive OPG results.

The relation between CI and OBF suggests that OBF may potentially be used to noninvasively estimate CI in some patients, particularly if a CI/OBF baseline is known. Our validation of the equation derived to predict CI from OBF measurements demonstrated the overall accuracy of this noninvasive technique compared with currently available invasive methods. Indicator dilution techniques of measuring CI have been reported to have a discrepancy of 11% to 22% between techniques of thermodilution method and dye method.12-21 Discrepancy between techniques could be related to variation in CI over time, variations in CI during various phases of the respiratory cycle, calibration error, and technical measurement error. Eight of 15 CI determinations fell within the range of the most accurate indicator dilution techniques, and all fell within 30% of predicted values. Nevertheless, given the overall marginal $r^2$ (.226) for the prospective series, it would appear that predicted value of OBF in isolation in determining CI is limited. In patients with known CI/OBF data, who subsequently clinically deteriorate after the catheter is removed, OPG-generated OBF may potentially be of clinical use in estimating CI before reinsertion of the catheter.

Transcranial Doppler measurements are those of blood flow velocities, not cerebral blood flow. In the setting of falling CI and falling CPP, the autoregulated bed of the brain would be expected to vasodilate to maintain cerebral blood flow. TCD-recorded MCA flow velocities might be expected to reflect the balance of two competing mechanisms: decreasing flow velocities with decreasing CPP coupled with a tendency for increasing blood flow velocities and blood flow that occurs by compensatory vasodilation of arterial beds.

We found MCA systolic velocity to have the best correlation with CI, with falling systolic velocity being linearly related to falling CI ($r = .45$). Normative studies of peak systolic blood flow velocities generated by TCD show a tendency to decrease with age.1 Although this may be a reflection of decreasing CBF or increasing arterial diameter with age, our data suggest that this observation may also be a reflection of decreasing CI as a function of age. Conversely, when TCD MCA systolic velocity values are diffusely low for the age of the patient, this may reflect poor CI rather than a focal obstruction to carotid outflow. Mean and diastolic blood flow velocities had an insignificant correlation with falling CI, thus implying that mean velocity and diastolic velocity may be better indicators of cerebral autoregulatory capacity than systolic velocity, since they remain unaffected by CI in the range of 2.0 to 4.5 L/min per square meter. We found no correlation of CI with intracranial ICA flow velocities, likely reflecting the more variable insonation angle of the carotid siphon.14

Because patients who were hemodynamically unstable or in cardiogenic shock were excluded from this study, the impact of critically low CI and OBF, OSP, and TCD-generated MCA blood flow velocities is not known, and the results of this study cannot be generalized to this patient population. More work is required to assess the effect of critically falling cardiac function on these parameters.

Fig 5. Bar graph depicts values predicted by noninvasive ocular blood flow vs thermodilution method measurement of cardiac index (CI) (in liters per minute per square meter) in a validation series of 15 patients. Solid bars indicate observed CI; stippled bars, predicted CI.
Acknowledgments

The authors are grateful to Kathleen Moser (Research Department, Lehigh Valley Hospital) for editorial assistance and manuscript preparation and also to Joan Longenecker and Donna Jenny (Neuroscience Research) and Bette Foulke, Judy Hutchison, and Eileen Gribben (Vascular Laboratory) for technical assistance.

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*Stroke*. 1993;24:1686-1690
doi: 10.1161/01.STR.24.11.1686

*Stroke* is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
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Print ISSN: 0039-2499. Online ISSN: 1524-4628

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