Dynamic Pressure–Flow Velocity Relationships in the Human Cerebral Circulation

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Background and Purpose—The pressure–flow velocity relationship in the cerebral circulation is characterized by the critical closing pressure (CCP), which is the pressure at which flow ceases, and the linear slope of a plot between pressure and flow velocity. It has been suggested, but not validated, that CCP can be determined from arterial blood pressure (ABP) and transcranial Doppler (TCD) recordings during the cardiac cycle. We studied a group of patients in whom ventricular fibrillation (VF) was induced. The time interval before defibrillation enabled calculation of CCP from data in which flow approached zero. These estimates were compared with values calculated before and after fibrillation and during regular heartbeats.

Methods—TCD velocities and ABP in the radial artery were recorded before, during, and after 28 episodes of VF in 13 patients. CCPs were calculated by 3 different methods: (1) linear extrapolation from data during VF (gold standard); (2) linear extrapolation from normal heartbeat data; and (3) first harmonic Fourier filtering of normal heartbeat data.

Results—The CCP during VF calculated from long diastoles was 32.9 ± 11 mm Hg (mean$\pm$SD). The regular heartbeat estimate was 6.0 ± 4.3 mm Hg lower ($P<0.05$). The CCP estimate with the use of a Fourier filter was 1.4 ± 3.9 mm Hg ($P=$NS) lower than during VF. During hyperemia after defibrillation, the CCP decreased by 13.3 mm Hg, while velocity increased by 63%. The decrease in CCP could explain half of the increase in flow velocity during hyperemia.

Conclusions—CCP can be accurately estimated from regular heartbeat data and is an important factor in regulation of the cerebral circulation. (*Stroke*. 2003;34:1645-1649.)

Key Words: cerebrovascular circulation ■ ultrasonography, Doppler, transcranial ■ vasoreactivity

The classic concept defining cerebrovascular tone is cerebral vascular resistance. This concept was developed from cerebral blood flow (CBF) determinations with the use of indicator methods such as nitrous oxide or ^{133}Xe. Basically this concept assumes that perfusion pressure and flow are linearly and proportionally related. It follows that flow stops only when the perfusion pressure is zero. However, when dynamic measurement techniques are used, such as electromagnetic flowmetry or ultrasound Doppler, the limitations of this concept become manifest.[1,2] Dynamically, flow may stop at pressure levels significantly higher than zero. The arterial blood pressure (ABP) level at which flow stops is defined as the critical closing pressure (CCP)[1–3] or, in cardiac literature, the zero-flow pressure ($P_{f=0}$).[4] Above the CCP, an approximately linear slope, sometimes referred to as the inverse flow resistance, defines the relation between pressure and flow, when these variables are plotted as an x-y function[1,2] (Figure 1). It follows that flow is linearly (but not proportionally) related to pressure and that it can be regulated by changes in both CCP (the x intercept) and slope. The pressure-flow relation is mainly a function of the peripheral resistance

cerebral vascular bed. It is, however, derived by measuring systemic arterial pressure and inflow through the cerebral conductance arteries, which contribute only minimally to the total cerebrovascular resistance.

With the use of ultrasound, the velocity of flow in the basal cerebral arteries can be assessed noninvasively from the Doppler shift. Because the calibers of the insonated vessels are not known precisely, this technique cannot be used to determine absolute values of flow. Therefore, the slope of the relationship between pressure and flow is less meaningful when Doppler techniques are used. Nonetheless, quantitative determinations of the CCP can be made if, as shown in some studies,[5,6] the vessel walls of the basal cerebral arteries are stiff and the caliber changes are small over the normal range of pressures. Comparisons of transcranial Doppler ultrasound (TCD) recordings in the middle cerebral artery (MCA) with electromagnetic flowmetry demonstrated good proportionality between Doppler estimates of velocity and volume flow.[7,8] Moreover, it is clear that at the zero-flow pressure, flow velocity must also be zero. In principle, the possibility exists that the CCP determined by ultrasound Doppler techniques
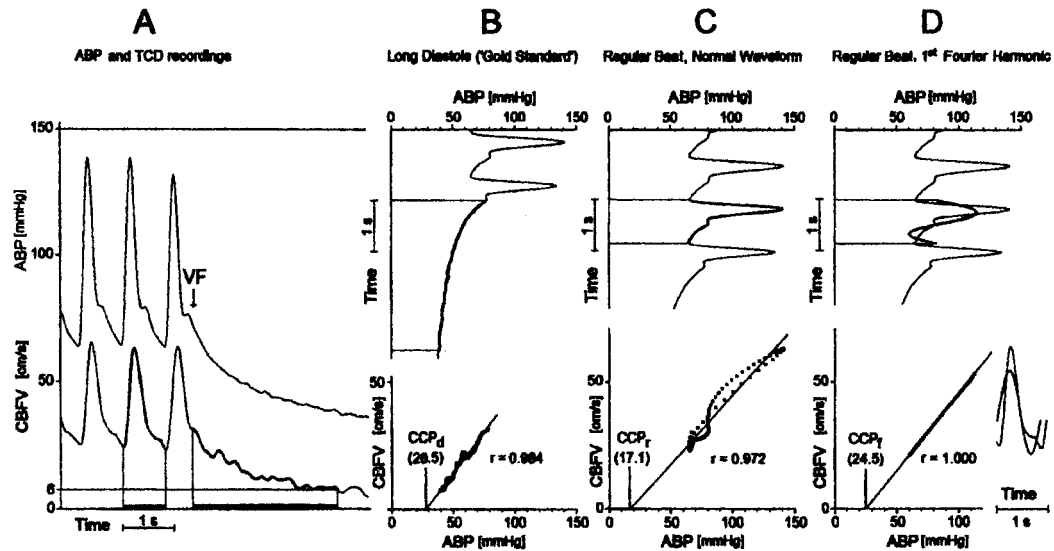
Figure 1. Methods used to determine CCP. A, Tracings of ABP and MCA CBFV. VF was induced as indicated by the arrow, and both ABP and CBFV descended in a curving manner. B, Determination of long diastole CCP, CCP_d, by linear extrapolation of the pressure-velocity data pairs. Regular heartbeat analysis is shown in C and D for determination of CCP_r and CCP_f, the difference being Fourier filtering used to eliminate as much as possible of the pressure waveform distortion in D.

may emerge as a physiologically relevant index of cerebrovascular tone.[9–17]

The dynamic pressure-flow relationships have been studied extensively in the coronary circulation.[4,18–21] The zero-flow pressure is significantly higher than the outflow pressure in the right atrium, and it reflects the level of vascular tone. Measurements in the coronary arteries of conscious humans showed a decrease in $P_{f=0}$ from 51.7 to 37.9 mm Hg after vasodilation with angiographic contrast media.[19] In the cerebral circulation, a 25.9% decrease in CCP and a 20.7% increase in flow velocity were reported after the subject breathed 5% CO_2 in air.[15] Vasoconstriction during moderate hyperventilation increased the CCP from 13 to 23 mm Hg.[17] These early reports suggest that the "back pressure" effect of the CCP is an important factor in the regulation of CBF.

In the heart, because of the complicated intramural distribution of pressure in systole, calculation of the zero-flow pressure requires either long diastoles induced experimentally[18] or slow heartbeats occurring naturally.[19] In the cerebral circulation, this complication does not exist, and normal heartbeats have been used for calculation of CCP.[1,2,9–17] However, this technique has not been validated against the prolonged diastole method, which would be expected to give more accurate estimates because data closer to the zero-flow intercept are used.

The aim of the present study was to validate estimates of CCP based on regular heartbeat data against long diastole (CCP_d) determinations after induced ventricular fibrillation (VF) during defibrillator testing. Two different regular beat methods were tested: (1) We used the conventional method[9–17] of determining the CCP by linear regression (CCP_r), using only mildly filtered recordings of pressure and flow velocity waveforms. (2) To minimize potential errors due to waveform distortion in the arm arterial system,[22] we also investigated whether using maximally filtered waveforms

would improve the estimates. For this purpose we determined the first harmonic Fourier filtered CCP (CCP_f). Furthermore, the study protocol allowed an assessment of the relative role of the decrease in back pressure in mediating the flow increase during reactive hyperemia.

Subjects and Methods

The study was conducted in a series of 13 patients in whom VF was induced for routine testing of implanted automatic cardiac defibrillators. The devices were implanted for treatment of potentially life-threatening arrhythmias. The mean age of the subjects was 54 years (range, 23 to 70 years); the group consisted of 1 woman and 12 men. This study was approved by the human subjects committee at the University of Washington School of Medicine, and informed consent was obtained from all patients. The normal routine testing protocol was not altered except for the TCD monitoring. General anesthesia was induced with a combination of ≥2 of the following: isoflurane, nitrous oxide, enflurane, midazolam, sodium thiopental, sufentanil citrate, vecuronium bromide, alfentanil hydrochloride, metocurine, and propofol. Dobutamine, calcium carbonate, phenylephrine hydrochloride, or epinephrine was administered when necessary for control of ABP. The patients were not receiving other medication that would have influenced the results of the study significantly. No medication changes were made within 3 minutes before or after induction of VF by either alternating current or rapid ventricular pacing.

Mechanical ventilation was used, and a constant hypocapnic end-tidal P_{CO_2} measured by a Datex 223 monitor was maintained. The left MCA velocity signals were obtained with the use of a 2-MHz probe held in position by a headband. The probe was connected to a TC2-64B TCD instrument (EME GmbH) with analog output of the CBF velocity (CBFV) spectral outline waveform. The ABP was recorded from a radial artery catheter. Care was taken to ensure that the ABP waveform was undamped by blockage or air bubbles. After sampling at 50 Hz and analog-to-digital conversion, CBFV, ABP, end-tidal P_{CO_2}, and ECG signals were stored on the hard disk of a PC-compatible laptop computer. The different estimates of CCP were determined offline from the stored data with the use of a custom program written in Visual C++ for Windows 2000. Microsoft Excel 97 was used for statistical calculations.

Processing of Long Diastole Data After Induced VF

Analysis of the long diastolic fall in pressure and flow after cessation of cardiac function is the "classic" approach to estimating the extrapolated zero-flow pressure intercept.[18] This procedure is illustrated by a representative case in Figure 1A and 1B. The flow velocity drops rapidly during the first 2.5 seconds after the induction of VF. Since Doppler instruments have high-pass filters to eliminate the artifacts from arterial wall movements, the quality of the spectral outline is poor at lower velocities. In the unit used, the filter cutoff was 150 Hz, corresponding to 6 cm/s. When the velocity falls below this level, noise will influence the output of the spectral outline estimator, and the waveform data are not reliable. As illustrated by the bar on the time axis in Figure 1A, the interval from the end of the dicrotic notch of the ABP wave to the point where CBFV fell below 6 cm/s was used for calculation of CCP_d. The 6 cm/s velocity end point was reached in 11 patients before a ventricular contraction occurred. In 2 subjects, systolic activity was seen in all tests before the 6 cm/s end point was reached. However, in 3 instances the diastolic period was >2.5 seconds, and these data were considered to qualify as long diastoles.

A total of 60 episodes of VF were recorded. Thirty-two of these were discarded from analysis because the VF was not complete (long diastoles interrupted by early systolic waves in the ABP) or because of spikes or noise in the TCD recording. The remaining 28 episodes were analyzed as the example shown in Figure 1B. Corresponding samples of ABP (x axis) and CBFV (y axis) were plotted throughout the long diastolic interval. Extrapolation to the zero flow velocity pressure was done by conventional linear regression analysis.

Processing of Regular Heartbeat Waveforms

The 8 heartbeats immediately before induction of VF were used for estimation of CCP_r. After low-pass filtering of both ABP and CBFV at 5 Hz (to eliminate high-frequency noise in the velocity), the computer plotted the data pairs of pressure versus velocity during the cardiac cycle for each of the 8 heartbeats immediately preceding VF. The plot from 1 such beat is shown in Figure 1C, and the linear extrapolation was done by the same procedure as for the prolonged diastoles. To compensate for time delays in pulse propagation and measurement systems, linear regression was performed with the velocity data delayed by up to 10 samples (=0.2 seconds). The delay that gave the highest r value was used for determination of the CCP_r. The results from the 4 beats with the highest r value of the linear regression were averaged.

For the determination of pressure–flow velocity relationships, both measurements should preferably be made in the same anatomic location. In the clinical environment this is difficult to achieve, and for ethical reasons the radial artery was the only available location from which a blood pressure recording could be made. The pressure waveform in this location will be somewhat distorted compared with the waveform in the cerebral vessels. This distortion is caused by the transmission of the pulse as well as by reflections of the pulse wave.[22] The higher-frequency components of the waveform are more likely to be distorted than the fundamental (first harmonic) component. Therefore, removing the higher frequency content before processing may possibly yield a more accurate estimate of CCP. A similar approach has been described earlier and used to estimate cerebral perfusion pressure.[23]

Fourier analysis is the preferred method to remove the higher harmonics from the data. The conventional Fourier transform was used to determine the amplitudes of the first harmonics (ABP_1 and $CBFV_1$) of pressure and velocity data from each of the 8 regular heartbeats. The corresponding time means of the waveforms in each beat were also calculated (ABP_0 and $CBFV_0$). The inverse Fourier transform can be used to reconstruct the filtered waveform, as shown in Figure 1D. Since the higher harmonics are eliminated, the regression analysis will be done on near-perfect linear data. Mathematically, the intercept on the pressure axis will therefore be given by the following equation[23]:

$$CCP_f = ABP_0 - CBFV_0 \times ABP_1 / CBFV_1.$$

The 2 highest and 2 lowest values of the 8 beats were discarded, and the remaining 4 intermediate values were averaged to determine the estimate of CCP_f used for comparison with CCP_d.

Processing of Data During Hyperemic Response After VF

A clear hyperemic response in CBFV was seen after ventricular defibrillation and heart restart in most of the recordings. However, in some recordings there was either no or only a weak response. Moreover, the response was sometimes masked by large changes, mostly increases, in the ABP level. The more detailed study of the hyperemic response was made with the use of the following selection criteria for recordings used: (1) an ABP difference of <10 mm Hg between the pre-VF and the hyperemic interval and (2) an increase in CBFV of >30%. Twelve episodes of VF from 6 patients met these criteria and were selected for further analysis. An interval of 8 heartbeats at the peak of the CBFV response was analyzed by the CCP_f calculation method, as described above.

Results

The mean end-tidal P_{CO_2} was 24.2±3 mm Hg in the series (all results are given as mean±SD), and the CBFV was 28.3±10 cm/s. ABP before VF was 79.1±11.1 mm Hg. Linear regression analysis of the pressure–flow velocity relationship during the long diastoles resulted in good correlations ($r=0.955±0.03$). Only 1 determination resulted in $r<0.9$. The CCP_d was 32.9±11 mm Hg (range, 13 to 56 mm Hg).

The linear regression analysis of the regular beat data also showed a high degree of linear correlation between ABP and CBVF ($r=0.978±0.010$). The average time delay giving the highest r values was 0.041 second, and the maximum delay was 0.08 second. The CCP_r was 26.9±11 mm Hg (range, 10 to 41 mm Hg). When compared with the CCP_d (from long diastoles), the CCP_r was 6.0±4.3 mm Hg lower. This difference was significant ($P<0.05$). The correlation with the gold standard CCP_d was good ($r=0.924$); the results are plotted in Figure 2A.

The first harmonic Fourier analysis–based method resulted in a CCP_f estimate of 31.5±10.9 mm Hg (range, 15 to 52 mm Hg). This was only 1.4±3.9 mm Hg lower than the gold standard CCP_d. This difference was not statistically significant at the $P<0.05$ level. The correlation between CCP_d and CCP_f was good ($r=0.935$); the individual data are shown in Figure 2B.

A comparison between the pressure–flow velocity relationships before VF (control state) and during peak hyperemia is shown in Figure 3. Flow velocity was normalized as 100% in the control period. During hyperemia, the pressure axis intercept (CCP) was shifted to the left by 13.3 mm Hg. Alone this shift would have resulted in an increase in CBFV to 131%, as illustrated by the dotted line and the circle in Figure 3. In addition, the slope of the relationship also increased so that the flow velocity at peak hyperemia was 163% of its pre-VF value. The mean ABP in hyperemia (80.6 mm Hg) was almost equal to the ABP in the control state (80.4 mm Hg).

Discussion

The present study was designed primarily to validate determinations of CCP based on regular beat data. Linear extrapolation estimates of CCP_d from long diastoles were used as a reference or gold standard. Of the 2 regular beat methods
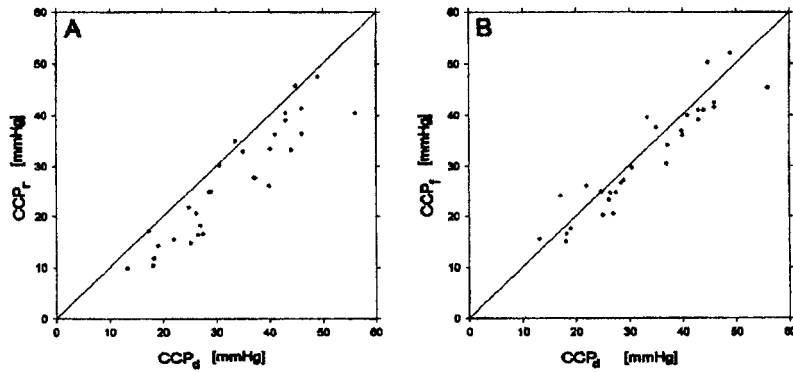
Figure 2. Comparison of individual estimates of CCP. The x axes are estimates of CCP_d based on prolonged diastoles. In A, the corresponding estimates based on regression analysis of regular heartbeats (CCP_r) are shown. B shows the individual results (CCP_f) obtained with the Fourier filtered data. The line of identity is indicated in both panels.

used, the estimates from the first harmonic Fourier filtered data, CCP_f, were more accurate than the estimates based on linear extrapolation from only slightly filtered waveforms, CCP_r. The Fourier filtered estimates had both a smaller absolute error as well as less deviation (scatter). This finding can be explained by an increase in the systolic amplitude of the blood pressure in the radial artery,[22] mostly affecting the unfiltered data. This effect produces a shift to the right of the systolic (upper right) part of the pressure–flow velocity data. The systolic right shift forces the extrapolated pressure axis intercept to the left. The beat shown in Figure 1C is an example of this effect. The waveform distortion in the arm arterial tree is affecting primarily the second and higher harmonics,[22] and therefore the first harmonic–filtered estimates should, in principle, be more accurate. The Fourier filtering technique is recommended for future studies. The errors due to wave distortion would likely have been even more serious if finger plethysmographic methods[14,15] were used to record ABP noninvasively. It remains doubtful whether such ABP recording methods can produce reliable estimates of CCP. Accurate blood pressure waveform rendering is a prerequisite for reliable assessment of CCP, and to our knowledge there is only 1 published noninvasive method that can document a level of accuracy comparable to invasive procedures.[24]
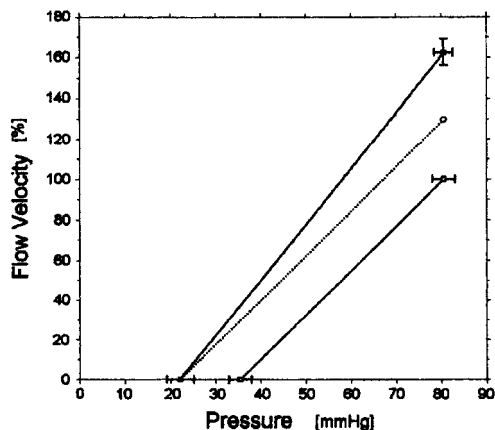

Figure 3. Cerebral pressure–flow velocity relationships during control state (open squares) and reactive hyperemia after VF (closed squares). The dotted line and the open circle describe the hypothetical effect on flow velocity due to changes in CCP alone (slope unchanged). Horizontal and vertical bars indicate the SEM of the data. See text for further description.

Vascular bed compliance has frequently been mentioned in the coronary hemodynamic literature as a factor that may cause errors in the estimates of the extrapolated zero-flow pressure.[18,20] In the cerebral circulation, this factor is of less concern because the cerebral arterial bed is stiff, with the total compliance—also referred to as "windkessel"—component of flow being 2% to 3% of mean flow during a heartbeat.[25] This estimate was based on the rapid inflow filling of the windkessel after release of common carotid artery compression maneuvers. In the formula used for calculating CCP_f, the second term contains the ratio of the first harmonic amplitude of ABP divided by the equivalent amplitude of flow velocity. If we assume that this ratio decreases by 2.5% (because of increase of the flow component into the windkessel), the CCP_f estimate would increase by approximately 1.5 mm Hg in our series. An error of this magnitude seems acceptable. Moreover, this is probably a conservative estimate of the error since the excursions in pressure during normal heartbeats are smaller than those provoked by the compression maneuver used to assess the compliance component of flow.[25]

While the aforementioned windkessel effect refers to the entire cerebral (precapillary) vascular bed, we also need to consider elastic properties of the arterial wall and their effects on the caliber of the conducting artery that is insonated. The cross-sectional area would increase slightly with increased pressure. Velocity is given as flow divided by area. Therefore, any (relative) velocity increase would be slightly less than the (relative) flow increase. The ratio $ABP_1/CBFV_1$ would increase because of this effect, and the CCP_f estimate would be lower. For a cross-sectional area variation of 5%, the underestimation of the CCP would be approximately 3 mm Hg. Again, this level of error should be tolerable. We shall also mention an interesting possibility: if the peripheral windkessel effect had the same numerical value as that from the elasticity of the insonated conductance artery, the errors due to these 2 phenomena would cancel out.

The concept of the CCP broadens our understanding of how flow in the cerebrovascular bed is regulated. The results summarized in Figure 3 show that, during the hyperemic phase, almost half (31%) of the increase in flow velocity can be explained by a reduction in the CCP. The remaining 32% increase can be attributed to the increase in slope. The slope can be defined as the inverse cerebrovascular resistance or the inverse of the resistance area product.[11] Similar to the coronary circulation,[19] flow in the cerebral vascular bed

seems to be regulated by 2 factors: CCP (back pressure) and slope ("resistance proper"). We should, however, caution that in a normal physiological state the relative contribution of each factor could be different than for the present data.

The CCP levels reported in this study were much higher than the cerebral venous sinus pressures and the intracranial pressure. For obvious reasons, we had no direct access to the intracranial pressure, but there were no indications that it was abnormal. Moreover, the CCP fell markedly during hyperemia. The vasodilation in the post-VF phase would have caused a substantial increase in intracranial pressure if it had been elevated. Weyland et al[17] had access to intracranial pressure recordings, and they showed that the CCP increased during vasoconstriction despite a decrease in intracranial pressure.

The CCP in the present series was also higher than previously reported.[13,15–17] This may possibly be explained by an increased cerebral vascular tone during the procedures. The low flow velocity (less than half the normal value, while the ABP was only slightly lower than normal) indicated vasoconstriction. Probably the vasoactive effects were caused mainly by the induced hypocapnia. Any effects of medication and/or anesthetic agents would have been overridden by the strong vasoconstrictive influence of an end-tidal P_{CO_2} of 24 mm Hg. With all the interventions/medications necessary for this type of validation study, the values found should not be considered "normal physiological values" of CCP.

While the results of this report are encouraging with respect to methodological aspects, further studies are necessary to establish normal values. In such studies, if radial artery ABP recordings are used, filtering of the data by Fourier transform techniques should produce estimates of CCP that are closely correlated to the gold standard method of CCP determination with the use of prolonged diastoles. It would also be of interest to study whether CCP can be assessed with sufficient accuracy by entirely noninvasive means, without having to use invasive ABP measurements.

Acknowledgment

References

1. Early CB, Dewey RC, Pieper HP, Hunt WE. Dynamic pressure-flow relationships of brain blood flow in the monkey. *J Neurosurg*. 1974;41: 590–596.
2. Dewey RC, Pieper HP, Hunt WE. Experimental cerebral hemodynamics: vasomotor tone, critical closing pressure, and vascular bed resistance. *J Neurosurg*. 1974;41:597–606.
3. Burton AC. On the physical equilibrium of the small blood vessels. *Am J Physiol*. 1951;164:319–329.
4. Bellamy RF. Diastolic coronary artery pressure-flow relations in the dog. *Circ Res*. 1978;43:92–101.
5. Giller CA, Bowman G, Dyer H, Mootz L, Krippner W. Cerebral arterial diameters during changes in blood pressure and carbon dioxide during craniotomy. *Neurosurgery*. 1993;32:737–741.
6. Giller CA, Aaslid R. Estimates of pulse wave velocity and measurement of pulse transit time in the human cerebral circulation. *Ultrasound Med Biol*. 1994;20:101–105.
7. Lindegaard K-F, Lundar T, Wiberg J, Sjøberg D, Aaslid R, Nornes H. Variations in middle cerebral artery blood flow investigated with noninvasive transcranial blood velocity measurements. *Stroke*. 1987;18: 1024–1030.
8. Newell DW, Aaslid R, Lam A, Mayberg TS, Winn HR. Comparison of flow and velocity during dynamic autoregulation testing in humans. *Stroke*. 1994;25:793–797.
9. Aaslid R. Cerebral hemodynamics. In: Newell DW, Aaslid R, eds. *Transcranial Doppler*. New York, NY: Raven Press; 1992:49–55.
10. Panerai RB, Coughtrey H, Rennie JM, Evans DH. A model of the instantaneous pressure-velocity relationships of the neonatal cerebral circulation. *Physiol Meas*. 1993;14:411–418.
11. Panerai RB, Kelsall AW, Rennie JM, Evans DH. Estimation of critical closing pressure in the cerebral circulation of newborns. *Neuropediatrics*. 1995;26:168–173.
12. Michel E, Zernikow B, von Twickel J, Hillebrand S, Jorch G. Critical closing pressure in preterm neonates: towards a comprehensive model of cerebral autoregulation. *Neurol Res*. 1995;17:149–155.
13. Richards HK, Czosnyka M, Pickard JD. Assessment of critical closing pressure in the cerebral circulation as a measure of cerebrovascular tone. *Acta Neurochir (Wien)*. 1999;141:1221–1227.
14. Dawson SL, Panerai RB, Potter JF. Critical closing pressure explains cerebral hemodynamics during the Valsalva maneuver. *J Appl Physiol*. 1999;86:675–680.
15. Panerai RB, Deverson ST, Mahony P, Hayes P, Evans DH. Effects of CO_2 on dynamic cerebral autoregulation measurement. *Physiol Meas*. 1999; 20:265–275.
16. Czosnyka M, Smielewski P, Piechnik S, Al-Rawi PG, Kirkpatrick PJ, Matta BF, Pickard JD. Critical closing pressure in cerebrovascular circulation. *J Neurol Neurosurg Psychiatry*. 1999;66:606–611.
17. Weyland A, Buhre W, Grund S, Ludwig H, Kazmaier S, Weyland W, Sonntag H. Cerebrovascular tone rather than intracranial pressure determines the effective downstream pressure of the cerebral circulation in the absence of intracranial hypertension. *J Neurosurg Anesthesiol*. 2000;12:210–216.
18. Dole WP, Bishop VS. Influence of autoregulation and capacitance on diastolic coronary artery pressure-flow relationships in the dog. *Circ Res*. 1982;51:261–270.
19. Dole WP, Richards KL, Hartley CJ, Alexander GM, Campbell AB, Bishop VS. Diastolic coronary artery pressure-flow velocity relationships in conscious man. *Cardiovasc Res*. 1984;18:548–554.
20. Hoffman JIE, Spaan JAE. Pressure-flow relations in the coronary circulation. *Physiol Rev*. 1990;70:331–389.
21. Jin XY, Gibson DG, Pepper JR. The effects of cardioplegia on coronary pressure-flow velocity relationships during aortic valve replacement. *Eur J Cardiothorac Surg*. 1999;16:324–330.
22. O'Rourke MF, Nichols WW. *McDonald's Blood Flow in Arteries: Theoretical, Experimental and Clinical Principles*. London, UK: Arnold Publishers; 1998:187–190.
23. Aaslid R, Lundar T, Lindegaard K-F, Nornes H. Estimation of cerebral perfusion pressure from arterial blood pressure and transcranial Doppler recordings. In: Miller JD, Teasdale GM, Rowan JO, Galbraith SL, Mendelow AD, eds. *Intracranial Pressure VI*. Berlin, Germany: Springer-Verlag; 1986:226–229.
24. Aaslid R, Brubakk AO. Accuracy of an ultrasound Doppler servo method for noninvasive determination of instantaneous and mean arterial blood pressure. *Circulation*. 1981;64:753–759.
25. Aaslid R, Newell DW, Stooss R, Sorteberg W, Lindegaard K-F. Assessment of cerebral autoregulation dynamics from simultaneous arterial and venous transcranial Doppler recordings in humans. *Stroke*. 1991; 22:1148–1154.