Editorial

Validity of Cerebral Arterial Blood Flow Calculations From Velocity Measurements

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It is obvious that a noninvasive technique that can provide continuous measurements of blood flow through a cerebral artery would be very valuable for clinical and investigative purposes. The most promising approach to the development of such a technique involves the use of ultrasound for the measurement of blood flow velocity. Since blood flow through a vessel is equal to the instantaneous average velocity times the cross-sectional area of the vessel, monitoring of velocity and vessel caliber provides the essential measurements that are needed to estimate blood flow. Busija et al[1] showed that such a method is both accurate and useful. They measured blood flow velocity in a cerebral artery in cats and dogs with an ultrasonic Doppler probe placed around the artery, and simultaneously they measured vessel diameter by direct visualization. They found that blood flow calculated from the velocity and vessel caliber correlated exceedingly well with blood flow measured directly with radioactive microspheres.

In this issue of *Stroke*, Aaslid and his colleagues[2] measured blood flow velocity in the middle cerebral artery of human volunteers to investigate the responses of cerebral blood flow to rapid decreases in arterial blood pressure. The approach developed by these authors involves certain important assumptions that can have a critical influence on the validity of the results. I examine the soundness of these assumptions and their potential consequences on the usefulness of the technique.

Two important features of the method used by Aaslid et al[2] should be borne in mind. First, these authors did not measure vessel caliber, and they assumed that the middle cerebral artery had a constant cross-sectional area throughout the interventions they used. Second, they did not measure average velocity through the middle cerebral artery but maximum velocity. The authors justified their assumption of an unchanging vessel caliber in the face of a sharp reduction in blood pressure on two grounds. First, the authors claimed that there was no significant change in Doppler signal power; theoretically, this variable should be proportional to the cross-sectional area of the vessel.[3] Values for Doppler signal power were given for normocapnia and hypocapnia only during the fourth second after the onset of hypotension. In the case of normocapnia, there was a mean±SEM decrease in Doppler signal power of 2.55±1.2%, which gives a t value of 2.13. Since 10 subjects, that is, 9 degrees of freedom, were involved, this decrease is significantly different from 0 at the 5% level (by one-tailed t test), contrary to what the authors state in their article. It is true that during hypocapnia the change in Doppler signal power was not significant, but one does not know what happened earlier. A second argument in their assumption of unchanging vessel caliber was that any changes in the caliber of the middle cerebral artery would be expected to be small. It is well known that in both humans and animals, in the steady state during reductions in blood pressure, there is a change in the caliber of large cerebral arteries, but it is also true that this change is relatively small, in general <5%.[4-7] Such changes in vessel radius represent much larger changes in cross-sectional area because of the quadratic relation between radius and area. For example, a 5% increase in vessel radius is equivalent to a 10% increase in cross-sectional area. A 10% increase in vessel radius would correspond to a 21% increase in cross-sectional area. The errors introduced by the assumption of unchanging vessel caliber may, therefore, be significant, although perhaps acceptable.

The substitution of maximum velocity for average velocity was justified by Aaslid et al[2] on the grounds that these two variables correlate in the femoral artery and that the blood flow velocity profile in the carotid artery would be expected to be relatively flat. It is not known how the relation between maximum and mean blood flow velocities changes with sharp changes in blood pressure or with alterations in vessel caliber. The only thing one can say is that there may be errors, perhaps of significant magnitude, introduced by this assumption.

It is clear that the method used by Aaslid et al[2] deviates significantly from the theoretically pre-

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scribed method of calculating blood flow from velocity measurements. It is, therefore, important to find out whether the accuracy of the technique can be verified empirically. In an earlier article,[8] these authors attempted to validate this technique by comparing velocity measured in the middle cerebral artery to blood flow measured directly with a flowmeter placed on the internal carotid artery in patients undergoing carotid endarterectomy. They assumed that blood flow in the middle cerebral artery would be a constant proportion of the blood flow in the internal carotid artery. To provide a practical estimate of blood flow, the relation between velocity and blood flow must be linear and the percent change in velocity must be related to the percent change in blood flow with an intercept of 0 and a slope of 1. None of these three conditions was attained. The relation between velocity and blood flow indicated by an electromagnetic flowmeter was curvilinear; however, the authors assumed a linear relation on the grounds that the coefficient of the quadratic term was relatively small and could be ignored without significant error.[8] The slope of the relation between the percent change in velocity and the percent change in blood flow was >1, and the intercept was significantly different from 0. However, the correlations they observed between velocity and blood flow were high. One may, therefore, conclude that changes in maximum velocity in patients of the type studied by these authors and under the conditions of these experiments might be useful as a measure of changes in blood flow.

Let us now consider the application of the same approach to the estimation of blood flow and the exploration of autoregulatory adjustments to changes in blood pressure by Aaslid et al.[2] In the experiments done during normocapnia shown in their Figure 2, most of the reduction in blood pressure was achieved in 1 second. Subsequently, blood pressure stayed relatively low for approximately 3–4 seconds and then began rising. The calculated cerebral blood flow showed a decrease less pronounced than the blood pressure decrease. As a result, the calculated cerebral vascular resistance decreased, showing a 9% decrease at the end of 2 seconds and a 13% decrease at the end of 3 seconds. These decreases in cerebral vascular resistance mean that there must have been significant dilation of the cerebral vessels within 1–2 seconds. These responses are much faster than the reported responses of cerebral vessels to arterial hypotension. In anesthetized cats, arterial hypotension caused significant dilation of cerebral arterioles and arteries, with a mean delay of 5.2 seconds, when the decreases in blood pressure were sharp and pronounced.[5] More slowly developing or less pronounced decreases in arterial blood pressure were associated with more delayed dilation.[5] It is difficult, therefore, to accept that active changes in vessel caliber in response to arterial hypotension occurred as rapidly as Aaslid et al[2] assert. A more likely explanation is that passive changes in vessel caliber occurred as a result of the decrease in blood pressure but were ignored. In fact, with sharp and pronounced decreases in blood pressure in experimental animals, there are passive decreases in vessel caliber that can be as large as 10% of the baseline values.[5] These passive changes in caliber do not involve active changes in the contractile activity of vascular smooth muscle and, therefore, can take place without delay. Recall that during normocapnia in the individuals studied by Aaslid et al[2] there was a significant decrease in Doppler signal power during the fourth second of hypotension, suggesting a decrease in vessel caliber. If this represents the passive decrease expected during hypotension, one would reasonably surmise that the decrease would have been even more pronounced earlier. If such a change in caliber occurred but was ignored, then the calculated blood flows are overestimates and the vascular resistances are underestimates. For example, in the second second during hypotension, a 3% decrease in the caliber of the middle cerebral artery, equivalent to a 6% decrease in cross-sectional area, would be sufficient to eliminate the calculated decrease in vascular resistance reported during normocapnia. I believe this is a more likely explanation for the observations made by Aaslid et al.[2] The first few seconds of the period during which the observations were made are likely to have been dominated by these passive phenomena. Therefore, the slopes that Aaslid et al calculated have nothing to do with the rate of autoregulation of the cerebral vascular bed. It is possible that autoregulation may have had an effect later and, perhaps, may have accounted for the secondary increase in blood flow velocity they observed as the blood pressure returned to baseline. The variation in the slopes they recorded with changes in the prevailing $Paco_2$ may have had to do with the degree of filling of the vascular bed rather than with the capacity of the vessels to autoregulate.

Regardless of the appropriateness of the method used for measuring or calculating cerebral blood flow, there are important conceptual problems in the specific application used in the experiments of Aaslid et al.[2] Consider what happens to the blood flow through any vascular bed when there is a sudden marked decrease in arterial blood pressure. Arterial inflow would decrease, but this decrease in blood flow would not occur instantaneously along the entire bed. The decrease in outflow, for example, will not occur until some time later.[9] Since outflow exceeds inflow for a period of time, the volume of blood in the vascular bed is reduced. When the arterial blood pressure is restored to its previous level, there is usually a reactive hyperemia, which will occur first in the artery and then in the vein. The excess blood flow during this hyperemia in the artery would be greater than that in the vein because part of the increased flow would be used to replace the volume of blood in the vascular

bed that was depleted during the period of hypotension.[9] If one were to calculate vascular resistance under these conditions, what is the appropriate blood flow that should be used in the calculation? The arterial inflow, the venous outflow, or some other measure of blood flow?

This difficulty illustrates the problems created when the conceptual model on which we base our interpretations is not appropriate for the experimental conditions we wish to investigate. The utility of changes in vascular resistance calculated by dividing the pressure drop across the vascular bed by the blood flow arises from the fact that we can use these changes to infer what happens to blood vessels. If vascular resistance is increasing, we conclude that the blood vessels are constricting; if vascular resistance is decreasing, we decide that the blood vessels are dilating. These relations apply only to conditions of steady flow in which there is no acceleration or deceleration of the blood. In the unsteady state, when there are rapid changes in blood pressure and blood flow, there are significant capacitance and inertial factors that render the interpretation of changes in vascular resistance less secure and, at times, misleading.

In conclusion, techniques for calculating cerebral blood flow based on the measurement of blood flow velocity in arterial vessels hold promise for providing useful measurements of blood flow to the brain for both clinical and investigational purposes. The accurate calculation of cerebral blood flow should be based on measurements of average blood flow velocity through the vessel as well as vessel caliber to calculate cross-sectional area. At present, applications based exclusively on the measurement of blood flow velocity represent risky shortcuts. They might provide useful approximations under steady-state conditions, in situations in which it is known that caliber changes in the vessel in which the velocity is measured are relatively small. Under conditions of rapidly changing blood flows and blood pressures, the results of such techniques are of doubtful value and may be misleading.

References

1. Busija DW, Heistad DD, Marcus ML: Continuous measurements of cerebral blood flow in anesthetized cats and dogs. *Am J Physiol* 1981;241:H228–H234
2. Aaslid R, Lindegaard K-F, Sorteberg W, Nornes H: Cerebral autoregulation dynamics in humans. *Stroke* 1989;20:45–52
3. Arts MGJ, Roevros JMJG: On the instantaneous measurement of bloodflow by ultrasonic means. *Med Biol Eng* 1972; 10:23–34
4. Heistad DD, Marcus AL, Abboud FM: Role of larger arteries in regulation of cerebral blood flow in dogs. *J Clin Invest* 1978;234:H371–H383
5. Kontos HA, Wei EP, Navari RM, Levasseur JE, Rosenblum WI, Patterson JL Jr: Responses of cerebral arteries and arterioles to acute hypotension and hypertension. *Am J Physiol* 1978;234:H371–H373
6. Harder DR: Pressure-dependent membrane depolarization in cat middle cerebral artery. *Circ Res* 1984;55:197–202
7. Radü EW, duBoulay GH: Paradoxical dilation of large cerebral arteries in hypocapnia in man. *Stroke* 1976;7:569–572
8. Lindegaard KF, Lundar T, Wiberg J, Sjoberg D, Aaslid R, Nornes H: Variations in middle cerebral artery blood flow investigated with noninvasive transcranial blood velocity measurements. *Stroke* 1987;18:1025–1030
9. Kontos HA, Mauck HP Jr, Patterson JL Jr: Mechanism of reactive hyperemia in limbs of anesthetized dogs. *Am J Physiol* 1965;209:1106–1114

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