Comparison of Flow and Velocity During Dynamic Autoregulation Testing in Humans

David W. Newell, MD; Rune Aaslid, PhD; Arthur Lam, MD; Teresa S. Mayberg, MD; H. Richard Winn, MD

Background and Purpose We compared relative changes in middle cerebral artery velocity and internal carotid artery flow during autoregulation testing to test the validity of using transcranial Doppler recordings of middle cerebral artery velocity to evaluate cerebral autoregulation in humans.

Methods Seven human volunteers had dynamic autoregulation tested during surgical procedures that included exposure of the internal carotid artery. The mean arterial blood pressure and middle cerebral artery velocity spectral outline (V_max), using transcranial Doppler, and ipsilateral internal carotid artery flow, using an electromagnetic flowmeter, were continuously and simultaneously recorded during transient sharp decreases in blood pressure that were induced by rapid deflation of thigh blood pressure cuffs. The resulting responses of velocity in the middle cerebral artery and flow in the internal carotid artery were compared.

Results Moderate decreases in blood pressure evoked responses in cerebral autoregulation. There were no significant (P=0.97) differences between the responses in middle cerebral artery velocity and internal carotid artery flow to the blood pressure decreases.

Conclusions Relative changes in V_max accurately reflect relative changes in internal carotid artery flow during dynamic autoregulation testing in humans. Therefore, alterations in middle cerebral artery diameter do not occur to the extent that they introduce a significant error in making these comparisons.

Key Words • autoregulation • carotid arteries • cerebral arteries • ultrasonics

Cerebral autoregulation has been defined as the ability to maintain a constant cerebral blood flow despite a changing cerebral perfusion pressure.1,2 The capacity for the human brain to regulate its blood flow was first demonstrated by performing repeated static measurements of brain perfusion at different blood pressures, thereby establishing the range of blood pressures in which this mechanism was effective.3 Most subsequent studies of autoregulation in humans, including those concerning disordered cerebral autoregulation, have used a similar static methodology using 133Xe.1,4,5

In contrast to static blood flow techniques, Aaslid et al6 described a new methodology to evaluate dynamic cerebral autoregulation in humans using transcranial Doppler (TCD). The TCD method measures relative changes in blood flow velocity, reflecting relative changes in cerebral blood flow, through the middle cerebral artery (MCA) during a rapid change in systemic blood pressure induced by the rapid deflation of thigh blood pressure cuffs. Dynamic autoregulation testing using TCD has two advantages compared with previous methods used to study the autoregulatory response: first, TCD allows continuous measurement of the autoregulatory response, which is not possible using the static measurement technique; second, it is noninvasive and does not require any medications to change the blood pressure. From a cybernetics viewpoint, a regulatory system such as the cerebral autoregulation is most thoroughly evaluated by introducing a stepwise disturbance to create an error signal and then observing the rapidity and the effectiveness of the response.7 Such an analysis, however, requires a continuous blood flow method that allows instantaneous analysis of changes in cerebral blood flow. Both TCD and electromagnetic flowmetry can provide such information.

The present study was designed to test the hypothesis that changes in the MCA velocity do not vary significantly from changes in internal carotid artery (ICA) blood flow during transient acute changes in systemic blood pressure. We compared changes in volume flow in the ICA with changes in MCA velocity spectral outline (V_max) during stepwise changes in blood pressure sufficient to induce a cerebral autoregulatory response. We also review here the rationale for using V_max instead of the other spectral indices to measure relative blood flow changes during autoregulation testing.

Subjects and Methods

Patients (n=7) selected for this study were individuals scheduled to undergo surgical exposure of the ICA either for carotid endarterectomy (CEA) (5 patients) or for proximal control of the carotid artery during aneurysm surgery (2 patients). The characteristics of the participants in the study are shown in the Table. All patients were under general anesthesia (isofluorane 0.5% to 1.0%) during the testing. All patients had recent computed tomographic scans before participation in the study, and no major cerebral infarctions were revealed. All patients also underwent recent cerebral angiography, and no patient demonstrated evidence of atherosclerosis or stenosis of the MCA. The 2 patients who underwent aneurysm surgery had unruptured aneurysms clipped. One of the patients had no history of subarachnoid hemorrhage. The

Received August 13, 1993; final revision received November 9, 1993; accepted January 6, 1994.

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was used as the first time point to calculate the beginning of the stepwise change in mean ABP was averaged and used as a baseline. The 5-second average baseline values for the MCA velocity and ICA flow were normalized to 100% and used to calculate a percent change over time for these parameters during each autoregulation test. The lowest blood pressure, of ABP, MCA velocity, and ICA flow immediately before the escape. This process was repeated four times for each patient. Continuously recorded arterial blood pressure (ABP) signals were obtained using intra-arterial catheters and transducers.

The data were analyzed using a custom software program to access the previously recorded signals. Each 5-second interval of ABP, MCA velocity, and ICA flow immediately before the stepwise change in mean ABP was averaged and used as a baseline. The 5-second average baseline values for the MCA velocity and ICA flow were normalized to 100% and used to calculate a percent change over time for these parameters during each autoregulation test. The lowest blood pressure, which occurred between 1 and 3 seconds after the cuff release, was used as the first time point to calculate the beginning of the response. The data from 20 subsequent 1-second intervals of each parameter (ABP, MCA velocity, and ICA flow) were then averaged for each test (Fig 2). These average values of all of the tests for each of the three different parameters from every time point, including the baseline and the subsequent 21 1-second intervals, were then analyzed. Four tests on each patient were reviewed, and 2 tests (on different patients) were excluded because the blood pressure drop occurred over a 5- to 6-second interval. The data from each parameter in the remaining 26 tests were averaged for each time point during the test. The ICA flow and MCA velocity data were then statistically compared using the repeat-measure ANOVA model, testing the interaction between the two measures and time, which is used to determine if the difference between the measures is constant over time. The ANOVA model also was used to test the difference between the two measures. The data also were treated as if coming from 7 different patients, every patient having repeat measurements. All results are given as the mean values at each time point for all the tests. Linear regression analysis was performed between the group average change in ICA flow and change in MCA velocity during the test interval, including the baseline values. To examine the variability between patients, analysis was performed of the

<table>
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<td>CEA</td>
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<td>M</td>
<td>Right carotid stenosis</td>
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<td>66</td>
<td>M</td>
<td>Left carotid stenosis</td>
<td>CEA</td>
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CEA indicates carotid endarterectomy; M, male; and F, female.
Results

The baseline average mean ABP (the 5-second interval before the drop) was 100.1 mm Hg, and after the drop it was 82.4 mm Hg, yielding an average drop of 17.7 mm Hg. The baseline average velocity (time-averaged mean) in the MCA trunk was 41.3 cm/s and was reduced to 80.2% of this value by the blood pressure drop. The baseline flow in the proximal ICA was 381.5 mL per minute and fell to 80.3% of this value as a result of the blood pressure drop. The average changes in mean ABP during the 26 autoregulation tests are illustrated in Fig 3, top left, and the responses of MCA velocity and ICA flow are illustrated in Fig 3, top right. Repeat-measure ANOVA revealed no change in the difference between MCA velocity and ICA flow over time (P =.0000). Repeat-measure ANOVA without interaction showed no significant difference between the two measurements (P =.97). Linear regression analysis between the group averages of percent ICA flow change and percent MCA velocity change over the time interval studied revealed a close linear relation (r =.995; P <.001; y =5.6 +.94x).

Analysis of the average ratio between MCA velocity and ICA flow of the 7 patients for all time points during the test is illustrated in Fig 3, bottom. The standard deviation of the values for the 7 individual patients is also given.

Discussion

In the present study we compared the temporal changes in MCA velocity measured by TCD with changes in ICA flow measured by electromagnetic flow.
metry during transient decreases in blood pressure. The temporal responses in MCA velocity and ICA flow did not differ. Thus, the results provide evidence that the $V_{\text{max}}$ in the MCA trunk can be used to accurately reflect relative changes in blood flow in the human cerebral circulation caused by a nonpharmacologically induced moderate step change in blood pressure, supporting earlier observations of Aaslid et al.\textsuperscript{6} Moreover, the identical temporal response of MCA velocity ($V_{\text{max}}$) and the ICA flow indicates stability of the following three parameters: the diameter of the MCA trunk, the MCA velocity profile, and the perfusion territory of the MCA relative to the ICA.\textsuperscript{9,10}

Before accepting the conclusion that the MCA diameter remains static during the autoregulatory testing described, several methodological aspects of our study need to be addressed. First, although we recorded changes in the cerebral circulation at two different sites (MCA and ICA), the majority of flow through the ICA is distributed to the MCA territory under normal circumstances. Thus, our observation that there was no difference between the measurements at the two sites indicates that the MCA velocity may be useful to estimate ICA flow changes during autoregulation. Second, we used a selected population (average age, 62 years) that may not represent the general population. Moreover, the MCAs of this older population may have been less responsive because of atherosclerosis. None of the patients, however, had evidence of atherosclerosis in the MCAs by either angiography or TCD. Both patients undergoing aneurysm surgery had unruptured aneurysms clipped and had no evidence of vasospasm. We therefore believe that these findings apply to the general population. In an earlier study, we used a younger cohort (average age, 33 years) with no evidence of atherosclerosis and also showed no evidence of MCA diameter changes during autoregulation testing.\textsuperscript{11}

The validity of using TCD for determining dynamic autoregulation in humans has been questioned\textsuperscript{12} because the autoregulation responses observed in humans using this method\textsuperscript{4} were faster than pial artery responses to acute hypotension demonstrated experimentally in cats.\textsuperscript{13} It was speculated that the MCA diameter may change during a step change in blood pressure, and thus the responses seen in MCA velocity may “have nothing to do with the rate of autoregulation of the cerebral vascular bed.”\textsuperscript{12} However, subsequent clarification indicated that the autoregulatory response in cats did begin after a similar latency period as was seen in humans using the TCD method,\textsuperscript{14} thereby making it unnecessary to invoke an alternative explanation for the responses seen in MCA velocity. It was also contended that the use of $V_{\text{max}}$, or the spectral outline velocity, as an index of relative blood flow change represents a “risky shortcut.”\textsuperscript{12} To address these criticisms, we review the TCD methodology and the rationale for using $V_{\text{max}}$ as an index to measure relative flow changes to assess the autoregulatory response.

Velocity is the parameter used in Doppler ultrasonography applications and is obtained by recording frequency shifts in ultrasound reflected from flowing blood. These frequency shifts are then coded by spectral analysis and can be used to display the range of flow velocities that normally occur. Under normal conditions in a relatively straight artery, a number of different frequency shifts occur during laminar flow because of the parabolic flow profile. These different frequency shifts are displayed on the spectrum analyzer as different velocities. Many Doppler instruments allow the user to display a “true mean” velocity and also a spectral outline or $V_{\text{max}}$. The true mean velocity is derived from average weighting of all the spectral signals from a cross section of the artery being recorded. The true mean includes the high-velocity signals at the center of the artery and the low-velocity signals near the walls. The spectral outline velocity, or $V_{\text{max}}$, is obtained by assigning an outline to the spectral tracing, thereby reflecting only the maximum velocities occurring at the central portion of the artery. A change in flow will produce proportional changes in $V_{\text{max}}$ and true mean, in the absence of any disturbance in the velocity profile.\textsuperscript{10}

Blood flow through an artery can be estimated by calculating the product of the true mean velocity and the cross-sectional area of the artery. This verified method has been used to measure blood flow in arteries of experimental animals,\textsuperscript{12} where active vessel diameter changes occur and are involved in the regulation of cerebral blood flow. TCD can also be used to estimate blood flow changes in the MCA in humans using a similar principle. The true mean velocity can be measured, and the reflected power of the ultrasound can be used as an index of MCA diameter. An index of relative flow can be obtained that would theoretically be unaffected by any transient diameter changes in the artery that is being insonated. Therefore, a transient decrease in arterial diameter caused by vasoconstriction, insufficient to affect flow, would cause the velocity to increase and the reflected power to decrease because of a reduction in cross-sectional area. Because the flow index is a product of the two measurements, this value would remain unchanged. We used this index previously in a set of experiments to validate the original observations of autoregulation.\textsuperscript{11} This approach has also been advocated by other investigators.\textsuperscript{15,16}

There are major disadvantages, however, of using a flow index derived from the true mean and reflected power for routine TCD recordings and autoregulation testing. A very high signal-to-noise ratio is needed to provide useful measurements, and most importantly, any small movement of the sample volume that is focused on the artery can cause a change in reflected power, which would give an erroneous reading of a change in flow. A similar movement of the sample volume would have little or no effect on $V_{\text{max}}$, which is a much more stable parameter than the true mean (Fig 4). If it can be established, as it has been in this study and in our previous study, that the MCA diameter does not change to a significant extent during the conditions of the test, the use of $V_{\text{max}}$ is not a risky shortcut\textsuperscript{12} but in fact a more reliable index of relative flow change. It must also be stated, however, that for each application where this measure is used, validation that a change in the MCA diameter does not produce an unacceptable error should be obtained. It has been demonstrated, for example, that certain pharmacologic interventions may induce disparities in flow and velocity, presumably due to effects on MCA diameter,\textsuperscript{17} and others may not.\textsuperscript{18} Moreover, recent direct observations of the MCA during cranietomy indicate that the diameter of this artery may change very slightly (2.5%) because of pharmacoc-
logically induced blood pressure changes that were considerably greater than the ones induced in our study. This degree of change, however, will probably not cause an unacceptable discrepancy between velocity and flow for most applications.

The TCD method may have many useful applications in the study of autoregulation in humans in normal as well as in pathological states. Further development of noninvasive methodologies for continuous ABP recording make the method completely noninvasive. The introduction of multichannel Doppler equipment with bilateral monitoring capability permits simultaneous testing of both cerebral hemispheres, making comparisons much more accurate. Further study is needed to compare dynamic autoregulation values obtained using this method to those values obtained using static cerebral blood flow methods. The ease and availability of this method, however, is certain to lead to the gathering of much needed information on cerebral autoregulation and its disorders in humans.

Acknowledgments

This study was supported in part by a National Stroke Association award and by National Institutes of Health 1 P50 NS-30305-01 (Dr Newell). Dr Newell is the recipient of a Clinician Investigator Development Award 1K08 NS-015969-01. The authors would like to thank Colleen Douville and Sheila Byrd for their assistance in performing Doppler examinations and data collection. We also wish to thank Dr Steven Nichols for referring one of the patients who participated in the study.

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Stroke. 1994;25:793-797
doi: 10.1161/01.STR.25.4.793

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