Transcranial Doppler pulsatility in vasodilation and stenosis

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Although blood velocity in the major intracranial vessels is readily measured with transcranial Doppler ultrasound (TCD), the interpretation of velocity changes is by no means straightforward. For example, a velocity increase can arise from either a local stenosis or a decrease in downstream resistance, and these mechanisms have contradictory implications for blood flow. To determine whether TCD pulsatility might distinguish these two mechanisms, Doppler ultrasonic readings were taken from an artificial vascular model under conditions of either stenosis or distal dilation. In addition, TCD studies of nine patients with unihemispheric arteriovenous malformations (AVM's) and 16 TCD studies of seven patients with unihemispheric aneurysmal vasospasm were reviewed, and pulsatility of the AVM's (representing decreased resistance) were compared with those of the vasospastic vessels (representing stenosis).

The average percentage drop in pulsatility in the vasodilated configuration of the model/percentage increase in velocity was 0.38 ± 0.08 (± standard error of the mean), while that for stenosis was 0.20 ± 0.01. Similar comparisons of the patient population yielded 0.67 ± 0.16 for the AVM group and 0.26 ± 0.04 for the vasospasm group. These differences were significant (p < 0.05). The fall in pulsatility associated with a given increase in velocity is significantly greater when the velocity increase arises from diminished downstream resistance than from stenosis.

KEY WORDS: stenosis, arterial, vasodilation, pulsatility, hemodynamics, ultrasound, Doppler velocimetry

TRANSCRANIAL Doppler ultrasound (TCD) has recently emerged as a useful method of assessment of cerebral hemodynamics.1-3,5,12 This non-invasive technique allows the measurement of blood velocity in the major intracranial vessels by means of ultrasound signals transmitted through bone. These studies can be performed rapidly and repeated, and have been used to investigate the hemodynamics of a variety of disease states including aneurysmal vasospasm,1,2,12,33 stroke,11,21,32,36 arteriovenous malformations (AVM's),13,14 and brain death.31

Despite this experience, TCD data can be difficult to interpret since measurements of blood velocity bear no direct relationship to those of flow. The interpretation of even a simple elevation in blood velocity may not be straightforward. Such an elevation may be due to either a stenosis at the insonation site6,7,20,34,39,40 or a decrease in downstream resistance as occurs in pial vasodilation or in the feeding system of AVM's.22,25,28,30,38 The former case is often associated with a decrease in flow, while in the latter case flow is usually elevated. These two interpretations of increased velocity have opposite implications for cerebral blood flow (CBF) and therefore may lead to different clinical decisions based on the TCD study. One might hope, however, that other information contained in the TCD waveform would distinguish these differing circumstances.

The TCD waveform is a graph of peak velocity plotted against time (Fig. 1).1,3,12 The shape of this waveform can be measured by the Gosling pulsatility method, defined as systolic minus diastolic velocity divided by mean velocity.1,3,12 A waveform with a rounded shape will have a lower pulsatility than a peaked waveform. Unfortunately, diminished pulsatility is induced both by stenosis6,7,20,34,39,40 and by a decrease in downstream resistance,22,25,28,30,38 and so cannot be used to distinguish these two causes of increased velocity.

It has been our clinical impression, however, that the magnitude of pulsatility decrease is greater at a given velocity for vasodilation than for stenosis, and might therefore indicate the mechanism of increased velocity. The purpose of this report is to support that impression based on a laboratory model of a vascular tree segment.
FIG. 1. Normal transcranial Doppler sonogram showing the waveform of middle cerebral artery velocity.

as well as the review of a series of patients with aneurysmal vasospasm (for stenosis) and AVM's (for decreased resistance).

Materials and Methods

Laboratory Model

A model of a vascular tree segment was constructed from Silastic intravenous tubing, consisting of a 4-cm straight segment ending in a single bifurcation. The inner diameter of the tubing was 2.5 mm. Fluid flowed into the straight segment by gravity from an overhead reservoir. Pulsatile flow was created at 60 cycles/min by means of a balloon encircling the tubing proximal to the straight segment, which was intermittently inflated by an animal ventilator* so as to narrow the tubing. Adjustments of ventilator parameters permitted appropriate modifications of the flow waveform.

The fluid used in the model was made by adding 3 gm of domestic cornstarch to 1 liter of water. This solution was chosen since it is readily available and is a colloid solution with non-Newtonian properties similar to those of blood. The 3 gm of cornstarch produced enough microparticles to be visible to the Doppler ultrasound system when in motion, and provided a viscosity equal to that of blood (see below).

A 2-MHz Doppler probe connected to a TCD device† was mounted at a 30° angle to the model axis and focused on the midportion of the straight segment (Fig. 2). An adjustable metal clamp was placed on the straight segment 5 mm proximal to the insonation site to create a stenosis and on each distal bifurcation branch to provide downstream resistance. Three configurations were studied (Figs. 2 and 3). A baseline configuration was made by placing clamps only on the distal branches and adjusting the clamps to yield a TCD velocity of 14 to 25 cm/sec. A vasodilated configuration was created by loosening these distal clamps to obtain a velocity increase of 100%, 130%, or 250%. The stenosis configuration was created by setting the distal clamps to their original position and adding the proximal clamp to achieve the same velocity increase as the vasodilated configuration (Fig. 3). Each configuration was studied five to 10 times at each level of velocity increase.

The percentage drop in mean pulsatility between the vasodilated and baseline configurations was calculated for each level of velocity increase (Fig. 4). A similar calculation was made for the stenosis configuration, and the pulsatility drops of vasodilation and stenosis configurations were compared at each level of velocity increase (Table 1). The average percentage pulsatility drop/percentage increase in velocity was calculated for the stenosis and vasodilated configurations and compared by a one-tailed t-test.

The viscosity of the colloid solution was obtained by measuring steady flow through a straight tube segment with water manometers, and computing the viscosity from the Poiseuille equation:

\[
flow = \frac{\text{radius}^2 \times \text{pressure drop}}{8 \times (\text{viscosity}) \times \text{length}}.
\]

Different hemodynamic systems can be effectively compared with various standard scaling indices. Pulsatile

* Respirator, Model 665, manufactured by Harvard Apparatus, Millis, Massachusetts.
† Doppler system, Model TC2-64, manufactured by Carolina Medical Electronics, Inc., King, North Carolina.
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**TABLE 1**

<table>
<thead>
<tr>
<th>% Velocity Increase</th>
<th>Vasodilated Configuration†</th>
<th>Stenosis Configuration†</th>
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<tbody>
<tr>
<td>97 ± 2.6</td>
<td>50 ± 2.7</td>
<td>19 ± 4.9</td>
</tr>
<tr>
<td>132 ± 3.7</td>
<td>49 ± 7.8</td>
<td>29 ± 8.4</td>
</tr>
<tr>
<td>256 ± 0.7</td>
<td>61 ± 2.4</td>
<td>44 ± 1.5</td>
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</tbody>
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* Means are presented ± standard errors of the mean.
† Percentage decrease from baseline.

Flow models are often characterized by the Reynolds number: (radius × density × velocity)/viscosity, and by the Womersley number: radius × (2π × frequency)/viscosity², and two systems with identical indices are likely to be hemodynamically similar. The Reynolds and Womersley numbers of our model were calculated from the measured viscosity, velocity, and tube diameter. To account for the probe angle, the velocity was multiplied by cos 30° to obtain true velocity. Based on reported values for blood viscosity and density, it was possible to calculate a real vessel diameter, velocity, and pulse that yielded the same hemodynamic indices as the model. These latter parameters are those of an actual vessel best described by our model.

Data were analyzed with Pearson’s correlation coefficient and one-tailed t-tests.

**Clinical Material**

The records of 19 patients with cerebral AVM’s and 30 patients with aneurysmal vasospasm who received TCD studies during the year previous to the study were examined. Nine of the AVM’s were fed by one middle cerebral artery (MCA) without contralateral MCA contribution, and seven of the aneurysm patients had TCD evidence of vasospasm in only one MCA (velocity ≥ 120 cm/sec) or only one anterior cerebral artery. In four of the aneurysm patients, unilateral vasospasm was confirmed by angiography. Nine TCD studies performed on the nine AVM patients and 16 studies performed on the seven aneurysm patients formed the basis of this analysis, with the AVM studies corresponding to the vasodilated configuration of our artificial model and the vasospasm studies corresponding to the stenosis configuration. Pulsatilities were averaged over four to five heartbeats.

The percentage difference between the AVM feeder and normal contralateral pulsatilities was calculated and plotted against velocity increase. None of the contralateral vessels used for comparison had any angiographic contribution to the AVM. Similar calculations were performed for the vasospasm group (Fig. 5). The contralateral vessels used for comparison in these cases either were of normal caliber (if angiograms were performed at the time of insonation) or had TCD velocities which were in the normal range throughout the hospital stay. Just as for the analysis of the artificial model, the average percentage fall in pulsatility/percentage increase

Fig. 3. Transcranial Doppler sonograms showing waveforms for baseline (left), vasodilated (center), and stenosis (right) configurations of model. The vasodilated waveform is of equal amplitude but lower pulsatility than the stenosis waveform.

Fig. 4. Pulsatility data in the artificial model showing the decreases obtained in the vasodilated and stenosis configurations as a percentage of baseline pulsatility plotted against the degree of velocity increase.
Table 2

<table>
<thead>
<tr>
<th>% Velocity Increase</th>
<th>Arteriovenous Malformation†</th>
<th>Aneurysmal Vasospasm†</th>
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<tbody>
<tr>
<td>≤ 100%</td>
<td>36 ± 6</td>
<td>18 ± 6</td>
</tr>
<tr>
<td>&gt; 100%</td>
<td>46 ± 5</td>
<td>30 ± 2</td>
</tr>
<tr>
<td>no. of cases</td>
<td>19</td>
<td>30</td>
</tr>
</tbody>
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* Means are presented ± standard errors of the mean.
† Percentage decrease from contralateral hemisphere.

Results

Laboratory Model

In the vasodilation model, the mean levels of the three induced velocity increases were 97% ± 2.6%, 132% ± 3.7%, and 256% ± 0.7% (± standard error of the mean) (Table 1). A linear relationship was seen between the percentage fall in pulsatility (as compared to baseline) and the percentage velocity increase, for both the vasodilated ($r^2 = 0.92$) and stenotic ($r^2 = 0.96$) configurations (Fig. 4). Furthermore, the pulsatility drop seen in the vasodilated configuration was significantly larger than that of the stenosis configuration at all levels of velocity increase (Table 1, $p < 0.05$). The average percentage drop in pulsatility/percentage increase in velocity for the vasodilated configuration was 0.38 ± 0.08 (± standard error of the mean), while that for the stenosis configuration was significantly lower at 0.20 ± 0.01 ($p < 0.05$).

When the Doppler ultrasound velocity was 20 cm/sec in our model, the Reynolds and Womersley numbers were the same as in a blood-filled artery of 1.9 mm diameter with a velocity of 30 cm/sec and pulse of 90 beats/min. Therefore, our model best describes a vessel such as the precommunicating segment of the posterior cerebral artery.

Clinical Material

The average percentage drop in pulsatility/percentage increase in velocity (as compared to the contralateral normal vessels) for the patients with AVM was 0.67 ± 0.16, while that for the patients with vasospasm was significantly lower at 0.26 ± 0.04 ($p < 0.05$). When only the patients with angiographically proven vasospasm were included in this calculation, the percentage drop in pulsatility/increase in velocity was even smaller (0.21 ± 0.03) and was again significantly different from the AVM group ($p < 0.01$).

As occurred in the artificial model, the pulsatility drop in the AVM group was significantly larger than that of the vasospasm group at either level of velocity increase ($p < 0.05$). The pulsatility drop also tended to increase at greater velocity increases (difference not significant in AVM group, $p < 0.05$ in vasospasm group).

Discussion

Although TCD has proved useful in the assessment of cerebral hemodynamics, TCD waveforms are difficult to interpret and can be misleading. One reason for this difficulty is that neither flow nor vessel caliber can be directly measured by TCD, and therefore inferences must be based solely on velocity and its waveforms. However, a change in blood velocity can arise from at least two fundamentally different mechanisms: either a local stenosis or a decrease in downstream resistance. Although the clinical setting and angiographic or CBF studies can often suggest the mechanism of increased velocity, it is nevertheless often unclear as to exactly which mechanism applies. A normal angiogram does not eliminate the possibility of vessel narrowing, since a significant velocity increase (such as by 20%) can arise from a small decrease (10%) in lumen diameter which may not be appreciated from a single angiogram. The vessel diameter changes under different conditions, which may add an error of as much as 10% to 15% to velocity measurements. Studies of the CBF may detect vasodilated states, but are relatively insensitive to precritical stenosis and cannot be performed frequently.

Although the TCD velocity may be equally elevated by stenosis or vasodilation, one might hope that the TCD waveform could distinguish the two situations. Pulsatility is a measure of waveform shape, but is unfortunately diminished by both a stenosis or vasodilation. A normal angiogram does not eliminate the possibility of vessel narrowing, since a significant velocity increase (such as by 20%) can arise from a small decrease (10%) in lumen diameter which may not be appreciated from a single angiogram. The vessel diameter changes under different conditions, which may add an error of as much as 10% to 15% to velocity measurements. Studies of the CBF may detect vasodilated states, but are relatively insensitive to precritical stenosis and cannot be performed frequently.

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a decrease in downstream resistance. Furthermore, the pulsatility arises from complex interactions between the blood pressure waveform, properties of the vessel wall, downstream impedance, and reflections along the vascular tree. Although pulsatility can be explicitly predicting in simple models, a priori deduction from measurable clinical parameters is not currently practical. However, pulsatility is readily measurable by TCD, and one might hope that the magnitude of pulsatility drop would distinguish stenosis from vasodilation. The ability to distinguish stenosis from downstream vasodilation on the basis of pulsatility might be helpful in several clinical situations. Velocity increases seen after subarachnoid hemorrhage can be due to either developing vasospasm or reactive pial vasodilation subsequent to ischemia or hypercarbia. Similarly, velocity increases seen after aneurysm clip placement might be due to vessel stenosis induced by the clip or might result from reactive hyperemia following temporary occlusion that may have been necessary for clip placement. Other scenarios in which the precise interpretation of TCD velocity changes would be important are readily conceivable.

In this report we show that the pulsatility drop associated with a decrease in downstream resistance is more pronounced at a given level of velocity increase than for stenosis both in an artificial model of a vascular segment and in review of patients with AVM’s and aneurysmal vasospasm. Resistance and stenosis were explicitly created in the model, while the AVM feeding vessels and spastic arterial segments were taken as paradigms of decreased resistance and stenosis, respectively.

Although a velocity increase is associated with a pulsatility drop for either stenosis or distal vasodilation, the exact relationship between velocity and pulsatility changes is complex. Data from our model suggest that this relationship is nonlinear; that is, a proportional change in velocity is not associated with an equal proportional change in pulsatility. This lack of a simple proportion factor is not surprising in light of the complex factors giving rise to pulsatility as discussed previously.

The artificial model employed pulsatile flow and contained a distal bifurcation in order to include flow reflections, which are known to significantly affect pulsatility. Use of a colloid solution allowed TCD detection of flow, and our colloid solution had measured viscosity identical to that of blood (0.035 poise). Although the flow rates used were somewhat lower than the situation in vivo, Reynolds and Womersley scaling showed that our model best describes a cerebral vessel of 1.9 mm when the pulse is 90 beats/min and velocity is 30 cm/sec, which are parameters very close to those of the proximal posterior cerebral artery.

Despite these design features, the model cannot fully recreate the exact physical conditions in the human cranium, and any extrapolation of results to the in vivo case must made with caution. Indeed, the waveforms generated by our physical model are somewhat different in shape from those seen in clinical practice. However, insofar as the same physical laws apply to cerebral arteries as to artificial tubes, the model suggests that downstream vasodilation will incur a greater fall in pulsatility than will stenosis.

Patients were chosen for review who had both an unaffected and affected hemisphere as revealed by cerebral angiography, and the velocity on the unaffected side was taken as a baseline. The normal and abnormal data were therefore recorded under identical conditions of blood pressure and pCO2. Normative data from TCD studies were not used for comparison because of the known high interindividual variation in TCD velocities. Error may nevertheless have been introduced by hemispheric comparison due to the normal slight interhemispheric asymmetry of velocity as well as the possibility of the normal hemisphere being affected by the contralateral lesion. In addition, the hemodynamics of the vasospastic segments were not purely those of stenosis due to the compensatory downstream vasodilation known to accompany vasospasm. Finally, the mechanical properties of the vessel may change in vasospasm and so induce a further hemispheric asymmetry.

The patients chosen in the vasospasm group were selected on the basis of angiography or TCD criteria. When the smaller group satisfying the more stringent requirement of angiographic spasm was used for calculation, the differences between the AVM and vasospasm were more pronounced. These errors may account for the greater scatter in the clinical data than in the laboratory model, but the greater effect of vasodilation on pulsatility drop was nonetheless significant.

Although the difference in pulsatility drop between the vasodilated and stenotic states is statistically significant, there is a degree of overlap between those two states in both the model and in the clinical review. Accordingly, comparisons of velocity and pulsatility changes are not absolute, and may be most relevant when the pulsatility changes are pronounced or when neither the clinical setting nor radiological studies dictate the mechanism of velocity increase. Pulsatility considerations also may arise since TCD studies are usually performed frequently and so may detect early hemodynamic changes before other more intermittent diagnostic modalities can be performed. Although care must be taken in interpreting results from artificial models and from retrospective series, the agreement between these two very different sources of data is striking and suggests that the demonstrated effects of pulsatility are in fact general properties of the vascular systems studied by TCD.

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References


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