Variations in Middle Cerebral Artery Blood Flow Investigated With Noninvasive Transcranial Blood Velocity Measurements

Karl-Fredrik Lindegaard, MD, Tryggve Lundar, MD, Jan Wiberg, MD, Dag Sjøberg, BSc, Rune Aaslid, PhD, and Helge Nornes, MD

Observations on blood velocity in the middle cerebral artery using transcranial Doppler ultrasound and on the ipsilateral internal carotid artery flow volume were obtained during periods of transient, rapid blood flow variations in 7 patients. Five patients were investigated after carotid endarterectomy. A further 2 patients having staged carotid endarterectomy and open heart surgery were investigated during nonpulsatile cardiopulmonary bypass. The patient selection permitted the assumption that middle cerebral artery flow remained proportional to internal carotid artery flow. The integrated time-mean values from consecutive 5-second periods were computed. The arithmetic mean internal carotid artery flow varied from 167 to 399 ml/min in individual patients, with individual ranges between ±15% and ±35% of the mean flow. The mean middle cerebral artery blood velocity varied from 32 to 78 cm/sec. The relation between flow volume and blood velocity was nearly linear under these conditions. Normalization of the data as percent of the individual arithmetic means permitted a composite analysis of data from all patients. Linear regression of normalized blood velocity (V) on normalized flow volume (Q') showed $V' = 1.05 Q' - 5.08$ ($r^2 = 0.898$).

From the Department of Neurosurgery and The Computer Department, Rikshospitalet, The National Hospital, University of Oslo, Oslo, Norway.

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Address for correspondence: Karl-Fredrik Lindegaard, MD, Department of Neurosurgery, Rikshospitalet, N-0027 Oslo 1, Norway.

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error. Second, it is assumed that the peripheral vascular beds supplied by the MCA and the anterior cerebral artery, respectively, are reasonably similar. Otherwise, systemic blood pressure variations might lead to an unequal division of QICA. This probably requires that no brain infarction is present and that the perfusion of the brain hemisphere is adequate during the investigation. Thus, a strict selection of patients was necessary. The measurements were obtained after CEA in patients treated for unilateral and relatively moderate ICA stenosis and having normal computed tomography (CT) scans.

Subjects and Methods

Patients

Seven patients, all men, were investigated after completed CEA. The treated lesions represented ICA lumen area reductions of from 50 to 75% measured on extracranial angiograms, and the contralateral ICA showed no stenosis. Cerebral angiograms, performed in 5 of the 7 patients, showed no stenosis of the intracranial ICA portion or its major branches and normal filing pattern of the cerebral arteries. Noninvasive measurements of blood velocity in basal cerebral arteries, performed preoperatively in all patients as previously described, were useful in further confirming near-normal intracranial hemodynamic conditions.

There was normal anterograde anterior cerebral artery flow, and the absolute value and pulsatility of the MCA velocity spectrum outline were within normal limits, ruling out significant intracranial artery stenosis.3

General anesthesia was induced with thiopentone and maintained with fentanyl, pancuronium bromide, and nitrous oxide using a volume-controlled respirator. An indwelling shunt was used during CEA. The ICA clamping time was <3.5 minutes. Two patients had one-stage CEA and open heart surgery. These patients were investigated following aortocoronary bypass grafting during nonpulsatile cardiopulmonary bypass (CPB) with hemodilution. The anesthetic regimen is detailed elsewhere.12,13 Informed consent was obtained in all patients. Clinical data are summarized in Table 1.

Systemic blood pressure was monitored using a radial artery cannula, and Paco2 and hematocrit were checked repeatedly. Changes in QICA occurred following the administration of metaraminol or thiopentone as indicated by the individual clinical situation, or were concomitant with spontaneous blood pressure fluctuations. During CPB, further changes in blood pressure and QICA resulted from changes in pump flow (Table 1).

Blood Velocity Measurements

The 2-MHz pulsed Doppler instrument and the transcranial Doppler investigation procedure have been described in detail previously.3,4 The probe was steadied against the underlying temporal squama, and this situation was maintained throughout the recording period. A software-implemented subroutine translated the velocity spectrum outline into an analog voltage (Figure 1). The spectrum outline represents the blood having the highest velocity in the vessel segment under study. The observed blood velocity is inversely related to the cosine of the angle of incidence between the ultrasound beam and the velocity vector. The MCA runs at a sharp angle to the ultrasonic beam, but the velocity vector is the cosine is 1. If the angle varies between 0 and 15°, the cosine remains >0.965. Within this range, any error produced remains <3.5%.

Flow Volume Measurements

Cuff probes with diameters ensuring a good fit were implanted on the ICA distal to the suture line and steadied to remain in position during the recordings. The external carotid artery was clamped. The probes were connected to a Nycotron A/S model N-3400

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Table 1. Clinical Description of Subjects

<table>
<thead>
<tr>
<th>Patient/age</th>
<th>Diagnosis</th>
<th>Operation</th>
<th>ICA stenosis (%) area</th>
<th>Mean blood pressure range (mm Hg)</th>
<th>Paco2 (mm Hg)</th>
<th>Body temperature (° C)</th>
<th>Hematocrit</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>1/56</td>
<td>TIA</td>
<td>CEA</td>
<td>70</td>
<td>98–134</td>
<td>35</td>
<td>37</td>
<td>41</td>
<td>1 mg metaraminol bitartrate</td>
</tr>
<tr>
<td>2/60</td>
<td>TIA</td>
<td>CEA</td>
<td>64</td>
<td>84–116</td>
<td>36</td>
<td>37</td>
<td>35</td>
<td>100 mg thiopentone sodium</td>
</tr>
<tr>
<td>3/56</td>
<td>TIA</td>
<td>CEA</td>
<td>50</td>
<td>86–138</td>
<td>35</td>
<td>37</td>
<td>39</td>
<td>1 mg metaraminol bitartrate</td>
</tr>
<tr>
<td>4/54</td>
<td>TIA</td>
<td>CEA</td>
<td>55</td>
<td>88–112</td>
<td>34</td>
<td>37</td>
<td>42</td>
<td>1 mg metaraminol bitartrate</td>
</tr>
<tr>
<td>5/49</td>
<td>TIA</td>
<td>CEA</td>
<td>60</td>
<td>82–104</td>
<td>36</td>
<td>37</td>
<td>40</td>
<td>100 mg thiopentone sodium</td>
</tr>
<tr>
<td>6/58</td>
<td>MS, IHD</td>
<td>CEA, ACB</td>
<td>75</td>
<td>60–108</td>
<td>37*</td>
<td>28</td>
<td>24</td>
<td>Heart-lung machine flow increased from 1.5 to 2.0 l/min/m²</td>
</tr>
<tr>
<td>7/61</td>
<td>TIA, IHD</td>
<td>CEA, ACB</td>
<td>75</td>
<td>41–73</td>
<td>36*</td>
<td>36</td>
<td>26</td>
<td>Heart-lung machine flow increased from 1.5 to 3.0 l/min/m²; 1.5 mg metaraminol bitartrate</td>
</tr>
</tbody>
</table>

*Paco2 corrected to 37° C.

All subjects were men. ICA, extracranial internal carotid artery; TIA, transient ischemic attack; MS, minor stroke with minimal residual deficit; IHD, ischemic heart disease; CEA, carotid endarterectomy; ACB, aortocoronary bypass grafting during nonpulsatile cardiopulmonary bypass.
square-wave electromagnetic flowmeter (Lier, Norway), and the calibration factor for each probe was set according to the manufacturer's specifications. A QICA of 0 was checked by clamping the proximal common carotid artery (CCA) for about 15 seconds. These test occlusions do, however, clearly invalidate the basis for considering ICA flow proportional to MCA flow. Therefore, findings during CCA clamping and within 1 minute after the test occlusions were omitted from the subsequent analysis.

Data Analysis

The analog outputs from the Doppler instrument and the electromagnetic flowmeter were tape-recorded (R-71 instrumentation tape recorder, Teac Corp., Tokyo, Japan) and played back through an analog-to-digital converter to a Hewlett-Packard HP-9816 microcomputer with Pascal programming environment (San Diego, Calif.). This system has a 25-Hz sampling frequency on each channel. Statistical tests were performed using SAS Institute Inc. software (Cary, N.C.) on a mainframe computer; \( p < 0.05 \) was considered significant.

Results

The variations in QICA were reflected in the VMCA recording when QICA changed due to systemic effects (Figure 2). Computing the time-mean values of QICA and VMCA from successive 5-second periods provided 52–123 data points from individual patients. The individual arithmetic mean QICA was between 167 and 399 ml/min with mean VMCA from 32 to 78 cm/sec. QICA ranged between about ± 15% and about ± 35% of the mean (Table 2) and indicated that cerebral perfusion...
remained adequate. Visual inspection of the plotted data confirmed a near-linear relation between these two parameters under these defined conditions (Figure 3). Linearity was further tested by fitting the data to the parabolic equation \( y = A + Bx + Cx^2 \). The numeric values for the coefficient \( C \) ranged from 0.002 to 0.012, median 0.008. For the present purpose, it therefore seemed permissible to treat the relation between VMCA and QICA as linear. The results of linear regression analysis of paired data from individual patients are shown in Table 2. The intercept, i.e., VMCA corresponding to QICA = 0, was significantly different from 0 in 2 patients. We emphasize, however, that a QMCA of 100% denotes 100%, permitting comparisons of relative changes in blood velocity and flow volume. The results of linear regression analysis of the normalized values for the coefficient \( C \) ranged from 0.002 to 0.012, median 0.008. For the present purpose, it therefore seemed permissible to treat the relation between VMCA and QICA as linear. The results of linear regression analysis of the normalized data (denoted \( V' \) and \( Q' \)) are shown in Table 3. Composite analysis of \( V' \) and \( Q' \) from all patients (579 data points) revealed a regression coefficient of 1.05, \( y \) intercept of \( -5.08 \), and \( r^2 \) of 0.898. Using this line as a calibration curve and given that \( V' \) changed from 100 to 75%, the \( Q' \) estimate was 76.2%, with 95% confidence limits of \( \pm 5.3 \% \) (Table 3, Figure 4).

**Discussion**

**Methodologic Considerations**

The present study compares maximum VMCA with QICA obtained simultaneously in a clinical model selected to permit the assumption that a relative change in QICA signaled a corresponding relative change in QMCA. Transcranial Doppler is reliable in detecting intracranial artery stenosis and collateral flow in the circle of Willis; hence, the validity of these assumptions in our highly selected patients could be confirmed even without cerebral angiography. Therefore, it seemed justified to accept the term \( Q' \) as denoting relative changes in QMCA.

The current Doppler technique did not permit measuring the cross-sectional average blood velocity, which is exactly proportional to flow volume given that the lumen area of the insonated vessel segment remains constant. The relation between the maximum and the average velocity is given by the velocity profile. In pulsatile flow, the instantaneous velocity profile varies from relatively flat in systole to more parabolic in diastole. In the femoral artery, the maximum blood velocity nevertheless follows changes in blood velocity.

### Table 2. Correlation Between ICA Flow Volume (QICA) and MCA Blood Velocity (VMCA)

<table>
<thead>
<tr>
<th>Patient</th>
<th>No. data points</th>
<th>ICA flow volume (ml/min)</th>
<th>MCA blood velocity (cm/sec)</th>
<th>Regression of VMCA on QICA</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Range</td>
<td>Mean</td>
<td>Range</td>
<td>Mean</td>
</tr>
<tr>
<td>1</td>
<td>94</td>
<td>164–224</td>
<td>197.4</td>
<td>46–65</td>
</tr>
<tr>
<td>2</td>
<td>52</td>
<td>210–272</td>
<td>234.3</td>
<td>44–58</td>
</tr>
<tr>
<td>3</td>
<td>61</td>
<td>148–194</td>
<td>167.2</td>
<td>56–75</td>
</tr>
<tr>
<td>4</td>
<td>88</td>
<td>150–228</td>
<td>190.0</td>
<td>64–96</td>
</tr>
<tr>
<td>5</td>
<td>70</td>
<td>202–274</td>
<td>241.1</td>
<td>49–67</td>
</tr>
<tr>
<td>6</td>
<td>123</td>
<td>251–526</td>
<td>398.7</td>
<td>46–106</td>
</tr>
<tr>
<td>7</td>
<td>91</td>
<td>174–328</td>
<td>246.9</td>
<td>23–44</td>
</tr>
</tbody>
</table>

ICA, extracranial internal carotid artery; MCA, middle cerebral artery. Each data point is time-average recorded simultaneously over 1–5 second period.

### Table 3. Correlation Between Q' and V'

<table>
<thead>
<tr>
<th>Patient</th>
<th>No. data points</th>
<th>Q' (% of mean) range</th>
<th>V' (% of mean) range</th>
<th>Regression of V' on Q'</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Slope</td>
</tr>
<tr>
<td>1</td>
<td>94</td>
<td>83–113</td>
<td>83–118</td>
<td>1.10*</td>
</tr>
<tr>
<td>2</td>
<td>52</td>
<td>89–116</td>
<td>91–120</td>
<td>0.99</td>
</tr>
<tr>
<td>3</td>
<td>61</td>
<td>88–116</td>
<td>88–118</td>
<td>1.01</td>
</tr>
<tr>
<td>4</td>
<td>88</td>
<td>79–120</td>
<td>82–123</td>
<td>1.01</td>
</tr>
<tr>
<td>5</td>
<td>70</td>
<td>84–114</td>
<td>82–113</td>
<td>0.97</td>
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<td>6</td>
<td>123</td>
<td>63–132</td>
<td>61–141</td>
<td>1.09*</td>
</tr>
<tr>
<td>7</td>
<td>91</td>
<td>70–133</td>
<td>72–137</td>
<td>0.98</td>
</tr>
<tr>
<td>Composite analysis, data from all patients (579 points)</td>
<td>1.05*</td>
<td>-5.08†</td>
<td>0.898</td>
<td>±5.3</td>
</tr>
</tbody>
</table>

Q' and V', flow volume and blood velocity normalized to the arithmetic mean in individual patients; 100% denotes individual mean (see Table 2). 95% confidence interval for estimating Q' given V' using regression line as calibration curve.

*Significantly different from 1 \( (p<0.05) \).
†Significantly different from 0 \( (p<0.05) \).
volume. Because flow in brain arteries is less pulsatile, the same should apply to the MCA.

**Blood Velocity vs. Flow Volume**

The regression coefficient for V on Q for the combined data was significantly greater than 1, mainly due to findings in 2 of the 7 patients (see Tables 1 and 3). One of these patients was investigated during nonpulsatile CPB. Differences related to hematocrit, flow pulsatility, and anesthesia do not, therefore, fully explain these findings. In determining the diameter of arteries, two opposing mechanisms operate: active contraction of smooth muscle within the vessel wall and passive dilation by transmural pressure. MCA transmural pressure cannot be assessed without knowledge of the intracranial pressure. However, the present results suggest a tendency for the MCA to contract when blood pressure and blood flow increase. Qualitatively, this is in keeping with experimental findings in vivo and in vitro. Arguably, smooth muscle contractility in large cerebral arteries could be less vigorous in aging humans with atherosclerotic arteries than in an animal model. Even the greatest regression coefficient found in the present series, 1.10, could be explained by an MCA diameter reduction of not more than 5%. Changes of this magnitude have been observed angiographically when arterial blood pressure increased from <76 to >100 mm Hg in patients under general anesthesia and moderate hypocapnia. The differences found in the present series might, therefore, reflect predictable individual variation. Although difficult to evaluate statistically, the linear relation between flow and blood velocity did not seem to be seriously offset by moderate therapeutic doses of metaraminol or thiopentone. Indeed, Olesen claimed that there was no change in the diameters of large intracranial arteries on angiograms following intracarotid epinephrine and norepinephrine infusions of 1–10 µg/min.

The electromagnetic flowmeter reading is inversely related to hematocrit. Nevertheless, since hematocrit was constant during the recordings, observations of Q should remain valid. Furthermore, the relative term Q cancels out individual differences in absolute flow volume and hematocrit.

**Clinical Implications**

The present study investigated changes in Q of up to ±35% of the arithmetic mean flow. In patients without significant extracranial or intracranial artery stenosis, the brain volume perfused by the MCA probably remains constant in the face of moderate changes in systemic blood pressure. Thus V may be regarded as reflecting changes in brain perfusion. It seems permissible to infer that under these defined conditions, this also applies to the anterior and posterior cerebral arteries. The 95% confidence interval for estimating Q given V was ±5.3%, which seems sufficiently accurate for clinical purposes. The recording of maximum blood velocity allows no calculations of absolute flow volume. Nonetheless, the transcranial Doppler method has an important advantage compared with existing techniques; the improved resolution in time permits investigating blood flow variations on a short and continuous timescale. Such information is difficult to obtain by other methods.
to obtain with other methods. Furthermore, continuous recordings over relatively long periods can be obtained.

The clinical model precluded comparison of Q’ and V when ICA flow is being closed down. However, in patients with chronic ICA stenosis or total occlusion, variations in brain perfusion during acute clamping of the carotid artery are anticipated to be near-linear even when the proximal MCA is being supplied partially or completely through the circle of Willis. Recording of VMCA shows particularly promise for monitoring brain perfusion during open heart surgery.\textsuperscript{12,13} Further investigation is, however, clearly needed to evaluate the relation between V’ and V and variations in brain perfusion during acute clamping of the carotid artery.

Using and interpreting blood velocity recordings for the purpose of monitoring brain perfusion are in a developing stage. Therefore, caution is recommended in extrapolating the present data to situations differing in important respects from those dealt with here. Possible differences between general anesthesia and the awake state remain to be elucidated. Finally, in the face of diameter changes in the proximal MCA, whether due to escalating vasospasm or induced pharmacologically, the relation between relative changes in blood velocity and flow volume will shift from unity.

References

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Key Words • cerebral blood flow • cerebral blood velocity • cerebral artery • cerebral perfusion • diagnostic ultrasound
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