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

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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  $\pm 15\%$  and  $\pm 35\%$  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  $V' = 1.05 Q' - 5.08$  ( $r^2 = 0.898$ ). (*Stroke* 1987;18:1025-1030)

Investigation of blood flow in defined cerebral artery systems by a continuous technique has considerable clinical value, as shown by Normes et al,<sup>1,2</sup> who used an electromagnetic flowmeter to investigate cerebral vasomotor responses during aneurysm surgery. More recently, advances in the field of Doppler techniques have permitted noninvasive measurements of blood velocity in defined basal cerebral arteries.<sup>3,4</sup> This continuous method provides means to diagnose and to quantify individual hemodynamic situations in patients with extracranial and intracranial artery stenosis,<sup>4,5</sup> cerebral vasospasm due to subarachnoid hemorrhage,<sup>6</sup> and arteriovenous malformations.<sup>7</sup>

The middle cerebral artery (MCA) carries about 80% of the flow volume received by the cerebral hemisphere.<sup>8</sup> The normal MCA blood velocity ( $V_{MCA}$ ) under resting conditions ranges from 35 to 90 cm/sec, with a mean of about 60 cm/sec.<sup>3,4</sup> This range probably reflects the well-known individual MCA diameter variation as well as individual differences in cerebral blood flow. In healthy individuals,  $V_{MCA}$  shows  $CO_2$  reactivity of  $3.4 \pm 0.8\%/mm\ Hg$ ,<sup>9</sup> which is very close to the  $4.1 \pm 1\%$   $CO_2$  reactivity of cerebral blood flow determined by means of the xenon washout technique.<sup>10</sup> Together, these data suggest the attractive possibility that investigating variations in  $V_{MCA}$  may provide a

good impression of variations in MCA flow volume ( $Q_{MCA}$ ).

The present study was conducted to examine in further detail the relation between concomitant variations in  $V_{MCA}$  and  $Q_{MCA}$  in clinical situations. A special emphasis was placed on evaluating blood velocity measurements as a clinical tool in labile vascular situations since flow measurements using the well-established xenon washout techniques have definite limitations under such circumstances.

## Clinical Model

Direct recording of  $Q_{MCA}$  using miniaturized cuff probes<sup>1,2</sup> is a highly specialized technique; moreover, this invasive method is incompatible with simultaneous transcranial blood velocity measurements in the clinical setting. However, during carotid endarterectomy (CEA), recording of the flow volume in the extracranial internal carotid artery (ICA) is available. This method provides a great number of sampling points from each individual investigated. Given that the ipsilateral MCA receives a constant proportion of the ICA flow volume ( $Q_{ICA}$ ), relative changes in  $Q_{ICA}$  will reflect relative changes in  $Q_{MCA}$ . This model includes some assumptions. First, since the ICA usually also supplies the anterior cerebral artery, a constant proportional relation between  $Q_{ICA}$  and  $Q_{MCA}$  can be assumed only when the carotid system investigated is neither receiving flow through collaterals nor supplying collaterals into other intracranial artery territories. This condition is met only when there is no cerebral artery stenosis either extracranially or intracranially. Flow in the ophthalmic artery and other small extradural ICA branches is low compared with total ICA flow and should not constitute an important source of

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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  $Q_{ICA}$ . 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 filling pattern of the cerebral arteries. Noninvasive measurements of blood velocity in basal cerebral arteries, performed preoperatively in all patients as previously described,<sup>4</sup> 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.<sup>5</sup>

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.<sup>11</sup> 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 by-

pass (CPB) with hemodilution. The anesthetic regimen is detailed elsewhere.<sup>12,13</sup> 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  $PCO_2$  and hematocrit were checked repeatedly. Changes in  $Q_{ICA}$  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  $Q_{ICA}$  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.<sup>3,4</sup> 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 when an "ultrasonic window" in the temporal region is being used. We have assumed that the incidence angle is  $0^\circ$ , in which case the cosine is 1. If the angle varies between  $0$  and  $15^\circ$ , 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

**Table 1. Clinical Description of Subjects**

Patient/age	Diagnosis	Operation	ICA stenosis (% area)	Mean blood pressure range (mm Hg)	$PaCO_2$ (mm Hg)	Body temperature ( $^\circ C$ )	Hematocrit	Comments
1/56	TIA	CEA	70	98–134	35	37	41	1 mg metaraminol bitartrate
2/60	TIA	CEA	64	84–116	36	37	35	100 mg thiopentone sodium
3/56	TIA	CEA	50	86–138	35	37	39	1 mg metaraminol bitartrate
4/54	TIA	CEA	55	88–112	34	37	42	1 mg metaraminol bitartrate
5/49	TIA	CEA	60	82–104	36	37	40	100 mg thiopentone sodium
6/58	MS, IHD	CEA, ACB	75	60–108	37*	28	24	Heart-lung machine flow increased from 1.5 to 2.0 l/min/m <sup>2</sup>
7/61	TIA, IHD	CEA, ACB	75	41–73	36*	36	26	Heart-lung machine flow increased from 1.5 to 3.0 l/min/m <sup>2</sup> ; 1.5 mg metaraminol bitartrate

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.

\* $PaCO_2$  corrected to  $37^\circ C$ .

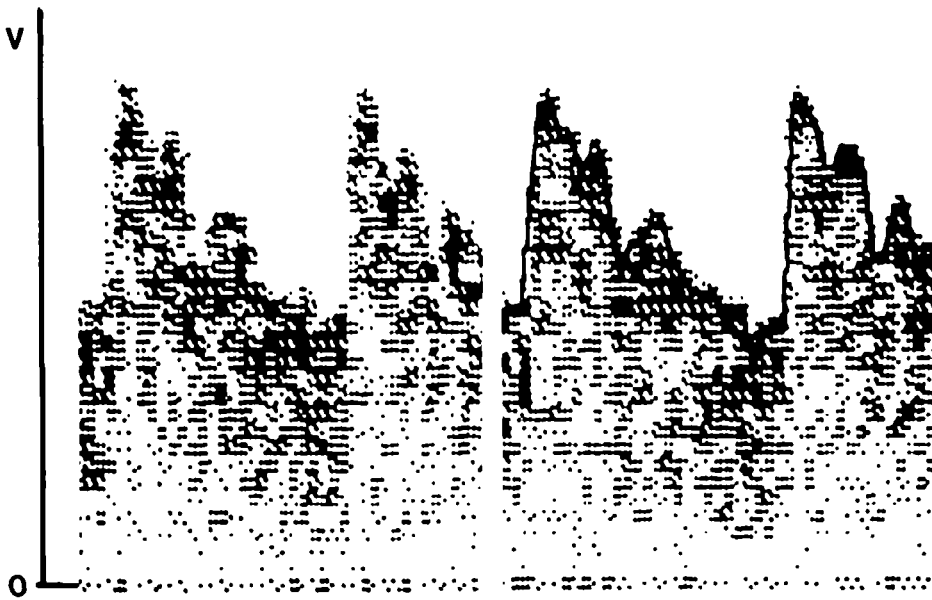


FIGURE 1. Blood velocity recording without (left) and with (right) software-implemented spectrum outline follower. Velocity spectrum outline is translated into an analog voltage output.

square-wave electromagnetic flowmeter (Lier, Norway), and the calibration factor for each probe was set according to the manufacturer's specifications. A  $Q_{ICA}$  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 microcom-

puter 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  $Q_{ICA}$  were reflected in the  $V_{MCA}$  recording when  $Q_{ICA}$  changed due to systemic effects (Figure 2). Computing the time-mean values of  $Q_{ICA}$  and  $V_{MCA}$  from successive 5-second periods provided 52–123 data points from individual patients. The individual arithmetic mean  $Q_{ICA}$  was between 167 and 399 ml/min with mean  $V_{MCA}$  from 32 to 78 cm/sec.  $Q_{ICA}$  ranged between about  $\pm 15\%$  and about  $\pm 35\%$  of the mean (Table 2) and indicated that cerebral perfusion

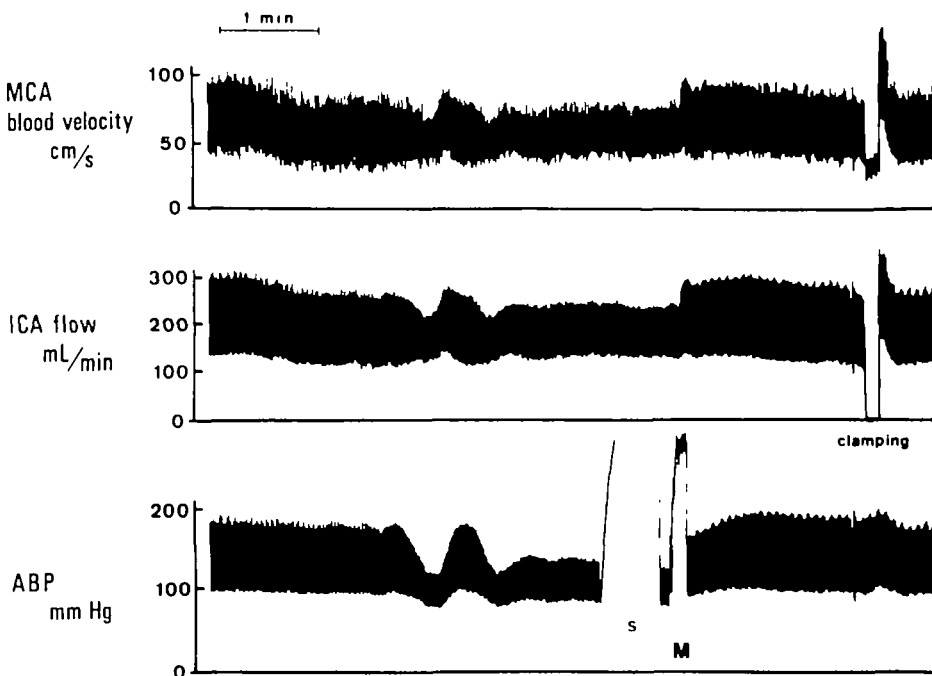


FIGURE 2. Patient 1. Recording after endarterectomy for carotid stenosis reducing lumen area by 60%. Recording of blood velocity in middle cerebral artery (MCA) (top) closely resembles that of flow volume in ipsilateral internal carotid artery (ICA) (middle). Responses are less pronounced than concomitant spontaneous fluctuations in systemic arterial blood pressure (ABP) (bottom). MCA flow is maintained through collaterals during test occlusion to check ICA flow of 0. Clinical model precluded comparison of blood velocity and flow volume under these circumstances (far right). S, sampling blood from radial artery cannula; M, 1 mg i.v. metaraminol bitartrate to counter decreasing blood pressure.

**Table 2. Correlation Between ICA Flow Volume ( $Q_{ICA}$ ) and MCA Blood Velocity ( $V_{MCA}$ )**

Patient	No. data points	ICA flow volume (ml/min)		MCA blood velocity (cm/sec)		Regression of $V_{MCA}$ on $Q_{ICA}$		
		Range	Mean	Range	Mean	Slope	y intercept	$r^2$
1	94	164–224	197.4	46–65	55.1	0.31	–5.77	0.940
2	52	210–272	234.3	44–58	48.2	0.20	0.54	0.883
3	61	148–194	167.2	56–75	63.5	0.38	–1.12	0.898
4	88	150–228	190.0	64–96	78.3	0.41	–0.54	0.956
5	70	202–274	241.1	49–67	59.4	0.24	1.74	0.944
6	123	251–526	398.7	46–106	75.2	0.21	–7.39	0.956
7	91	174–328	246.9	23–44	32.1	0.13	0.63	0.942

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

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  $V_{MCA}$  and  $Q_{ICA}$  as linear. The results of linear regression analysis of paired data from individual patients are shown in Table 2. The y intercept, i.e.,  $V_{MCA}$  corresponding to  $Q_{ICA} = 0$ , was significantly different from 0 in 2 patients. We emphasize, however, that a  $Q_{MCA}$  of 0 is vastly outside the ranges investigated here. Therefore, the y intercept should be regarded as only a descriptive characteristic of individual sets of data, and not as applicable to clinical situations with cerebral blood flow approaching zero.

$V_{MCA}$  and  $Q_{ICA}$  measured in individual patients were normalized, with the arithmetic mean of both variables denoting 100%, permitting comparisons of relative changes in blood velocity and flow volume. 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<sup>14</sup> 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  $V_{MCA}$  with  $Q_{ICA}$  obtained simultaneously in a clinical model selected to permit the assumption that a relative change in  $Q_{ICA}$  signaled a corresponding relative change in  $Q_{MCA}$ . Transcranial Doppler is reliable in detecting intracranial artery stenosis and collateral flow in the circle of Willis<sup>4,5</sup>; 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  $Q_{MCA}$ .

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 flow

**Table 3. Correlation Between  $Q'$  and  $V'$** 

Patient	No. data points	$Q'$ (% of mean) range	$V'$ (% of mean) range	Regression of $V'$ on $Q'$			95% confidence interval
				Slope	y intercept	$r^2$	
1	94	83–113	83–118	1.10*	–10.29†	0.940	$\pm 3.4$
2	52	89–116	91–120	0.99	1.13	0.883	$\pm 4.0$
3	61	88–116	88–118	1.01	–1.77	0.898	$\pm 3.3$
4	88	79–120	82–123	1.01	–0.69	0.956	$\pm 4.1$
5	70	84–114	82–113	0.97	2.92	0.944	$\pm 3.4$
6	123	63–132	61–141	1.09*	–9.83	0.956	$\pm 7.4$
7	91	70–133	72–137	0.98	1.99	0.942	$\pm 7.0$
Composite analysis, data from all patients (579 points)				1.05*	–5.08†	0.898	$\pm 5.3$

$Q'$  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 ( $p < 0.05$ ).

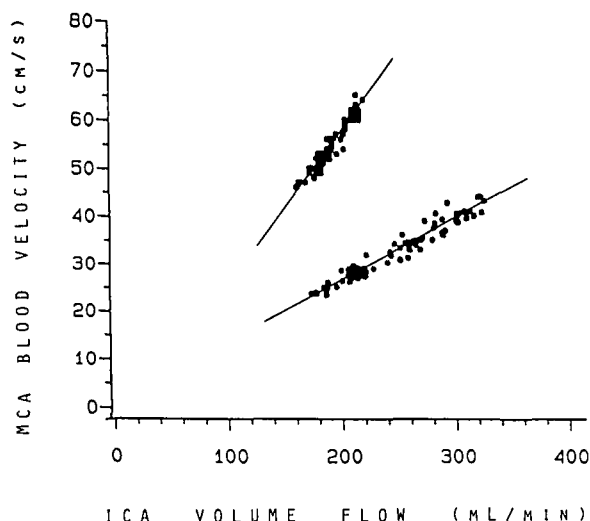


FIGURE 3. Plot of simultaneous observations of middle cerebral artery (MCA) blood velocity ( $V_{MCA}$ ) and internal carotid artery (ICA) flow volume ( $Q_{ICA}$ ). Each point is time-mean value from 1 5-second period. Upper line: Patient 1 (94 points, continuous tracings in Figure 2).  $V_{MCA} = 0.31Q_{ICA} - 5.77$ ;  $r^2 = 0.940$ . Lower line: Patient 7 (91 points).  $V_{MCA} = 0.13Q_{ICA} + 0.63$ ;  $r^2 = 0.942$ . Note individual difference in  $V_{MCA}$  for given  $Q_{ICA}$ .

volume.<sup>15</sup> 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 a 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*<sup>16,17</sup> and *in vitro*.<sup>18</sup> 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.<sup>19</sup> 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 metaminal or thiopentone. Indeed, Olesen<sup>20</sup> claimed that there was no change in the diameters of large intracranial arteries on angiograms following intracarotid epinephrine and norepinephrine infusions of 1–10  $\mu\text{g}/\text{min}$ .

The electromagnetic flowmeter reading is inversely related to hematocrit.<sup>21</sup> 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  $Q_{MCA}$  of up to  $\pm 35\%$  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  $\pm 5.3\%$ , 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

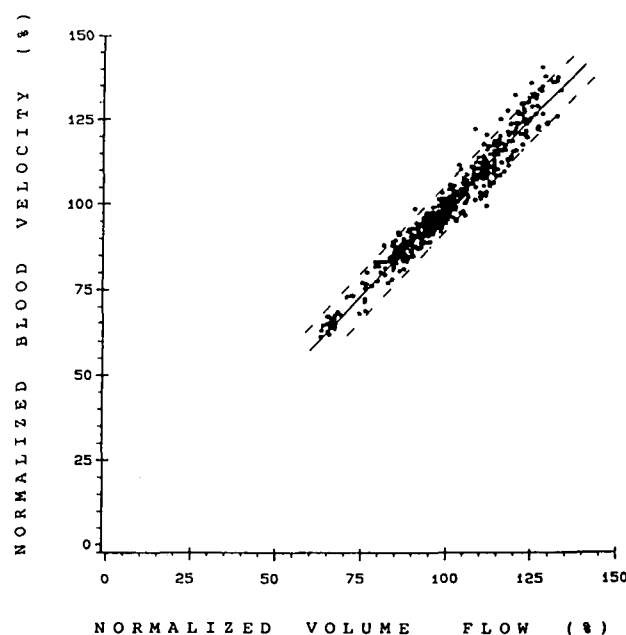


FIGURE 4. Absolute values for middle cerebral artery blood velocity and internal carotid artery flow volume in individual patients normalized with arithmetic means representing 100% ( $V'$  and  $Q'$ , respectively) for all patients combined. Regression line,  $V' = 1.05Q' - 5.08$ , drawn in. 95% confidence interval (---) for estimating  $Q'$  when  $V'$  is known was  $\pm 5.3\%$ .

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 and under similar conditions, MCA diameter and extent of the MCA perfusion territory probably change relatively little when systemic blood pressure changes. Therefore, the relation between  $Q'$  and  $V'$  could be anticipated to be near-linear even when the proximal MCA is being supplied partially or completely through the circle of Willis. Recording of  $V_{MCA}$  shows particular promise for monitoring brain perfusion during open heart surgery.<sup>12,13</sup> Further investigation is, however, clearly needed to evaluate the relation between  $V'$  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.

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KEY WORDS • cerebral blood flow • cerebral blood velocity • cerebral artery • cerebral perfusion • diagnostic ultrasound