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Flow Velocity Measurements as an Index of Cerebral Blood Flow

Validity of Transcranial Doppler Sonographic Monitoring during Cardiac Surgery

Andreas Weyland, M.D., Heidrun Stephan, M.D.,† Stephan Kazmaier, M.D.,* Wolfgang Weyland, M.D.,* Bernd Schorn, M.D.,‡ Frank Grüne, M.D.,§ Hans Sonntag, M.D.,‖*

Background: **Transcranial Doppler sonography is increasingly used to monitor changes in cerebral perfusion intraoperatively. However, little information is available about the validity of velocity measurements as an index of cerebral blood flow (CBF). The purpose of this study was to compare invasive and Doppler-derived measurements of cerebral hemodynamic variables during coronary artery bypass graft surgery.**

Methods: **In 15 male patients, measurements of CBF and middle cerebral artery flow velocity (V_{MCA}) were performed before and after induction of fentanyl–midazolam anesthesia, during hypothermic cardiopulmonary bypass (CPB), and at the end of the surgical procedure. Transcranial Doppler sonography recordings of systolic, diastolic, and mean V_{MCA}, and derived parameters such as pulsatility (PI) and resistance (RI) indexes were recorded from the proximal segment of the right middle cerebral artery. CBF was measured by the Kety-Schmidt inert gas saturation method with argon as a tracer. To facilitate comparisons of CBF and V_{MCA} measurements, changes between consecutive measurements were expressed as percentage values. Calculations of cerebral perfusion pressure and cerebral vascular resistance (CVR) were based on jugular bulb pressure. The cerebral metabolic rate for oxygen was calculated from CBF and the arterial − cerebral venous oxygen content difference.**

Results: **Changes in mean V_{MCA} paralleled changes in mean CBF except for hemodynamic changes associated with hypothermic CPB. At this stage of surgery, mean V_{MCA} increased while actual CBF decreased. Separate analysis of the periods before and after CPB revealed a poor association between percentage changes in CBF and V_{MCA} ($r = 0.26$, $P = 0.36$; $r = 0.51$, $P = 0.06$, respectively). Mean values of CVR, PI, and RI showed consistent changes after induction of anesthesia. After termination of CPB, mean CVR significantly decreased, whereas mean PI and RI remained virtually unchanged. Neither before nor after CPB was a clinically useful correlation found between percentage changes in PI, RI, and CVR (PI $r = 0.28$, $P = 0.34$; $r = -0.47$, $P = 0.09$, respectively; RI $r = 0.16$, $P = 0.59$; $r = -0.53$, $P = 0.06$, respectively).**

Conclusions: **Hypothermic CPB seems to alter the relation between global CBF and flow velocity in basal cerebral arteries. Inconsistency in directional changes in CBF and V_{MCA} at this stage of surgery might be attributable to changes in middle cerebral artery diameter, red blood cell velocity spectra, and regional flow distribution. Although changes in mean V_{MCA} before and after CPB appear to parallel changes in mean CBF, individual responses of V_{MCA} cannot reliably predict percentage changes in CBF. Furthermore, Doppler sonographic PI and RI cannot provide an approximation of changes in CVR during cardiac surgery. (Key words: Brain: cerebral blood flow; cerebral vascular resistance. Measurement techniques: transcranial Doppler; Kety-Schmidt technique. Surgery, cardiac: cardiopulmonary bypass.)**

TRANSCRANIAL Doppler sonography (TCD) purportedly allows for noninvasive measurements of blood flow velocity in basal cerebral arteries. Since the introduction of TCD into clinical practice by Aaslid and coworkers,[1] TCD has been used primarily for diagnostic investigations in patients with cerebrovascular disease.[2,3] Because of the on-line availability of TCD, it is used increasingly for intraoperative monitoring of cerebral perfusion as well. The influence of various surgical and anesthesiologic interventions on blood flow velocity in the middle cerebral artery (V_{MCA}) has been investigated.[4–6] However, the validity of velocity mea-

* Staff Anesthesiologist.

† Associate Professor of Anesthesia.

‡ Staff Surgeon, Department of Cardiothoracic and Vascular Surgery.

§ Research Associate in Anesthesia.

‖ Professor of Anesthesia.

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Address reprint requests to Dr. Weyland: Department of Anesthesiology, Emergency, and Intensive Care Medicine, Georg-August-Universitat Göttingen, Robert-Koch-Str. 40, D-37075 Göttingen, Germany.

surements as an index of flow is based on the assumption that the cross-sectional area and the flow profile of these vessels remain constant during the period of investigation.[7]

This investigation was designed to compare TCD and invasive measurements of cerebral flow-related parameters in patients undergoing open heart surgery.

Materials and Methods

After institutional approval by the local Ethical Committee on Human Research written informed consent was obtained from each patient. Fifteen male patients were studied during elective coronary artery bypass graft surgery. Their mean age was 55 yr (range 46–66 yr), their mean body height and weight were 173 ± 5 cm and 80.5 ± 10.3 kg, respectively (mean ± SD). 11 patients had a history of moderate hypertension that pharmacologically was controlled by preoperative use of β-adrenergic antagonists or calcium entry blockers. All patients received nitrates until the night before surgery. According to clinical and ultrasonic examination none of the patients showed preoperative evidence of cerebrovascular disease. Preanesthetic medication consisted of 2 mg flunitrazepam on the evening and on the following morning before the surgical procedure, individual preoperative medication of patients was continued until the day of surgery.

Before induction of anesthesia, routine hemodynamic monitoring was established and included electrocardiography (leads II and V_5) and arterial, central venous, and pulmonary arterial catheterization. Additionally, a jugular bulb catheter (6-French, Goodale-Lubin, USCI, CR Bard, Billerica, MA) was inserted by retrograde puncture of the right internal jugular vein. The correct position of the catheter tip was verified by fluoroscopic control to prevent inadvertent extracerebral contamination of blood samples. Induction of anesthesia was performed by administration of 10 $\mu g \cdot kg^{-1}$ fentanyl and 0.2 $mg \cdot kg^{-1}$ midazolam, tracheal intubation was facilitated by 0.1 $mg \cdot kg^{-1}$ pancuronium bromide. Anesthesia was maintained with 10 $\mu g \cdot kg^{-1} \cdot h^{-1}$ fentanyl and 0.15 $mg \cdot kg^{-1} \cdot h^{-1}$ midazolam. Additional doses were administered when necessary. Intraoperative hypertension unresponsive to bolus administration of fentanyl–midazolam was treated with phentolamine. No other vasoactive drugs and no inhalational anesthetics were given to avoid additional pharmacologic alterations of cerebral blood flow (CBF) and arterial diameter.

For cardiopulmonary bypass (CPB), a nonpulsatile flow of 1.8–2.4 $l \cdot m^{-2} \cdot min^{-1}$ was established with a centrifugal pump (Sarns Delphin, 3 M Health Care, Ann Arbor, MI) and a membrane oxygenator (Bard HF 5000, W. Harvey, Tewksbury, MA). The priming of CPB consisted of lactated Ringer's solution 1000 ml, 5% glucose 500 ml, 20% albumin 400 ml, and sodium bicarbonate 100 ml. Cardiac arrest and myocardial protection were obtained by administration of Bretschneider's cardioplegic solution at 4°C (Custodiol). Patients were cooled to 26°C applying α-stat acid–base management: arterial carbon dioxide tension was maintained at 40 mmHg measured at 37°C; no carbon dioxide was added to the oxygenator; and arterial carbon dioxide tension was regulated by adjusting gas flow through the oxygenator.

Measurements were carried out in the awake patient before anesthesia (I), 15 min after induction of anesthesia before surgery (II), during hypothermic CPB (III), and at the end of the surgical procedure after closure of the chest (IV). Measurements during CPB were performed under steady-state conditions, when arterial and venous blood temperatures were stable at 26°C for at least 10 min and when α-stat acid–base conditions had been verified by blood gas analysis. Pump flow and temperature were kept constant in each patient for the study period. At each measurement arterial, central venous, pulmonary arterial, pulmonary wedge, and jugular bulb pressures were recorded on an eight-channel chart recorder; thermodilution measurements of cardiac output were taken at three random times during the respiratory cycle (Polymed CO computer, System 1281, Siemens, Munich, Germany). During CPB, measurements of pump flow were obtained from an electromagnetic flow meter (Sarns Delphin, 3 M Health Care). Cerebral perfusion pressure was derived from mean arterial and jugular bulb pressure. Cerebral vascular resistance (CVR) was calculated according to standard formula.

CBF was measured by the Kety-Schmidt inert gas saturation technique with argon as a tracer.[9] Wash-in periods of 10 min were used for all measurements. A preprepared gas mixture containing 70% argon and 30% oxygen was administered to the awake patient *via* a tight-fitting face mask, to the anesthetized patient *via* the endotracheal tube, and *via* the membrane oxygenator during CPB. Simultaneous blood samples from the arterial and the jugular bulb catheter were withdrawn at a constant rate during the saturation period in duplicate by use of a high-precision aspiration pump

(Braun, Melsungen, Germany) with glass syringes. The catheters had an identical dead space and were known to exhibit only minimal loss of inert gas by diffusion. Triple determinations of argon concentrations in each arterial and cerebral-venous blood sample were carried out after vacuum extraction by gas chromatography and ionization detection.[10] A brain–blood partition coefficient of 1.10 was used for calculation of CBF. Saturation of cerebral tissue with argon was verified by comparison of arterial and cerebral-venous argon concentrations from blood sampled instantaneously at the end of each saturation period, when cerebral venous argon concentration was 91 ± 4% of arterial argon concentration (mean ± SD).

Blood samples for measurements of electrolyte concentrations (Nova Electrolyte Analyser 1, Nova Biomedical, Waltham, MA), viscosity (Cone/Plate Viscosimeter LVT, Wells-Brookfield, Stoughton, MA), glucose and lactate concentrations (standard test combination, Boehringer Mannheim, Mannheim, Germany), oxygen saturation and hemoglobin concentration (CO-Oximeter IL 282, Rotron Manufacturing, Woodstock, NY), and oxygen and carbon dioxide tensions (ABL 3, Radiometer, Kopenhagen, Denmark) were drawn twice, at the beginning and at the end of each argon wash-in period. Measurements of viscosity were performed at the actual blood temperature. Cerebral metabolic rates for oxygen (CMR_{O_2}), glucose (CMR_{gluc}), and lactate were calculated from CBF times the respective arterial − cerebral venous content difference.

A 2-MHz pulsed Doppler ultrasound device (TC 2000 S, EME, Überlingen, Germany) was used for transcranial measurements of red blood cell velocity from the right posterior "temporal window" just above the zygomatic arch. After identification of the right anterior and middle cerebral artery (MCA) the depth was adjusted in 2 mm increments to obtain signals from the proximal segment of the MCA. The mean insonation depth was 51 ± 3 mm. Meticulous care was taken to ensure a constant position of the ultrasound probe during the investigation by use of a suitable holder attached to the patient's head (IMP 2 monitoring probe holder, EME). After individual adjustment of Doppler parameters, such as gain, sample volume, and power of ultrasound, these were not changed over the study period. A mean power of ultrasound of 134 ± 43 $mW \cdot cm^{-2}$ *in situ* intensity was used for the TCD recordings. Time averaged determinations of flow velocity were based on envelope curves of maximal intravascular velocity. Mean flow velocity was derived from on-line integration of envelope curves (sample rate 52 Hz) and continuously recorded on a microcomputer (sample rate 0.8 Hz) by use of the long-term monitoring option of the Doppler device. For comparison with CBF measurements, mean flow velocity was averaged over the 10 min period from the beginning to the end of each argon wash-in maneuver. Simultaneously, end-expiratory carbon dioxide concentrations (Capnomac, Datex Instrumentarium, Helsinki, Finland) were recorded to ensure stability of the carbon dioxide tension during argon saturation. During CPB, continuous monitoring of carbon dioxide and oxygen tensions was performed by use of an in-line blood gas monitoring system (CDI 400, 3 M Health Care, Tustin, CA). Indexes of pulsatility and resistance[11,12] (PI and RI, respectively) were calculated at the beginning and at the end of each measurement from two 10-s recordings of the envelope curves of maximal intravascular velocity according to the following formulas:

$$PI = \frac{V_{MCA\ systolic} - V_{MCA\ diastolic}}{V_{MCA\ mean}}$$

$$RI = \frac{V_{MCA\ systolic} - V_{MCA\ diastolic}}{V_{MCA\ systolic}}.$$

Results are expressed as mean ± standard deviation. For statistical analysis paired Student's *t* tests were used to compare the mean of hemodynamic and metabolic variables between consecutive measurements. Because multiple tests (measurement I *vs.* II, II *vs.* III, and III *vs.* IV) were necessary to assess the time course of each variable, the levels of significance were adjusted by a sequentially rejective multiple test procedure according to Holm[13] to reduce the probability of type I errors. To facilitate comparisons between invasive and Doppler-sonographic measurements, changes in flow- and resistance-related parameters were calculated as differences between consecutive measurements and expressed as percentage of the immediately preceding values. Pearson correlation coefficients were calculated to evaluate the relation between changes in CBF and V_{MCA}, CVR and PI, and CVR and RI. Because replicate measurements in the same patient could not be treated as independent observations, correlation analyses were separately performed for the different periods to include only one data set per patient in each analysis. All calculations were performed on a microcomputer with the SPSS/PC+ software package.

Results

One patient had to be excluded from the evaluation of Doppler-derived parameters because sufficient quality of sonographic signals could not be obtained within the ultrasound power range of the TCD device. In all other patients the quality of Doppler spectra was appropriate for the on-line determination of envelope curves and the calculation of derived parameters throughout the study period (fig. 1).

Hemodynamic, metabolic, and blood gas data are presented in table 1. Normocapnia (arterial carbon dioxide tension measured at 37°C) could be provided at all stages of the surgical procedure by adjustment of respirator settings and gas flow of the oxygenator. After induction of anesthesia and during CPB mean CBF significantly decreased from 48 to 34 and 28 $ml \cdot min^{-1} \cdot 100\ g^{-1}$, respectively. During the postbypass period mean CBF significantly increased from 28 to 43 $ml \cdot min^{-1} \cdot 100\ g^{-1}$.

Changes in CBF were paralleled by changes in CMR_{O_2} and CMR_{gluc}. However, during hypothermic CPB the decrease of CMR_{O_2} and CMR_{gluc} was more pronounced than the decrease of CBF. The cerebral metabolic rate for lactate did not demonstrate any significant changes during the study period.

Between the first and the last two measurements mean TCD measured V_{MCA} closely paralleled changes in CBF, however, during hypothermic CPB mean V_{MCA} slightly increased whereas corresponding CBF values showed a significant decrease (fig. 2).

The evaluation of individual data exhibited consistent directional changes in CBF and V_{MCA} in 96% of paired data between measurements I and II and between III and IV. However, this was only true in 29% of changes between measurements II and III, when cerebral hemodynamic changes were associated with hypothermic CPB (fig. 3).

Because of these divergent reactions, measurements during CPB were excluded from further analysis. For a quantitative assessment of the relation between changes in CBF and V_{MCA}, differences between consecutive measurements before and after CPB were expressed as percentage of the preceeding values. Figure 4 gives the correlation of these relative changes. Although the pooled data suggest a linear relation between the two variables, separate analysis of the periods before and after CPB revealed a poor association between percentage changes in CBF and V_{MCA} ($r = 0.26$, $P = 0.36$; $r = 0.51$, $P = 0.06$, respectively).

The decrease of CBF after induction of anesthesia was associated with a concomitant increase in CVR from 2.0 to 2.8 $mmHg \cdot min \cdot ml^{-1} \cdot 100$ g. After termination of extracorporeal circulation mean CVR significantly decreased when compared with prebypass values. Despite these substantial changes in CVR by +40% and −43% mean RI demonstrated only minimal changes by +8% and −4%. However, the small increase in RI after induction of anesthesia was significant.

Analogous to the evaluation of changes in CBF and V_{MCA}, individual differences between consecutive measurements of CVR and RI were calculated as percentage values (fig. 5). Correlation analyses of the two periods did not show a significant linear relation between these variables ($r = 0.16$, $P = 0.59$; $r = -0.53$, $P = 0.06$, respectively).

The time course of mean PI closely resembled that of RI. Correlation coefficients between relative changes in CVR and PI before and after CPB were 0.28 ($P = 0.34$) and −0.47 ($P = 0.09$), respectively.

Discussion

A simple and noninvasive method for assessing CBF would be of considerable value. This is particularly true with respect to CPB because of the recent interest in the effects of CPB on brain and efforts to understand neurologic dysfunction. However, most methods for direct measurement of CBF are difficult to apply in the operating room or limited with respect to the number and the frequency of repeated measurements.

TCD sonography enables noninvasive on-line measurements of blood flow velocity in basal cerebral arteries.[1] Because TCD cannot provide information on volumetric blood flow, various factors theoretically could influence the estimation of cerebral circulatory changes. Initial work with TCD assumed a close relation between flow velocity and blood flow because changes of V_{MCA} during hypo- or hypercapnia, cardiovascular exercise, and carotid endarterectomy were analogous to changes of CBF in previous studies.[14,15] At that time and more recently, some investigations have evaluated the relation by simultaneous measurements of CBF and V_{MCA} in humans.[16–19] However, only preliminary data are available from method comparison studies during cardiac surgery.[20]

Mean baseline values of CBF were within the normal range obtained with the Kety-Schmidt technique.[19,21] Induction of anesthesia was associated with a 30% decrease in CBF and a concomitant reduction of CMR_{O_2} and CMR_{gluc}. CBF values during fentanyl–midazolam

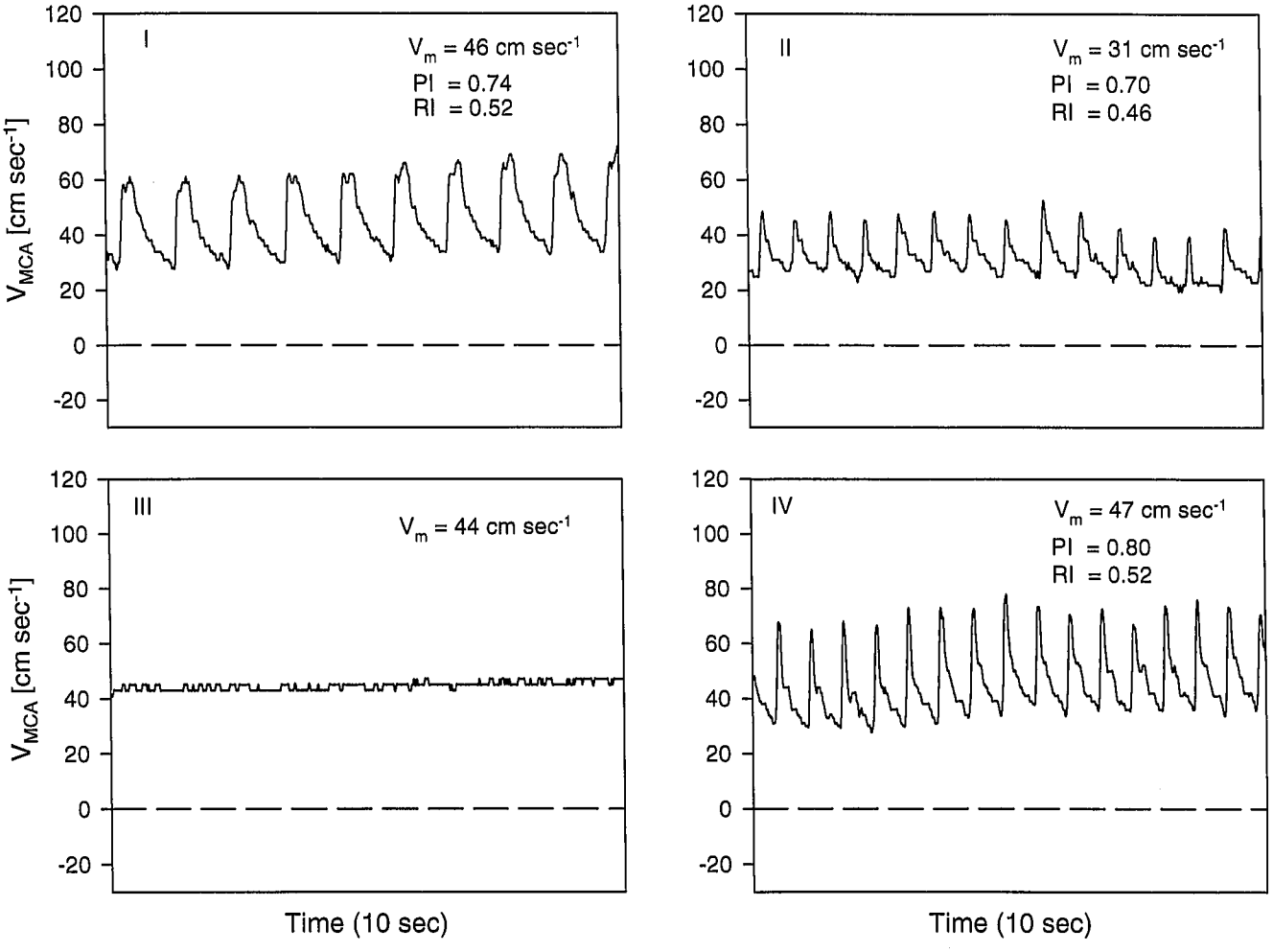

Fig. 1. Envelope curves of transcranial Doppler spectra in a single patient, recorded from the right middle cerebral artery with a 2-MHz pulsed Doppler ultrasound probe at a depth of 48 mm. I = awake; II = after induction of anesthesia; III = during nonpulsatile cardiopulmonary bypass at 26°C; IV = end of surgery.

anesthesia corresponded well to the results of Soma and coworkers,[22] who found a mean prebypass CBF of 30.6 ml · min^{-1} · 100 g^{-1} by using a modification of the Kety-Schmidt technique with mass-spectrometric detection of argon. After induction of anesthesia, CMR_{O_2} and CMR_{gluc} changed to the same extent, indicating that aerobic metabolism was not impaired by anesthesia. This was also true during hypothermic CPB when CMR_{O_2} and CMR_{gluc} further decreased. From the hypothermia-induced reduction of CMR_{O_2} a Q_{10} value (ratio of metabolic rates at two temperatures separated by 10°C) of 2.8 can be calculated. This is in close agreement with Q_{10} values found by other investigators for the human brain[23] and for the reduction of total body oxygen uptake.[24]

After termination of hypothermic CPB, mean CBF increased to a level that exceeded prebypass values. This finding is consistent with data from previous studies[22,25] and may in part be attributed to the decreased viscosity after CPB in our patients.

Mean V_{MCA} before induction of anesthesia and at the different stages of surgery corresponded to the range reported by other investigators.[20,26] The assessment of directional changes in cerebral perfusion in individual patients revealed a high level of agreement between changes in CBF and V_{MCA} except for during hypothermic

Table 1. Hemodynamic and Metabolic Variables, Hemoglobin Concentration, *p*H, and Blood Gas Values

	I	II	III	IV
HR (min)	64 ± 10	74 ± 25	—	92 ± 18*
CI (L/min)	2.8 ± 0.5	2.5 ± 0.6	2.0 ± 0.2*	2.9 ± 0.5*
MAP (mmHg)	100 ± 17	100 ± 18	79 ± 14*	78 ± 12
$P_{J\ Bulb}$ (mmHg)	8.4 ± 2.5	10.4 ± 2.0	9.6 ± 5.2	12.5 ± 2.3
CPP (mmHg)	92 ± 17	89 ± 17	69 ± 14*	64 ± 12
CBF ($ml \cdot min^{-1} \cdot 100\ g^{-1}$)	48 ± 9	34 ± 8*	28 ± 5*	43 ± 10*
V_{MCA} ($cm \cdot s^{-1}$)	45 ± 9	30 ± 8*	34 ± 11	46 ± 13*
CVR ($mmHg \cdot min \cdot ml^{-1} \cdot 100\ g$)	2.0 ± 0.5	2.8 ± 0.8*	2.5 ± 0.8	1.6 ± 0.4*
RI	0.51 ± 0.05	0.55 ± 0.08*	—	0.52 ± 0.06
PI	0.74 ± 0.11	0.88 ± 0.25*	—	0.81 ± 0.18
Hb (g/dl)	13.8 ± 1.0	12.7 ± 1.2*	8.4 ± 1.3*	9.1 ± 1.4
pH_{art}	7.37 ± 0.03	7.39 ± 0.03*	7.39 ± 0.03	7.37 ± 0.04
pH_{cv}	7.32 ± 0.03	7.32 ± 0.03	7.34 ± 0.03	7.31 ± 0.03
Pa_{CO_2} (mmHg)	41 ± 3	39 ± 3*	39 ± 3	39 ± 3
Pa_{O_2} (mmHg)	123 ± 22	148 ± 51	223 ± 31*	90 ± 23*
CMR_{O_2} ($ml \cdot min^{-1} \cdot 100\ g^{-1}$)	3.2 ± 0.6	2.6 ± 0.7*	1.0 ± 0.3*	2.3 ± 0.4*
CMR_{lact} ($\mu mol \cdot min^{-1} \cdot 100\ g^{-1}$)	−2.3 ± 2.3	−1.4 ± 1.4	−0.5 ± 1.6	0.84 ± 3.1
CMR_{gluc} ($mg \cdot min^{-1} \cdot 100\ g^{-1}$)	4.3 ± 1.1	3.2 ± 1.0*	1.2 ± 0.5*	3.1 ± 1.9*
Visc (mPa/s)	4.6 ± 0.5	4.4 ± 0.6*	4.0 ± 1.0	3.2 ± 0.6*
NPT (°C)	36.1 ± 0.3	35.3 ± 0.5*	26.3 ± 0.5*	36.1 ± 0.5*

Values are mean ± SD.

I = awake; II = after induction of anesthesia; III = during CPB at 26°C; IV = end of surgery; HR = heart rate; CI = cardiac index; MAP = mean arterial pressure; $P_{J\ Bulb}$ = jugular bulb pressure; CPP = cerebral perfusion pressure; CBF = cerebral blood flow; V_{MCA} = mean flow velocity (middle cerebral artery); CVR = cerebral vascular resistance; RI = resistance index; PI = pulsatility index; Hb = hemoglobin concentration; pH_{art} = arterial *p*H; pH_{cv} = cerebral venous *p*H; Pa_{CO_2} = arterial P_{CO_2}; Pa_{O_2} = arterial P_{O_2}; CMR_{O_2} = cerebral metabolic rate for oxygen; CMR_{lact} = cerebral metabolic rate for lactate; CMR_{gluc} = cerebral metabolic rate for glucose; Visc = viscosity; NPT = nasopharyngeal temperature.

* Significantly differs from preceding measurement; $P < 0.05$, sequentially adjusted for multiple test procedures.

CPB: in less than 30% of patients consistent estimations of the direction of CBF changes could be obtained by TCD between measurements II and III. This discrepancy was also evident in the time course of mean CBF and mean V_{MCA}. Although hypothermic CPB caused a significant reduction of CBF, mean V_{MCA} slightly increased. Different mechanisms might be responsible for this finding. First, the overestimation of CBF changes by V_{MCA} measurements during CPB might be related to hypothermia-induced vasoconstriction of basal cerebral arteries. This hypothesis is consistent with the direction of estimated changes: a decrease in MCA diameter would consequently increase V_{MCA} for a given flow value. However, in children undergoing profound hypothermia real-time ultrasound scanning of the MCA did not demonstrate temperature-induced alterations of vascular diameter.[27] Similarly, in our patients the time course of V_{MCA} cannot completely be explained by temperature-induced alterations of vascular diameter. If hypothermia-induced changes of MCA diameter exclusively would be responsible for the discrepancy of CBF and V_{MCA} changes during CPB, reverse reactions should be expected after rewarming. This was not observed.

Second, changes of intraarterial flow velocity profiles should be considered. Such changes might be related to hemodilution and to the nonpulsatile flow pattern. As velocity measurements were based on spectral envelope curves, changes of arterial velocity profiles might have biased the results of TCD monitoring. Time-averaged envelope curves from maximal intravascular velocity commonly are believed to parallel mean velocity and intensity-weighted mean velocity under physiologic conditions; nevertheless, this might not be true for changes in flow pattern and for conditions of substantially altered viscosity.[28,29]

Anesthesia-related drugs might also influence the relation between flow and velocity due to vasoactive properties on basal cerebral arteries. As demonstrated by simultaneous measurements of cerebral circulation by TCD and single photon emission computed tomography, vasodilators like nitroglycerin have to be considered as a reason for inconsistent reactions of CBF and V_{MCA}.[30] The only vasoactive medication used for

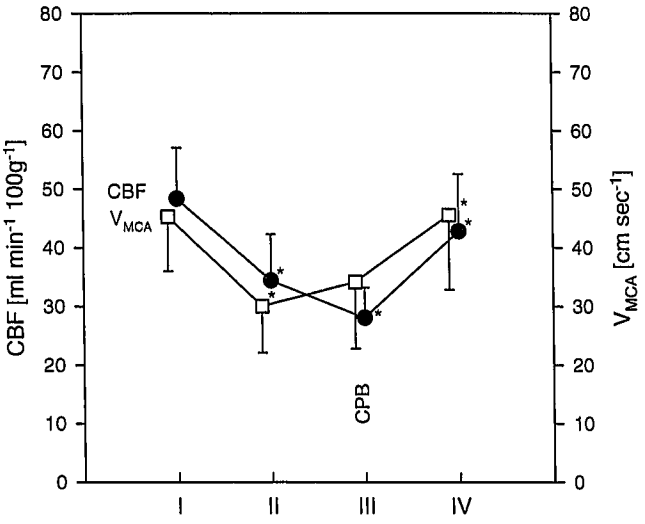

Fig. 2. Time course of mean cerebral blood flow (CBF) and mean middle cerebral artery flow velocity (V_{MCA}) (±SD). Inconsistent changes in flow and V_{MCA} occurred after the initiation of CBP. I = awake; II = after induction of anesthesia; III = during nonpulsatile cardiopulmonary bypass at 26°C; IV = end of surgery. *Differs significantly from preceding measurement ($P < 0.05$, sequentially adjusted for multiple test procedures).

the treatment of hypertension during CPB was phentolamine. However, vasodilation cannot explain the observed discrepancy between flow and velocity changes because an increase in MCA diameter would have caused an underestimation of CBF by TCD measurements. Furthermore, the consistency of changes from control values in the awake patient to postinduction values of CBF and V_{MCA} does not suggest any major pharmacologic influence of fentanyl–midazolam anesthesia. This is in agreement with a previous method comparison study on the effects of sufentanil.[31] Anesthesia-related effects on MCA diameter, however, had been postulated for halothane.[5]

Inconsistent changes in CBF and V_{MCA} additionally may be explained by changes in the regional distribution of CBF. V_{MCA} reflects blood flow in the proximal MCA whereas modifications of the Kety-Schmidt technique measure global CBF. Consequently, changes in regional flow distribution associated with hypothermia may also contribute to the discrepancy between CBF and V_{MCA} changes during CPB.

For a quantitative analysis of the relation between CBF and V_{MCA} a comparison of absolute values seemed inappropriate because a close linear relation between Doppler-derived velocity and flow could only be expected if the cross-sectional area of the insonated vessel would be identical in all patients. Therefore, only relative changes in CBF and V_{MCA} were analyzed. Individual

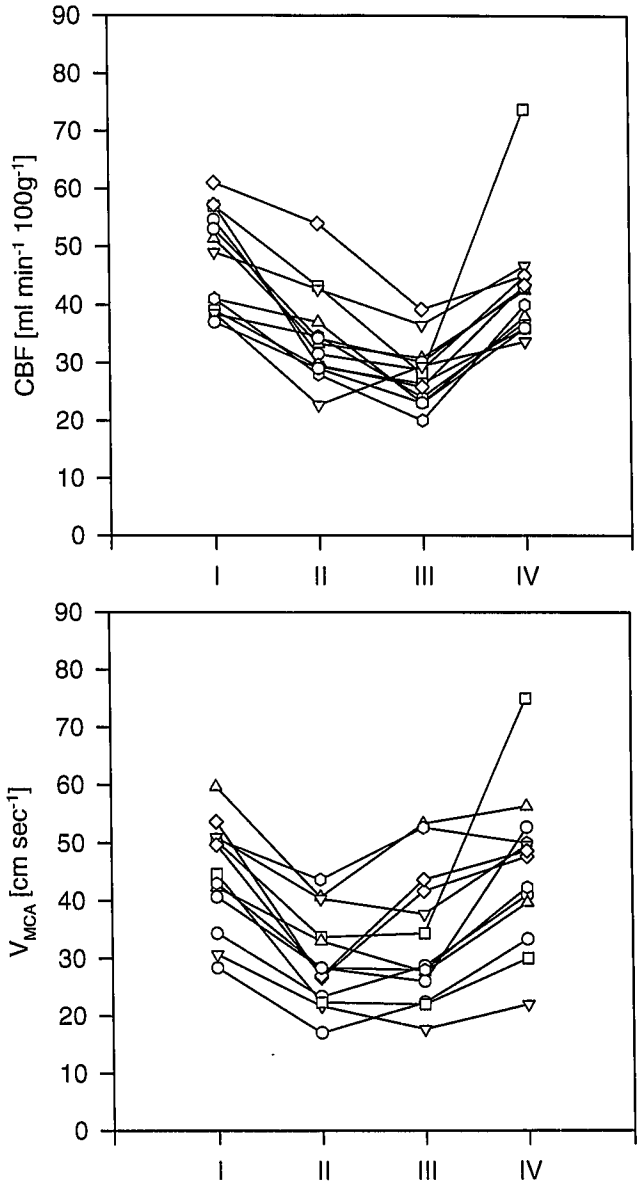

Fig. 3. Time course of individual cerebral blood flow (CBF) and middle cerebral artery flow velocity (V_{MCA}) data. Consistent directional changes in CBF and V_{MCA} occurred in 96% of data between measurements I and II and between III and IV, but in only 29% of changes between measurements II and III, when cerebral hemodynamic changes were associated with hypothermic cardiopulmonary bypass. I = awake; II = after induction of anesthesia; III = during nonpulsatile cardiopulmonary bypass at 26°C; IV = end of surgery.

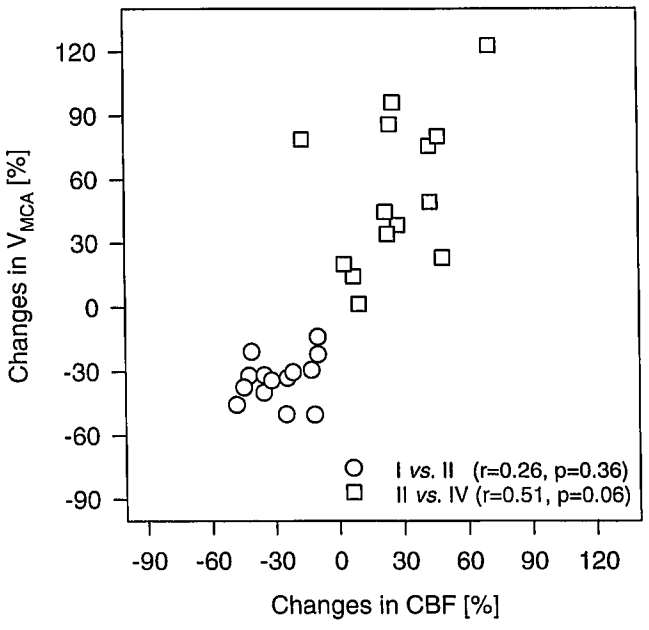

Fig. 4. Scatterplot of relative changes in cerebral blood flow (CBF) and middle cerebral artery flow velocity (V_{MCA}). Measurements during cardiopulmonary bypass were excluded from analysis. To facilitate comparisons of flow and velocity measurements, differences between consecutive measurements were expressed as percentage values. I = awake; II = after induction of anesthesia; IV = end of surgery.

pre- and postbypass changes in CBF and V_{MCA}, however, did not reveal clinically useful correlations. TCD measured flow velocity in our patients thus could not predict individual changes in CBF during the different periods.

Bishop and coworkers[16] investigated hypercapnia-induced changes in V_{MCA} and regional CBF by intravenous xenon 133 in symptomatic patients with cerebrovascular disease. They found a poor direct relation between these parameters, but changes of CBF and V_{MCA} expressed as a reactivity index showed a high coefficient of correlation (r = 0.849). However, this study was based on a single variation of CBF in awake patients. Comparing individual reactions to carotid occlusion during carotid endarterectomy, Halsey *et al.*,[17,18] using intracarotid injections of xenon 133, found a considerable variability in the reaction of regional CBF and V_{MCA}. From a methodologic point of view, the authors pointed out that regional CBF and TCD measurements are qualitatively different indexes of the cerebral circulation. Measurements of regional CBF by xenon 133 are heavily weighted toward cortical blood flow. TCD measurements are indexes of flow in the proximal segment of the MCA and thus also reflect, although proportionally less than cortical blood flow, circulation of deep white and gray matter supplied by the lenticulostriate arteries. The Kety-Schmidt technique, as applied in our investigation, basically represents global average CBF which also does not completely match the sample of the cerebral circulation assessed by TCD.

Only recently, CBF measurements made by the Kety-Schmidt technique in the desaturation mode have been compared with V_{MCA} measurements in healthy volunteers.[19] The authors found divergent results obtained when changes in V_{MCA} and global average CBF were simultaneously assessed during dynamic exercise. Beside potential technical limitations of TCD, a reduction in the diameter of the MCA was suggested as the most likely hypothesis to explain the divergent results of both techniques.

In most previous methodologic studies, measurements were performed in awake persons under well-controlled conditions. Until now, no comparison between direct measurements of CBF and V_{MCA} has been performed during cardiac surgery and extracorporeal circulation. Van der Linden and coworkers[20] studied seven patients undergoing cardiac operations with deep hypothermia by using a thermodilution technique for

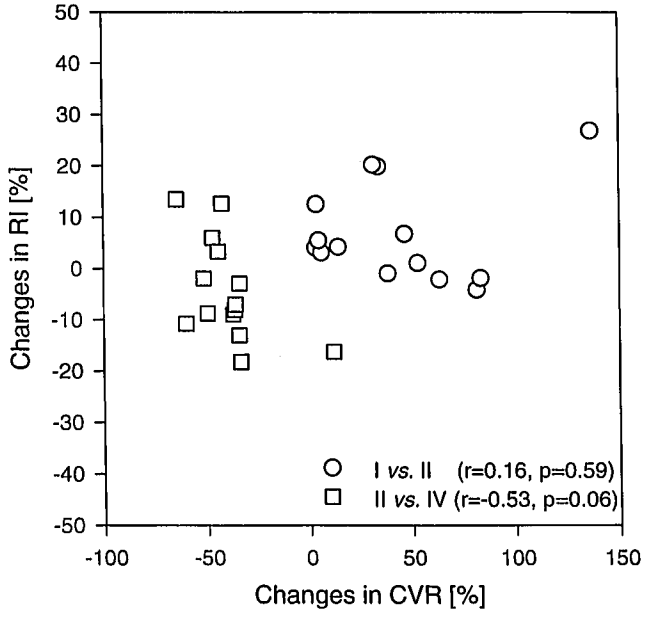

Fig. 5. Scatterplot of relative changes in cerebral vascular resistance (CVR) and resistance index (RI). To facilitate comparisons of CVR and RI, differences between consecutive measurements were expressed as percentage values. I = awake; II = after induction of anesthesia; IV = end of surgery.

determination of jugular venous blood flow as an index of CBF. Mean V_{MCA} and jugular venous blood flow showed consistent changes at virtually all stages of the surgical procedure. The greatest differences between normalized flow and velocity measurements were also found during CPB. The overall correlation of these variables was good ($r = 0.77$), however, the slope and intercept of the regression lines were considerably different from the line of identity in all but one patient. This finding should not only be attributed to a systematic underestimation of CBF changes by TCD, but might as well indicate a bias of flow estimation by jugular vein thermodilution measurements.

To our knowledge, no comparison between CVR and TCD-derived indexes has been performed until now. The two most commonly calculated indexes, RI and PI, both had been introduced as downstream indexes, that is, as a measure of vascular resistance distal to the site of insonation.[11,12] In our study, variations of CVR may primarily be attributed to effects of anesthesia and changes in blood viscosity. The increase in mean CVR after induction of anesthesia was associated with a small but significant increase in mean RI and PI. Both indexes, however, did not follow the marked decrease in CVR after termination of CPB. This finding may partly be explained by the concomitant decrease in viscosity. Because pulsatility of flow in peripheral arteries is known to be related to cardiac pump function and viscosity, changes of these variables might have masked resistance-related changes of Doppler indexes. Neither before nor after CPB did individual changes in RI and PI show a linear relation to changes in CVR. This indicates that serial determinations of Doppler indexes were not predictive for changes in CVR during cardiac surgery. However, these limitations might not refer to other pharmacologic effects on CVR and to the evaluation of downstream stenosis in cerebrovascular disease.

In summary, this study compared invasive and TCD measurements of spontaneous changes in cerebral hemodynamic variables associated with cardiac surgery. Changes in cerebral perfusion associated with hypothermic CPB could not be estimated by TCD monitoring. Consistent directional changes in CBF and V_{MCA} were observed in less than 30% of patients during this stage of surgery. This finding may be related to alterations of MCA diameter, changes of intraarterial velocity spectra and changes of regional flow distribution. Although changes in mean V_{MCA} before and after CPB paralleled changes in mean CBF, individual responses of V_{MCA} could not reliably predict percentage changes in CBF. Doppler-derived PI and RI that are supposed to reflect downstream vascular conditions were not reliably related to variations of CVR.

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