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Cerebrovascular CO_2 Reactivity during Anesthesia in Patients with Diabetes Mellitus and Peripheral Vascular Disease

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Background: **Diabetes mellitus (DM) and systemic atherosclerosis are risk factors for stroke. Although the origins of increased risk are complex, one possibility is that cerebrovascular reactivity is impaired and does not allow the brain to compensate for aberrations in physiology. The current study tested this issue by evaluating mean blood flow velocity of the middle cerebral artery (Vmca) and carbon dioxide reactivity during anesthesia in patients with DM and peripheral vascular disease (PVD).**

Methods: **Fifty-two patients were observed: 20 patients with DM (the DM group), 12 patients with PVD (the PVD group), and 20 patients classified as American Society of Anesthesiologists physical status 1 or 2 (the control group). The Vmca was measured using transcranial Doppler ultrasonography during isoflurane–nitrous oxide anesthesia. After measuring baseline Vmca at a partial pressure of carbon dioxide in arterial blood (Pa_{CO_2}) of 37.7 ± 4.5 mmHg (mean ± SD), measurements were repeated at a Pa_{CO_2} of 44.2 ± 3.8 mmHg, and the carbon dioxide reactivity (absolute value: $cm \cdot s^{-1} \cdot mmHg^{-1}$; relative value: percentage of baseline Vmca/mmHg) was calculated.**

Results: **The baseline Vmca of the DM group (51 ± 12 cm/s) was significantly greater than those of the control group (42 ± 6 cm/s) and the PVD group (42 ± 13 cm/s). The absolute and relative values of carbon dioxide reactivity in the DM group (3.1 ± 1.3 $cm \cdot s^{-1} \cdot mmHg^{-1}$; 6.3 ± 2.4%/mmHg) were significantly greater than or equivalent to those of the control group (2.3 ± 0.8 $cm \cdot s^{-1} \cdot mmHg^{-1}$; 5.3 ± 1.7%/mmHg), respectively. In the PVD group, the baseline Vmca was equivalent to the control group, but the carbon dioxide reactivity (1.1 ± 0.5 $cm \cdot s^{-1} \cdot mmHg^{-1}$; 2.8 ± 1.2%/mmHg) was significantly less.**

Conclusions: **The patients with DM have increased baseline cerebral blood flow velocity and normal carbon dioxide reactivity during anesthesia. The patients with PVD have decreased carbon dioxide reactivity, but baseline flow velocity is maintained. (Key words: Cerebral blood flow velocity; glycosylated hemoglobin [hemoglobin AIC]; stroke risk; transcranial Doppler ultrasonography.)**

DIABETES mellitus (DM) and atherosclerosis are risk factors for ischemic cerebrovascular disease.[1–3] Although the origins of increased risk are complex, one possibility is that cerebrovascular reactivity is impaired and does not allow the brain to compensate for aberrations in physiology. Results of some previous studies were inconsistent regarding basal cerebral blood flow (CBF) and cerebrovascular reactivity in awake diabetic humans.[4–8] To the best of our knowledge, no study has evaluated cerebral circulatory state and cerebrovascular reactivity during anesthesia in patients with DM or peripheral vascular disease (PVD) in the lower extremities. The current study, therefore, was designed to evaluate cerebral circulatory state, including carbon dioxide reactivity, during general anesthesia in patients with DM and PVD using noninvasive transcranial Doppler ultrasonography.

Materials and Methods

Patients and Preoperative Assessment

Fifty-two patients scheduled for nonneurosurgical elective surgery during general anesthesia were enrolled in the study: 20 patients with DM (the DM group), 12 patients with PVD (the PVD group) of the lower extremities, and 20 patients who were age matched and classified as American Society of Anesthesiologists physical status 1 or 2 (the control group). The patients with apparent histories of ischemic cerebrovascular disease were excluded from the study. The study protocol was

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approved by the Ethical Committee for Human Study of the Yamaguchi University Hospital, and informed consent was obtained from each patient.

The day before surgery, blood pressure and heart rate were measured and recorded while the patients were resting. Patient medical histories, including ischemic heart disease and diabetic complications, were obtained from interviews and the clinical recordings.

Anesthesia and Monitoring

All patients fasted from midnight on the night before surgery. All oral hypoglycemic agents and insulin were withheld on the morning of surgery in patients in the DM group. The patients were premedicated with 0.25 to 0.5 mg atropine sulfate and 25 to 50 mg hydroxyzine or 2 or 3 mg midazolam administered intramuscularly. Anesthesia was induced with 4 mg/kg thiopental and 0.15 mg/kg vecuronium, tracheas were intubated, and the lungs were mechanically ventilated. Anesthesia was maintained with 1% isoflurane (end-tidal) in 50% nitrous oxide and oxygen. In addition, fentanyl was administered intermittently (total dose, 100–200 μg). Acetate and Ringer's solution was infused intravenously (5–8 $ml \cdot kg^{-1} \cdot h^{-1}$), and the blood glucose concentration was measured by enzymatic analysis (Accutrend, Boehringer-Mannheim, Mannheim, Germany). The procedures were orthopedic surgery or laparotomy in the control and DM groups and aortofemoral bypass, femoropopliteal bypass, or both, in the PVD group. Before induction of anesthesia, an epidural catheter was inserted in patients scheduled for laparotomy, but no drug was administered *via* the epidural catheter until all study measurements were obtained. A radial artery was cannulated for direct monitoring of arterial blood pressure, for arterial blood sampling for blood gas analysis, and to determine hemoglobin, blood glucose, and electrolyte concentrations. The nasopharyngeal temperature (Temp) was monitored and maintained using a warming blanket (Medi-Therm II, Gaymar, New York, NY). Pulse oximetry was monitored, and end-tidal carbon dioxide tension and concentrations of isoflurane and nitrous oxide were assessed continuously with an infrared analyzer (CAPNOX; Nippon Colin, Komaki, Japan).

Determination of Vmca and Cerebrovascular Carbon Dioxide Reactivity during Anesthesia

After induction of anesthesia, a 2-MHz pulsed transcranial Doppler probe was attached to the patient's head at the left "temporal window," and the mean blood flow velocity of the middle cerebral artery (Vmca) was measured continuously (TC 2–64; EME, Überlingen, Germany). After the appropriate signals were identified at a depth of 45–55 mm, the probe was fixed using a probe holder (model IMP-F/536B; EME), so as not to change the insonating angle. Because the velocity fluctuated with the respiration cycle, the value during end-expiration was recorded.

More than 1 h (≈1.5 h after anesthesia induction) after making the incision, we measured baseline Vmca (at an end-tidal carbon dioxide tension of approximately 35 mmHg), while anesthesia was maintained with isoflurane, 1%, (end-tidal) in 50% nitrous oxide and oxygen. After obtaining baseline Vmca and blood samples for analysis of blood gases, blood glucose, hemoglobin, and electrolyte concentrations, we increased the end-tidal carbon dioxide tension by adding a dead-space tube of approximately 100-ml volume to the endotracheal tube and reducing the ventilatory frequency by 1 or 2 breaths/min. This resulted in an increase in the partial pressure of carbon dioxide in arterial blood (Pa_{CO_2}) of approximately 7 or 8 mmHg within a few minutes. Measurements were repeated when the end-tidal carbon dioxide tension was increased and remained stable for 5–10 min. Small doses of vecuronium (2 mg) were administered intravenously to prevent spontaneous respiration during hypercapnia.

The carbon dioxide reactivity in each patient was calculated as both the absolute change in Vmca ($cm \cdot s^{-1} \cdot mmHg^{-1}$) and the percentage change in Vmca (percentage of the baseline Vmca/mmHg) per each millimeter of mercury change in Pa_{CO_2} using the following formula:

The absolute carbon dioxide reactivity

$$(cm \cdot s^{-1} \cdot mmHg^{-1}) = \Delta \text{ Vmca}/\Delta \text{ Pa}_{CO_2}$$

The relative carbon dioxide reactivity

$$(\text{percentage of the baseline Vmca/mmHg}) = \Delta \text{ Vmca}/\Delta \text{ Pa}_{CO_2}/\text{baseline Vmca}) \times 100$$

where Δ Vmca is the difference between the flow velocity after Pa_{CO_2} elevation and the baseline flow velocity, and Δ Pa_{CO_2} is the difference between the final Pa_{CO_2} and the baseline Pa_{CO_2}.

Statistical Analysis

All data are reported as mean ± SD. An analysis of variance was used for intergroup comparisons of preoperative physiologic data and calculated carbon dioxide reactivity. The chi-squared test was used to compare the

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Table 1. Patient Characteristics

	Control (n = 20)	DM (n = 20)	PVD (n = 12)
Age (yr)	54 ± 16	59 ± 11	68 ± 8
Gender (male/female)	13/7	14/6	10/2
Height (cm)	160 ± 10	161 ± 10	155 ± 8
Weight (kg)	56 ± 11	56 ± 9	50 ± 9
MAP at rest (mmHg)	90 ± 9	92 ± 14	97 ± 14
HR at rest (beats · min^{-1})	69 ± 7	72 ± 10	72 ± 12

Values are mean ± SD.

MAP = mean arterial pressure; HR = heart rate; DM = diabetes mellitus; PVD = peripheral vascular disease.

gender distribution. Repeated-measures analysis of variance was used for intergroup comparisons of physiologic data (including Vmca) during the carbon dioxide reactivity study. Fisher's protected least significant difference was used for *post hoc* test. $P < 0.05$ was considered significant.

Results

Table 1 shows patient characteristics. There were no significant differences among the three groups in age, gender distribution, height, weight, or resting mean arterial pressure and heart rate.

Tables 2 and 3 show clinical data and Vmca in the DM and the PVD groups, respectively. One patient (patient 6) had diabetic retinopathy and nephropathy and was taking no medication at admission, but no other patients had such diabetic complications. Nine of 12 PVD patients were hypertensive, and 8 patients were prescribed antihypertensive drugs.

Table 4 shows the values for Vmca, Pa_{CO_2}, Pa_{O_2}, mean arterial pressure, heart rate, temperature, hemoglobin, and blood glucose. There were no significant changes in mean arterial pressure, heart rate, temperature, and hemoglobin, blood glucose, and electrolyte concentrations (data not shown) during the study. The baseline Vmca in the DM group was significantly greater than that of the control and the PVD group, but there was no significant difference between the PVD and the control group. The Vmca (post) values in all groups were significantly increased with Pa_{CO_2} elevation.

Figure 1 shows the cerebrovascular carbon dioxide reactivity. The absolute value of carbon dioxide reactivity in the DM group (3.1 ± 1.3 cm · s^{-1} · $mmHg^{-1}$) was significantly greater than in the control group (2.3 ± 0.8 cm · s^{-1} · $mmHg^{-1}$), although the relative value (6.3 ± 2.4%/$mmHg^{-1}$) was not different from control (5.3 ± 1.7%/$mmHg^{-1}$). The absolute value (1.1 ± 0.5 cm · s^{-1} · $mmHg^{-1}$) and the relative value (2.8 ± 1.2%/$mmHg^{-1}$) of carbon dioxide reactivity in the PVD group were significantly less than in the control group and the DM group. In two diabetic patients with PVD (patients 2 and 11), the Vmca and carbon dioxide reactivity were similar to those of other patients with PVD.

Discussion

The principal findings of the current study are (1) that the baseline Vmca in the DM group was significantly greater than in the control group; (2) that the absolute and relative values of carbon dioxide reactivity in the DM group were significantly greater than or equivalent to the control group, respectively; and (3) that the baseline Vmca in the PVD group was equivalent to the control group, but the carbon dioxide reactivity was significantly less than in the control group.

In interpreting our results, it seems justified to first consider the validity of the transcranial Doppler ultrasonography and the possibility of the influence of surgical stimulation. The flow velocity determined by transcranial Doppler ultrasonography is not equivalent to CBF. However, an excellent correlation between relative changes in flow velocity and changes in CBF has been reported.[9] In the current study, the baseline Vmca in the control group was 42 ± 6 cm/s (Pa_{CO_2} 37 ± 3 mmHg) during isoflurane, 1%, and 50% nitrous oxide anesthesia supplemented with fentanyl. Because we did not measure flow velocity while the patients were awake, we do not know whether flow velocity was increased or decreased by this anesthetic regimen. The observed carbon dioxide reactivity of 2.3 ± 0.8 cm · s^{-1} · $mmHg^{-1}$ (5.3 ± 1.7%/mmHg) in the control group is comparable to that reported by others.[10] The current study was performed during surgery using a stable general anesthetic. Surgical procedures are not identical, but we chose study periods when the surgical stimulation intensity was considered to be minimal. The mean arterial pressure and the heart rate during the study periods were nearly equal to the preoperative resting values, with minimum fluctuation, and did not differ among the three groups. Therefore, we think that the influence of the difference in the magnitude of surgical stimulation is minimal.

Cerebral Blood Flow Velocity and Cerebrovascular Carbon Dioxide Reactivity in Diabetic Patients

In diabetic patients, the baseline Vmca was significantly greater than in the control group (51 ± 12 *vs.*

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Table 2. Clinical Data and V_{mca} of DM Patients

Patient Number	Age (yr)	Gender	Fasting Blood Glucose (mg · dl^{-1})	HbA_{1c} (%)	Therapy	Diabetic Complications	CAD	Other Complications	Other Medications	V_{mca} (cm · s^{-1}) Baseline	V_{mca} (cm · s^{-1}) Post
1	58	F	248	9.9	Glibenclamide	(−)	(−)	(−)	(−)	42	72
2	72	M	160		None	(−)	(−)	(−)	(−)	44	64
3	70	F	170	8.0	Insulin	(−)	(−)	(−)	(−)	56	86
4	41	F	202		Glibenclamide	(−)	(−)	(−)	(−)	32	46
5	65	M	116		Diet	(−)	(−)	(−)	(−)	42	62
6	47	F	268	13.8	None	ret/neph	(−)	(−)	(−)	72	86
7	50	M	118		Diet	(−)	(−)	(−)	(−)	62	96
8	70	M	100	4.3	Diet	(−)	(−)	(−)	(−)	54	72
9	41	F	165	9.7	Diet	(−)	(−)	(−)	(−)	64	94
10	58	M	142		Diet	(−)	(−)	HT	Ca channel blocker	52	94
11	66	M	162		Glibenclamide	(−)	(−)	(−)	(−)	66	110
12	52	M	157	7.3	Insulin	(−)	(−)	(−)	(−)	46	60
13	62	F	189	9.9	Insulin	(−)	(−)	(−)	(−)	64	86
14	68	M	122	5.6	Insulin	(−)	(−)	HT	Ca channel blocker	58	70
15	54	M	120	6.7	Insulin	(−)	(−)	(−)	(−)	56	72
16	66	M	102	5.0	Diet	(−)	(−)	HT	(−)	50	62
17	79	M	117	7.2	Diet	(−)	(−)	(−)	(−)	24	36
18	68	M	138		Insulin	(−)	(−)	(−)	(−)	44	52
19	40	M	112		Glibenclamide	(−)	(−)	(−)	(−)	46	60
20	58	M	223	15.0	Insulin	(−)	(−)	(−)	(−)	50	58

F = female; M = male; HbA_{1c} = glycosylated hemoglobin (normal value 4.3–5.8%); DM = diabetes mellitus; ret = retinopathy; neph = nephropathy; HT = hypertension; CAD = coronary artery disease; V_{mca} = mean blood flow velocity of middle cerebral artery; Baseline = V_{mca} before CO_2 challenge; Post = V_{mca} after CO_2 challenge.

42 ± 6 cm/s). The higher CBF has been reported in patients with short-duration insulin-dependent diabetes mellitus who have no diabetic complications[4] and in patients with long-duration but well-controlled insulin-dependent diabetes.[5] However, Wakisaka *et al.*[6] reported reduced regional CBF in elderly patients with long-standing non-insulin-dependent diabetes. Thirty percent of these patients had retinopathy, neuropathy, nephropathy, or all of these complications. Rodriguez *et al.*[7] observed an inverse correlation between basal global CBF and the duration of DM. It is not clear why these contradictory results (decreased, unchanged, or even increased CBF) have been observed. We assume that differences in the level and duration of hyperglycemia

Table 3. Clinical Data and V_{mca} of PVD Patients

Patient Number	Age (yr)	Gender	ABI	Other Complications	Medication	CAD	V_{mca} (cm · s^{-1}) Baseline	V_{mca} (cm · s^{-1}) Post
1	52	M	0.48	HT	Ca channel blocker	(−)	52	66
2	66	M	0.75	HT, DM	Ca channel blocker	(−)	56	78
3	60	M	0.43	HT	β blocker	(−)	34	40
4	64	M	0.40	HT	Ca channel blocker, nitrate	(+)	38	48
5	81	F	0	HT	(−)	(−)	29	36
6	70	M	0.52	HT	Ca channel blocker	(−)	63	69
7	58	M	0.55	(−)	(−)	(−)	46	50
8	72	M	0.52	(−)	(−)	(−)	32	42
9	70	M	0.45	HT	Ca channel blocker	(−)	56	60
10	72	F	0.58	Asthma	Theophylline	(−)	28	32
11	72	M	0.61	HT, DM	Ca channel blocker, insulin	(−)	50	56
12	75	M	0.73	HT	Ca channel blocker	(−)	22	28

ABI = Ankle–brachial index, the ratio of systolic blood pressure in the ankle to the systolic blood pressure in the arm (The reported value of an individual patient is the lower one of the two measured sides.); HT = hypertension; DM = diabetes mellitus; CAD = coronary artery disease; PVD = peripheral vascular disease; V_{mca} = mean flow velocity of middle cerebral artery; Baseline = V_{mca} before CO_2 challenge; Post = V_{mca} after CO_2 challenge.

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Table 4. Physiological Data during CO_2 Reactivity Study

		Control (n = 20)	DM (n = 20)	PVD (n = 12)
V_{mca} (cm · s^{-1})	Baseline	42 ± 6	51 ± 12†	42 ± 13
	Post*	60 ± 9	72 ± 19†	50 ± 16
Pa_{CO_2} (mmHg)	Baseline	37 ± 3	37 ± 3	38 ± 4
	Post*	44 ± 4	44 ± 3	45 ± 5
Pa_{O_2} (mmHg)	Baseline	245 ± 54	254 ± 48	220 ± 60
	Post	236 ± 46	235 ± 53	207 ± 56*
MAP (mmHg)	Baseline	81 ± 15	87 ± 12	81 ± 12
	Post	82 ± 15	87 ± 12	81 ± 13
HR (beats · min^{-1})	Baseline	78 ± 11	81 ± 12	69 ± 10
	Post	77 ± 11	79 ± 11	70 ± 10
Temp (°C)	Baseline	35.9 ± 0.7	36.0 ± 0.5	35.8 ± 0.5
	Post	35.7 ± 0.3	36.0 ± 0.5	35.8 ± 0.6
Hb (g · dl^{-1})	Baseline	12.5 ± 1.8	11.8 ± 1.6	11.4 ± 1.7
	Post	12.4 ± 1.9	11.8 ± 1.5	11.5 ± 1.7
Blood glucose (mg · dl^{-1})	Baseline	120 ± 20	143 ± 39	129 ± 38

Values are mean ± SD.

V_{mca} = mean blood flow velocity of middle cerebral artery; MAP = mean arterial pressure; HR = heart rate; Temp = nasopharyngeal temperature; Hb = hemoglobin; Baseline = before CO_2 challenge; Post = after CO_2 challenge; DM = diabetes mellitus; PVD = peripheral vascular disease.

* Significantly different from baseline value ($P < 0.05$).

†Significantly different from the control group and the PVD group ($P < 0.05$).

and in the severity of vascular disease may be responsible for the difference in reported results.

Sieber *et al.*[11] reported in dogs that chronic hyperglycemia associated with pancreatectomy increased CBF and the cerebral metabolic rate for oxygen. However, their subsequent study did not show any differences in CBF or the cerebral metabolic rate for oxygen between the control (nonhyperglycemic) and chronic diabetic (hyperglycemic) dogs when they were either awake or anesthetized with pentobarbital and fentanyl.[12] The authors speculated that the different results were caused by the elimination of the acute surgical stress in the latter study. Because we did not measure flow velocity in awake patients or in those without surgical stress, we cannot rule out the possibility of differential sensitivity to surgical stress or anesthetics in diabetic patients.

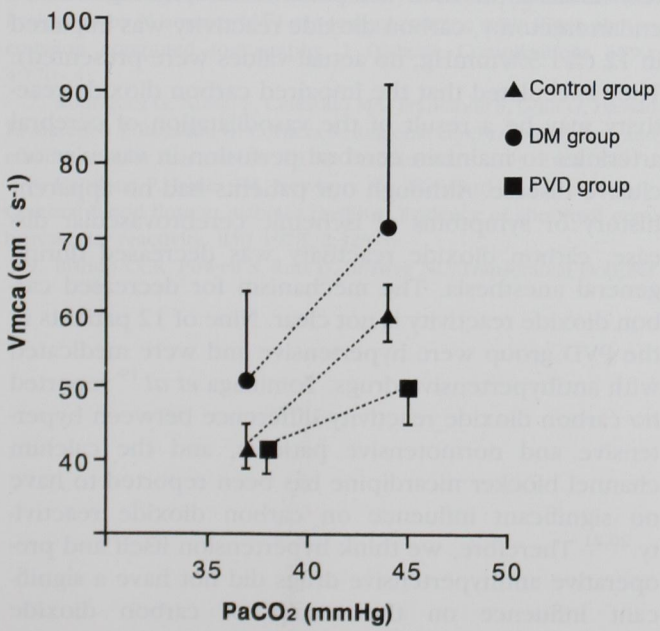

Fig. 1. Cerebrovascular carbon dioxide reactivity. The absolute value but not the relative value of carbon dioxide reactivity in the diabetes mellitus group was significantly greater than in the control group. Carbon dioxide reactivity (absolute and relative values both) in the peripheral vascular disease group was significantly less than in the control and the DM group.

For cerebrovascular carbon dioxide reactivity, Dandona *et al.*[8] reported that CBF decreased in response to the inhalation of 5% carbon dioxide in 45% of diabetic patients (CBF was increased in 38% of patients and unchanged in 17%). They concluded that diabetic persons are at increased risk of cerebrovascular disease because they cannot compensate with an increased CBF when necessary. These abnormalities were attributed to microangiopathy in the cerebral vessels. Griffith *et al.*[4] also reported some DM patients with decreased carbon dioxide reactivity. In rats, Pelligrino and Albrecht[13] reported unchanged carbon dioxide reactivity in the early and late stages (prolonged duration) of a streptozotocin-induced hyperglycemia model, despite the apparent blunted response or loss of vasodilative response to insulin-induced hypoglycemia. This suggested that there was selective suppression of the cerebral vasodilatory

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capacity in the chronically hyperglycemic diabetic patients. The authors speculated that the difference between their study and previous studies could be a result of the species or the differences in the severity and stability of hyperglycemia during an extended period. The latter may lead to a variability in vascular disease and reactivity.

It has long been believed that cerebrovascular carbon dioxide reactivity is influenced by basal cerebrovascular resistance (conductance),[14] and thus the higher the baseline flow, the steeper the carbon dioxide reactivity. In the current study, when evaluated with the absolute carbon dioxide reactivity, carbon dioxide reactivity in the DM group was significantly greater than in the control group (3.1 ± 1.3 *vs.* 2.3 ± 0.8 $cm \cdot s^{-1} \cdot mmHg^{-1}$), and this agrees with that assumption. However, when evaluated with the relative carbon dioxide reactivity, no statistical significance was seen between the DM and the control group (6.3 ± 2.4 *vs.* 5.3 ± 1.7%/mmHg). Because the transcranial Doppler ultrasonography method does not provide absolute changes but gives relative changes in CBF, carbon dioxide reactivity might be best assessed by the relative changes. Considering this methodologic characteristic, our results indicate that the DM patients examined in the current study have a maintained carbon dioxide reactivity (not increased). However, it deserves discussion concerning the heterogeneity in the DM group. Although the available data were limited in the current study (only in 12 patients), the recent glycosylated hemoglobin (hemoglobin A1c) value and carbon dioxide reactivity were correlated inversely, suggesting that the poor glycemic control exhibits the possibility of reduced reactivity of cerebral vessels. The most diabetic patients in this study were free from clinical symptoms of microangiopathy (retinopathy, nephropathy) and macroangiopathy (coronary artery disease, carotid artery disease, and so forth). Although not completely ruled out, atherosclerosis in our DM patients may not be a major factor affecting the results. Our results may indicate that the diabetic patients with poor glycemic control may be at increased risk of ischemia because of impaired cerebrovascular reactivity, although this ought to be further determined in a much larger population of diabetic patients.

Cerebral Blood Flow Velocity and Cerebrovascular Carbon Dioxide Reactivity in Peripheral Vascular Disease

The patients with PVD are considered to have generalized atherosclerosis that increases a risk of cerebral infarction, myocardial infarction, renal dysfunction, and so forth. Although we could not afford to perform angiography to assess the cerebral arteries and carotid arteries before operation, atherosclerotic changes in these arteries most likely were present. A decreased CBF might be anticipated in the patients with atherosclerosis in the cerebral arteries and carotid arteries, but in the current study the baseline Vmca during general anesthesia was not different from that of control patients (42 ± 13 *vs.* 42 ± 6 cm/s). Sugimori *et al.*[15] showed no differences in the average Vmca among patients with or without carotid artery occlusive disease and minor stroke. Heistad *et al.*[16] also showed that baseline CBF was similar in monkeys with or without atherosclerosis of the carotid arteries.

Regarding the carbon dioxide reactivity, absolute and relative values of carbon dioxide reactivity both were decreased compared with the control group (2.3 ± 0.8 *vs.* 1.1 ± 0.5 $cm \cdot s^{-1} \cdot mmHg^{-1}$; 5.3 ± 1.7 *vs.* 2.8 ± 1.2%/mmHg). Some previous studies reported impaired cerebrovascular carbon dioxide reactivity in patients with ischemic cerebrovascular disease[17] and in those with carotid artery disease.[18] Thiel *et al.*[18] studied preoperative cerebrovascular carbon dioxide reactivity using transcranial Doppler ultrasonography in carotid artery disease. In their 94 patients undergoing carotid endarterectomy, carbon dioxide reactivity was impaired in 12 ($\leqq$1.5%/mmHg, no actual values were presented). They speculated that the impaired carbon dioxide reactivity may be a result of the vasodilatation of cerebral arterioles to maintain cerebral perfusion in vascular occlusive disease. Although our patients had no apparent history or symptoms of ischemic cerebrovascular disease, carbon dioxide reactivity was decreased during general anesthesia. The mechanism for decreased carbon dioxide reactivity is not clear. Nine of 12 patients in the PVD group were hypertensive and were medicated with antihypertensive drugs. Tominaga *et al.*[19] reported no carbon dioxide reactivity difference between hypertensive and normotensive patients, and the calcium channel blocker nicardipine has been reported to have no significant influence on carbon dioxide reactivity.[20,21] Therefore, we think hypertension itself and preoperative antihypertensive drugs did not have a significant influence on the results of carbon dioxide reactivity. Whatever the mechanism for decreased carbon dioxide reactivity, our results indicate that when patients with PVD are anesthetized, even if they have no apparent history of ischemic cerebrovascular disease, they are at risk for cerebral hemodynamic impairment

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because they may exhibit poor reserve to increase CBF when necessary.

In conclusion, the baseline Vmca was increased and the carbon dioxide reactivity was maintained in the diabetic patients during anesthesia. In the patients with PVD, the baseline Vmca was maintained, but the carbon dioxide reactivity was decreased.

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