

Jugular Venous Bulb Oxygen Saturation in Patients with Preexisting Diabetes Mellitus or Stroke during Normothermic Cardiopulmonary Bypass

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Background: The authors hypothesized that patients with cerebrovascular abnormalities or metabolic disorders may experience abnormality in cerebral circulation more frequently than patients without these risks. The current study attempted to assess jugular venous bulb oxygen saturation (S_{jvO_2}) in patients with preexisting diabetes mellitus or stroke undergoing normothermic cardiopulmonary bypass.

Methods: Thirty-nine patients undergoing elective coronary artery bypass graft surgery were studied, including 19 age-matched control patients, 10 diabetic patients, and 9 patients with preexisting stroke. A 4.0-French fiberoptic oximetry oxygen saturation catheter was inserted into the right jugular bulb to continuously monitor internal S_{jvO_2} . Hemodynamic parameters and arterial and jugular venous blood gases were measured at seven time points: (1) after the induction of anesthesia and before the start of surgery, (2) just after the beginning of cardiopulmonary bypass, (3) 20 min after the beginning of bypass, (4) 40 min after the beginning of bypass, (5) 60 min after the beginning of bypass, (6) just after the cessation of bypass, and (7) at the end of the operation.

Results: No significant differences were seen in mean arterial pressure, arterial carbon dioxide tension (P_{aCO_2}), or hemoglobin concentration among the three groups during the study. The S_{jvO_2} value did not differ among the three groups after anesthesia induction and before surgery, just after the beginning of cardiopulmonary bypass, 60 min after the beginning of bypass, just after the end of bypass, or at the end of the operation. Significant differences between the control group and the diabetic and stroke groups were observed, however, at 20 min and 40 min after the beginning of bypass (at 20 min: control group $62.2 \pm 6.8\%$, diabetes group $48.4 \pm 5.1\%$, stroke group $45.9 \pm 6.3\%$; at 40 min: control group $62.6 \pm 5.2\%$, diabetes group $47.1 \pm 5.2\%$, stroke group $48.8 \pm 4.1\%$ [values expressed as the mean \pm SD]; $P < 0.05$). Also, values in the diabetes and stroke groups were decreased at 20 min and 40 min after the beginning of bypass compared with before the start of surgery.

Conclusions: A reduced S_{jvO_2} value was observed more frequently in patients with preexisting diabetes mellitus or stroke during normothermic cardiopulmonary bypass. It is possible that cerebral circulation during normothermic bypass is altered in patients with risk factors for cerebrovascular disorder. (Key words: Cerebral ischemia; extracorporeal circulation; metabolic disorder; neurologic complication.)

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CENTRAL nervous system complications continue to be a major cause of injury and death after cardiac surgery. Neuropsychologic dysfunction after cardiopulmonary bypass (CPB) has been reported in as many as 79% of patients during the early postoperative period.²

Patients undergoing elective coronary artery bypass graft surgery often have diabetes mellitus (DM) and cerebrovascular disease,¹ each of which presents risk factors for cerebral circulatory disturbance. In addition, patients with DM or preexisting stroke undergoing coronary artery bypass graft surgery may be at risk for cerebral ischemia, especially during normothermic CPB. Goto *et al.*³ reported that patients with preexisting cerebral neurologic disorders showed a greater degree of jugular venous desaturation than did patients without neurologic disorders during hypothermic CPB. Similarly, Croughwell *et al.*⁴ reported that patients with DM showed abnormal cerebral autoregulation during CPB.

CEREBRAL OXYGENATION DURING CPB

Table 1. Demographic Data for the Three Groups

	Normal Group	Diabetic Group	Stroke Group
LVEF (%)	60 ± 7 (52–71)	59 ± 10 (47–75)	57 ± 9 (49–72)
Total CPB time (min)	172 ± 37 (109–211)	144 ± 34 (111–195)	135 ± 29 (89–174)
Aortic clamping time (min)	122 ± 28 (91–167)	114 ± 24 (77–166)	107 ± 20 (74–148)

Values are mean ± SD (range). No statistical differences among the three groups.

LVEF = left ventricular ejection fraction; CPB = cardiopulmonary bypass.

These reports led us to consider the question of whether there is a difference in the incidence of jugular venous oxygen desaturation during normothermic CPB between patients with and those without such complications.

Materials and Methods

After obtaining the approval of the ethical committee of our institution and written informed consent from the patients, 19 age-, weight-, and height-matched control patients (control group), 10 diabetic patients (DM group), and 9 patients with preexisting stroke (stroke group) undergoing elective coronary artery bypass graft surgery were studied. The clinical data of DM and stroke groups are shown in tables 1–3. The stroke group had no diabetic disease. None of the patients had pulmonary, renal, or hepatic disease.

All patients received 10 mg oral diazepam 1 h before administration of anesthesia. A cannula was inserted in the left radial artery to monitor arterial blood pressure. Anesthesia was induced with 25 µg/kg intravenous fentanyl, 0.2 mg/kg midazolam, and 0.2 mg/kg vecuronium, and the trachea then was intubated. After induction of anesthesia, the pulmonary arterial catheter (Vigilance Swan-Ganz CCO Thermodilution Catheter; Baxter, Irvine, CA) was inserted through the right internal jugular

vein. For continuous monitoring of jugular vein oxygen saturation ($SjvO_2$), a 4.0-French fiberoptic oximetry catheter (Dual-lumen Oximetry Catheter; Baxter) was passed to the right jugular bulb retrogradely from the internal jugular vein using a modified Seldinger technique. Proper position of the top of the catheter was verified by radiograph. This catheter was connected to an analysis system (Explorer; Baxter) and calibrated *in vivo* by drawing a blood sample from the catheter. The arterial and jugular venous blood gases were analyzed (Stat Profile Ultima; NOVA Biomedical, Boston, MA). All patients were ventilated with 50% oxygen and 50% nitrogen. End-tidal carbon dioxide concentration was monitored (Ultima; Datex, Helsinki, Finland) and maintained between 35 and 45 mmHg. After induction of anesthesia, 4 mg · kg⁻¹ · h⁻¹ propofol was infused using a syringe pump and continued until the patients were placed in the intensive care unit. Relaxation was maintained with an intermittent administration of vecuronium. No volatile anesthetics were administered. The tympanic membrane temperature also was monitored continuously (Mon-a-Therm; Mallinckrodt, St. Louis, MO) as an indicator of brain temperature.

Cardiopulmonary bypass was primed with a crystalloid, non-glucose-containing lactate Ringer's solution, and a nonpulsatile pump flow rate of 2.2–2.5 l · min⁻¹ · m⁻² was maintained. A membrane oxygenator and a 40-µm

Table 2. Clinical Data of Diabetic Patients

Patient Number	Fasting Blood Glucose (mg/dl)	HbA1c (%)	Therapy	Diabetic Complications
1	187	8.1	Glibenclamide	Retinopathy + nephropathy
2	107	5.1	Diet	(–)
3	222	7.4	Insulin	(–)
4	154		Glibenclamide	Nephropathy
5	198	8.1	Insulin	Retinopathy
6	217		Glibenclamide	(–)
7	149	5.4	Glibenclamide	Retinopathy
8	147	6.4	Glibenclamide	(–)
9	165	6.6	Insulin	(–)
10	111	7.2	Glibenclamide	(–)

HbA1c = glycosylated hemoglobin (normal value 4.3–5.8%).

Table 3. Clinical Data of Stroke Patients

Patient Number	Brain CT Examinations
1	Multiple lacunar infarction
2	Small cerebral infarction
3	Multiple lacunar stroke
4	Small cerebral infarction
5	Multiple lacunar infarction
6	Broad infarction
7	Small cerebral infarction
8	Small cerebral infarction
9	Multiple lacunar stroke

CT = computerized tomography.

arterial line filter were used, and arterial oxygen tension (Pa_{CO_2}) uncorrected for temperature was adjusted to normocapnic levels (35–45 mmHg) by varying fresh gas flow to the membrane oxygenator. The target tympanic temperature was 35°C.

Hematocrit was maintained at more than 20% during CPB, with the addition of blood as needed. Phenylephrine infusions were used during CPB to maintain mean arterial pressure of 50–90 mmHg.

Cerebral perfusion pressure (CPP) was defined as mean arterial pressure minus internal jugular venous pressure. Internal jugular pressure was measured by monitoring pressure at the distal end of the Sjv_{O_2} catheter. All hemodynamic transducers were referenced to atmospheric pressure at the level of the external auditory meatus.

After the end of CPB, catecholamines, such as dopamine and dobutamine, were infused to maintain the cardiac index above $2.2 \text{ l} \cdot \text{min}^{-1} \cdot \text{m}^{-2}$. No patients needed infusion of epinephrine or norepinephrine to maintain the cardiac index above $2.2 \text{ l} \cdot \text{min}^{-1} \cdot \text{m}^{-2}$.

Antegrade blood cardioplegia was administered intermittently from the aortic root at 37°C. Distal coronary and proximal anastomoses were performed during a single aortic cross-clamping.

Hemodynamic parameters, arterial and jugular venous blood gases, and internal jugular venous pressure were measured (1) after the induction of anesthesia and before the start of surgery, (2) just after the beginning of CPB, (3) 20 min after the beginning of CPB, (4) 40 min after the beginning of CPB, (5) 60 min after the beginning of CPB, (6) just after the cessation of CPB, and (7) at the end of the operation.

Intraoperative epiaortic ultrasonography confirmed that none of the patients had moderate or severe atherosclerotic lesions in the ascending aorta.

Statistical Analysis

All data were expressed as the mean \pm SD. After the study was completed, we evaluated the sample size. The sample size calculation was based on the hypothesis that the Sjv_{O_2} value in diabetic or stroke patients would be decreased by 10% compared with that in control patients. The sample size provides 80% power to detect a 20% difference between groups with a 5% probability of an α -type error. Changes in mean values were compared with the baseline values using an analysis of covariance. Contrast was used to compare the differences among the three groups at each time point. Statistical significance was set at $P < 0.05$.

All calculations were performed on a Macintosh computer with SPSS (Chicago, IL) and Stat View 4.5 software packages (Abacus Concepts, Berkeley, CA).

Results

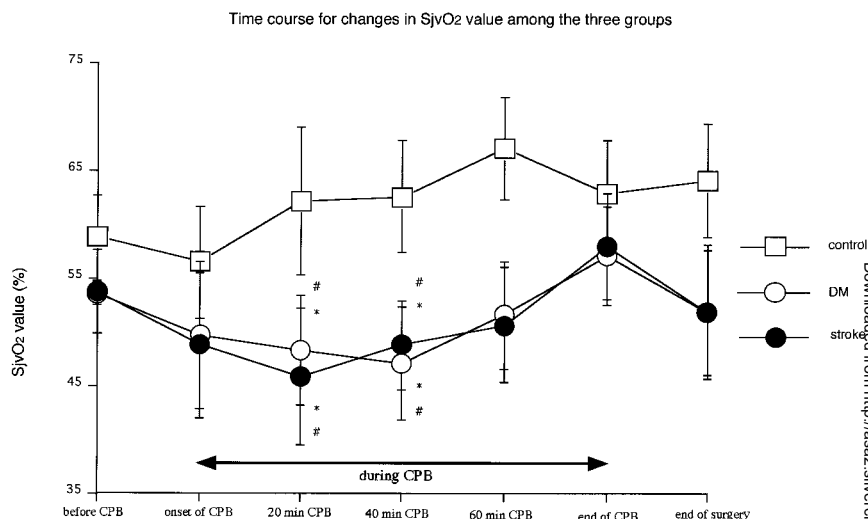
Postoperative neurologic dysfunction did not develop in any patient. There was no significant difference in preoperative blood pressure among the three groups (data not shown). Table 4 shows the time course for changes in variable parameters among three groups. Mean arterial pressure, cardiac index, hemoglobin, $\text{qIpa}_{\text{CO}_2}$, internal jugular pressure, and CPP among the three groups did not differ significantly at any time.

Figure 1 shows the time course for changes in Sjv_{O_2} among the three groups. Sjv_{O_2} did not differ among the three groups after anesthesia induction and before surgery, just after the beginning of CPB, 60 min after the beginning of CPB, just after the end of CPB, or at the end of the operation. Significant differences between the control group and the diabetic and stroke groups were observed, however, at 20 min and 40 min after the beginning of CPB (at 20 min: control group $62.2 \pm 6.8\%$, diabetes group $48.4 \pm 5.1\%$, stroke group $45.9 \pm 6.3\%$; at 40 min: control group $62.6 \pm 5.2\%$, diabetes group $47.1 \pm 5.2\%$, stroke group $48.8 \pm 4.1\%$ [values expressed as the mean \pm SD]; $P < 0.05$). Also, Sjv_{O_2} values in diabetic and stroke groups were decreased at 20 min and 40 min after onset of CPB compared with before the start of surgery. There was no significant difference in Sjv_{O_2} values between the diabetic group and the stroke group during at any point of the study.

Discussion

The principal findings of this study are that (1) patients with preexisting DM or stroke had a reduced Sjv_{O_2} com-

Fig. 1. The time course for changes in jugular venous bulb oxygen saturation ($SjvO_2$) among the three groups in the current study. $SjvO_2$ did not differ among the three groups after anesthesia induction and before surgery, just after the beginning of cardiopulmonary bypass, 60 min after the beginning of bypass, just after the end of bypass, or at the end of the operation. Significant differences between the control group and the diabetic and stroke groups were observed, however, at 20 min and 40 min after the beginning of cardiopulmonary bypass ($\#P < 0.05$ compared with control group). Also, $SjvO_2$ in the diabetic and stroke groups was decreased at 20 min and 40 min after the beginning of cardiopulmonary bypass, compared with before the start of surgery ($*P < 0.05$). There was no significant difference in $SjvO_2$ between the diabetic group and the stroke group at any point of the study. Values are expressed as the mean \pm SD.



imbalance in CBF and cerebral metabolic rate of oxygen consumption might have resulted from impaired cerebral circulatory disturbance in patients with preexisting stroke, and they considered the fact that patients with risk factors for cerebral circulatory disturbance were unable to preserve effective CBF if systemic hypoperfusion occurred. From the results of our study, we also concluded that patients with DM or stroke may be at a much higher risk of cerebral oxygenation abnormality than otherwise normal patients.

In the current study, multiple linear regression analysis indicated that either DM or preexisting stroke was a single determining factor of $SjvO_2$ value during normothermic CPB. CPP, Pa_{CO_2} , and arterial oxygen tension did not differ among groups. $SjvO_2$ did not correlate with CPP during normothermic CPB in the control group. There have been some reports describing the correlation between CPP and $SjvO_2$ during CPB. Grubhofer *et al.*¹⁰ reported that an increase in CPP in response to administering phenylephrine (from 47 to 93 mmHg) induced increases in $SjvO_2$ by 4.9% during hypothermic CPB. Furthermore, they considered this finding to suggest impaired cerebral autoregulation, and they recommended administration of phenylephrine to increase CPP in patients with lower $SjvO_2$ during CPB. In contrast, Hessel¹¹ commented that the poor correlation between slopes obtained during the rise versus the decline in arterial pressure ($r = 0.10$) in the report of Grubhofer *et al.*¹⁰ was disturbing. We suspect that the differences between our study and the one by Grubhofer *et al.*¹⁰ could be a result of the different species studied, anes-

thetic conditions, management of CPB, preoperative baseline mean arterial pressure, or mean arterial pressure during CPB.

The finding that control patients with normothermic CPB did not show any reduction in $SjvO_2$ is inconsistent with findings both of Cook *et al.*⁹ and of our previous studies.^{12,13} It is possible that many factors such as age, species, anesthetic drugs, Pa_{CO_2} , arterial oxygen tension, and blood viscosity influence $SjvO_2$ during normothermic CPB. $SjvO_2$ in our control group had tended to increase over time during CPB. Cook *et al.*⁹ reported that the increase in $SjvO_2$ appeared to be adapting to CPB flow conditions with time.

Croughwell *et al.*¹⁴ reported that reduced $SjvO_2$ during CPB was a risk factor for cerebral ischemia. There has been some controversy, however, regarding interpretation of $SjvO_2$ during CPB.^{15,16} Dexter and Hindman¹⁵ recently reported that a high $SjvO_2$ value during hypothermic CPB indicated impaired oxygen transfer from hemoglobin to the brain. They also found that during normothermia, increased oxygen extraction reduced $SjvO_2$, but that this reduction does not indicate an imbalance in either CBF or metabolism. In contrast, Hanel *et al.*¹⁷ reported that maximal reduction in the $SjvO_2$ value did not occur when blood-brain temperature gradients were at their maximum but rather occurred when the temperature gradients were small. To date, it is not clear whether reduced $SjvO_2$ during hypothermic or normothermic CPB indicates an imbalance in CBF and metabolism.

Whether SjvO_2 influences neurologic outcome after cardiac surgery remains unclear.¹⁸ Murkin *et al.*¹⁹ suggested that neurologic outcome may be poorer in patients with higher SjvO_2 during CPB. Patients with risk factors for cerebral circulatory disturbance, however, have not been studied extensively in terms of whether the state of cerebral oxygenation as measured by the SjvO_2 value has some effect on their neurologic outcome. Using a routine postoperative neurologic assessment, we did not detect any neurologic disorders in any of the patients. The possibility exists, however, that an extensive assessment of neurologic and cognitive function might have detected minor neurologic abnormalities. Further studies are needed to determine if any correlation exists between SjvO_2 reduction and neurologic disorders.

In conclusion, reduced SjvO_2 was observed more frequently in patients with preexisting DM or stroke during normothermic CPB. It is possible that cerebral circulation during normothermic CPB is altered in patients with risk factors for cerebrovascular disorder.

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