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Study on the Associating Factors with Regional Cerebral Oxygen Saturation Values during Cardiopulmonary Bypass

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Abstract **Background:** Regional cerebral oxygen saturation (rSO_2) is a pivotal indicator of brain ischemia during cardiovascular anesthesia. We evaluated the factors that might affect the rSO_2 values, examining the physiological parameters in two different time points during cardiopulmonary bypass (CPB). **Methods:** Fifty-nine patients undergoing cardiovascular surgery with CPB were retrospectively enrolled and their rSO_2 values were measured 30 min after aortic clamping (T1) and 30 min after the T1 measurement (T2). At each time point, the $PaCO_2$ was measured by arterial blood samples. Percent changes in the rSO_2 values were compared with percent changes in all parameters at each time point. **Results:** Percent changes in the rSO_2 values significantly correlated with percent changes in the $PaCO_2$ values on the left and right sides of the forehead ($r = 0.417$ vs. $r = 0.387$; both $P < 0.005$). **Conclusions:** Although perfusion pressure and Hb values are not changed during CPB, changes in the $PaCO_2$ values may have affected the rSO_2 values. These changes may indicate that keeping or adjusting the $PaCO_2$ values may be the most important factor for correcting the rSO_2 values during CPB.

Key words: arterial blood gas analysis, carbon dioxide, cardiopulmonary bypass, cardiovascular anesthesia, regional cerebral oxygen saturation

Introduction

Near-infrared spectroscopy is currently used for vital sign monitoring in various medical settings.[1] It is highly sensitive to relative changes in blood flow.[2] In particular, the regional oxygen saturation (rSO_2) can be measured in real time and with minimal invasiveness. rSO_2 values are the first-line indicator for detecting marked decreases in cerebral blood flow, which occur during carotid endarterectomy and neurosurgery, operative techniques that require temporary blocking of the carotid arterial blood flow.[3] Furthermore, it is important to monitor the onset of widespread cerebral ischemia during cardiopulmonary bypass (CPB).[4] For instance, when using a CPB system during cardiovascular surgery, a protruding aortic atheroma may cause organ damage such as stroke, due to the non-physiological circulation.[5]

Moreover, on the basis of the measurement principle of near-infrared spectroscopy, factors, other than cerebral blood flow, that may affect rSO_2 values have been suggested. These include hemoglobin (Hb) concentration, cerebrospinal fluid volume, and probe attachment site. Therefore, the measurements should be interpreted carefully.[6-8]

Changes in the partial pressure of carbon dioxide ($PaCO_2$) tension affect the cerebral blood vessel diameter, which may in turn affect cerebral blood flow. During CPB, clinical engineers manage the blood flow, body temperature, and adjustments of oxygenation and CO_2 tension. Additionally, arterial blood

gas analysis is used during CPB, allowing the effect of $PaCO_2$ on cerebral blood flow to be ascertained.

Few studies have investigated cerebral vascular responsiveness associated with $PaCO_2$ by using rSO_2 values as evaluation criteria during CPB under mild hypothermic conditions, and few studies have reported on the effects of $PaCO_2$ on rSO_2 values during CPB.[9] Therefore, in the present study, we used the $PaCO_2$ values obtained from arterial blood gas analysis, which is routinely performed during CPB, and compared these values to the corresponding rSO_2 values to determine factors that affect the rSO_2.

Materials and Methods

Subjects

Among adult patients who underwent cardiovascular surgery with CPB at Tokuyama Central Hospital between June 2012 and February 2014, 59 patients were retrospectively evaluated. We excluded those who underwent implantation of a vascular prosthesis to replace the aortic arch and those who underwent a second operation during the same period. At the time of this study, the need for informed consent for this study was waived by the Ethical Committee of our institution.

Measurements

The INVOS™ 5100C cerebral oximeter (Medtronic Japan, Tokyo, Japan) was used to measure the rSO_2. The ABL-725 blood gas analyzer (Radiometer™, Copenhagen, Denmark) was used to perform arterial blood gas analysis. To measure rSO_2, probes were attached to the left and right sides of the patient's forehead at the time of anesthesia induction; rSO_2 values were recorded at 1-min intervals throughout the surgery. $PaCO_2$ was adjusted during CPB using the α-stat mode. The INVOS™ 5100C auto macro tool (Somanetics™ Corp., Troy, MI, USA), a dedicated software for analyzing data from the INVOS™ 5100C cerebral oximeter, was used to record and save the values.

Anesthetic management

Premedication was not used in any of the cases. To induce anesthesia, the following drugs were used: sevoflurane (3-5 %), fentanyl (2 μg/kg), and remifentanil (0.3-0.5 μg/kg/min). To maintain anesthesia before CPB, sevoflurane (1.5-2 %) and remifentanil (0.2-0.3 μg/kg/min) were used. To maintain hemodynamics before and during CPB, phenylephrine and milrinone were used as required. The anesthetic agents used during CPB were propofol (3-5 mg/kg/h) and remifentanil (0.25-0.3 μg/kg/min). By using perfusion pressure as a reference, the administered volume was adjusted as required.

CPB

In all cases, CPB was performed under conditions of mild hypothermia. In the cases requiring insertion of intra-aortic balloon pumping (IABP), pulsatility was maintained during CPB on the internal trigger mode. Patients' body temperature was controlled during CPB and was maintained from 30℃ to 32℃ for each point of measurement using the esophageal and rectal temperatures as references, using the esophageal and rectal temperatures as references. Perfusion pressures were maintained at 50 mmHg, considered to represent the ideal value. During CPB, phenylephrine and milrinone were continuously administered if necessary. The perfusion rate was maintained at 1.5-2.5 L/min.

Assessment of factors that affect rSO_2 values

To determine the factors that affect rSO_2 values, data were extracted from two independent points in the records of CPB: 30 min after aortic clamping (T1), and approximately 30 min after T1 (T2). Arterial blood samples were collected twice, at T1 and T2, and blood gas analysis was performed immediately. At each time point, the $PaCO_2$, esophageal temperature, rectal temperature, and perfusion pressure were obtained by referring to values recorded as blood gas analysis and physiological parameters by the clinical engineer during CPB. We calculated the percent change ([T2 value − T1 value] ÷ T1 value) from the rSO_2 and arterial blood gas analysis values obtained at the two time points of blood sampling. Simultaneously, the rate of change in rSO_2 values and the esophageal temperature, rectal temperature, and perfusion pressure were compared. Furthermore, correlations

between rSO_2 values and the data of T1 and T2 were assessed.

Statistical analysis

A paired t-test was used to compare the values of $PaCO_2$ and the physiological parameters between the measurement values from the first and second arterial blood samples. Furthermore, the values of $PaCO_2$ and the physiological parameters were compared to each rSO_2 value, and the respective correlations were evaluated. The correlation coefficient was obtained by using the Pearson equation. GraphPad Prism 5 (GraphPad Software, Inc. La Jolla, CA) was used to analyze the data. Continuous data are expressed as mean ± standard deviation. Variables were considered significant at $p < 0.05$.

Results

Patients' ages ranged from 51-86 years; 28 were men and 31 were women. The weight, CPB time, and aortic clamping time are presented in Table 1. Overt cerebrovascular accidents did not occur postoperatively.

Fifty-four patients underwent elective cardiac surgery, and five underwent emergency surgery. Eight patients received an IABP before anesthesia was induced due to critical coronary artery disease. The preoperative diagnoses and operative procedures are shown in Table 2.

The values at T1 and T2 for the esophageal and rectal temperatures, perfusion pressure, and rSO_2 of both sides, and the values of $PaCO_2$ are presented in Table 3. Between the arterial blood sampling measurements at T1 and T2, significant changes were observed for the rectal temperature and perfusion pressure (both $p = 0.0004$).

The percent change in the rSO_2 values of both sides showed no significant correlations with the percent change in esophageal temperature, rectal temperature, and perfusion pressure, as shown in Table 4. However, the percent

Table 1 Preoperative and Intraoperative Valuables

Valuables	Values
Ages (years)	72 ± 8 (51-86)
Gender (male : female)	28 : 31
Weight (kg)	57 ± 15 (29-104)
CPB time (min)	196 ± 53 (131-413)
ACC time (min)	126 ± 43 (41-250)

CPB, cardiopulmonary bypass; ACC, aortic cross-clamping; mean ± SD with range

Table 2 The preoperative diagnoses and the performed operations

	n
Preoperative diagnosis	
Aortic stenosis	30
Mitral regurgitation	18
Coronary artery disease	14
Aortic regurgitation	9
Mitral stenosis	4
Atrial tumor	4
Atrial septal defect	3
Surgical procedure	
Aortic valve replacement	38
Coronary artery bypass graft	14
Tricuspid annuloplasty	9
Mitral valve replacement	8
Mitral valve plasty	7
Mitral annuloplasty	4
Atrial tumor removal	4
Atrial septal defect closure	3
Maze procedure	2
Dor procedure	1
Ventricular septal perforation surgery	1

n, number of cases

change in rSO_2 values was significantly correlated with the percent change in $PaCO_2$ (left side: r = 0.417, right side: r = 0.387; p < 0.005, both; Table 4, Fig. 1 A, B).

Discussion

Factors that affect rSO_2 values do not solely originate from cerebral blood flow. Various other factors, notably Hb concentration, have been already reported.[6,8] As reported by Yoshitani et al., serum Hb and hematocrit values are generally thought to affect rSO_2 values because of their effect on the optical path length.[6] They also indicated that the area of the cerebrospinal fluid layer, mean arterial pressure, and skull thickness affect rSO_2 values. Their report was based on single-point measurements for analyzing the factors related to rSO_2, and their findings may have been affected by other factors attributed to individual variability.

It is likely that various physiological factors, such as perfusion pressure, which is maintained by systemic circulation, are more likely artificially and homeostatically maintained during CPB than during other states of circulatory maintenance. During

Table 3 Measurements of all values obtained from the physiological parameters and the other parameters at T1 and T2

	T1	T2	P
Temperature (℃)			
Esophageal	32.4 ± 1.7	32.4 ± 1.2	0.900
Rectal	33.3 ± 1.5	32.9 ± 11	0.0004
Perfusion Pressure (mmHg)	43 ± 16	48 ± 13	0.0004
rSO_2-L(%)	67 ± 9	67 ± 9	0.820
rSO_2-R (%)	66 ± 10	66 ± 10	0.941
$PaCO_2$ (mmHg)	43.5 ± 3.5	43.4 ± 2.7	0.904
PaO_2 (mmHg)	345 ± 52	330 ± 64	0.0007
Hemoglobin (g/dL)	7.5 ± 1.3	8.0 ± 1.2	< 0.0001

T1, the time within 30 min after aortic clamping; T2, 30 min after T1; P, p value of paired t-test; rSO_2-L, regional cerebral oxygen saturation at left hemisphere; rSO_2-R, regional cerebral oxygen saturation at right hemisphere; Pa, partial pressure in arterial blood; CO_2, carbon dioxide; O_2, oxygen; Data are shown as the mean ± SD.

Table 4 Correlations between the percent change in rSO_2 and the percent change of the other parameters

	rSO_2-L		rSO_2-R	
	r	p	r	p
Temperature (℃)				
Esophageal	-0.106	0.423	0.567	0.242
Rectal	0.019	0.889	-0.034	0.800
Perfusion Pressure (mmHg)	-0.076	0.567	-0.058	0.662
$PaCO_2$ (mmHg)	0.417	0.001	0.387	0.003

rSO_2-L, regional cerebral oxygen saturation at left hemisphere; rSO_2-R, regional cerebral oxygen saturation at right hemisphere; r, correlation coefficient; P, p-value; Pa, partial pressure in arterial blood; CO_2, carbon dioxide

the transition phase to CPB, physiological parameters, such as blood flow, Hb concentration, and body temperature, show sudden changes;[10] however, after aortic clamping, the systemic circulation becomes completely dependent on the artificial cardiopulmonary system.[11] To determine adequate sequences of values, we therefore selected two time points for blood gas measurements, considering the stabilization of physiological parameters during CPB.

Our findings suggest that rSO_2 may be significantly affected by changes in $PaCO_2$, even though these were within their normal

Table 5 Correlations between the values of rSO_2 and the other parameters at T1 and T2

		T1		T2	
		r	p	r	p
rSO_2-L	Temperature (℃)				
	Esophageal	-0.050	0.708	-0.153	0.247
	Rectal	-0.048	0.716	-0.164	0.214
	Perfusion Pressure (mmHg)	-0.016	0.904	0.118	0.373
	$PaCO_2$ (mmHg)	0.237	0.071	-0.027	0.838
	PaO_2 (mmHg)	0.048	0.719	-0.004	0.974
	Hemoglobin (g/dL)	0.449	0.0004	0.265	0.043
rSO_2-R	Temperature (℃)				
	Esophageal	-0.732	0.582	-0.023	0.863
	Rectal	-0.064	0.628	-0.070	0.597
	Perfusion Pressure (mmHg)	-0.031	0.819	0.173	0.190
	PaO_2 (mmHg)	0.284	0.029	-0.052	0.698
	PaO_2 (mmHg)	0.159	0.229	0.193	0.143
	Hemoglobin (g/dL)	0.457	0.0003	0.289	0.026

rSO_2-L, regional cerebral oxygen saturation at left hemisphere; rSO_2-R, regional cerebral oxygen saturation at right hemisphere; r, correlation coefficient; P, p-value; Pa, partial pressure in arterial blood; CO_2, carbon dioxide; O_2, oxygen

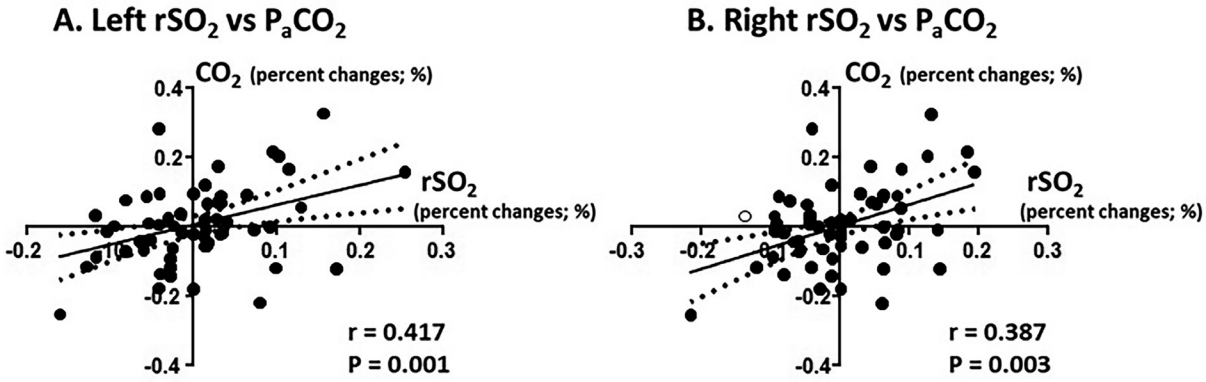

Fig. 1
Correlation between the percent change in the regional cerebral oxygen saturation values and the percent change in the $PaCO_2$ values at each time point (Pearson correlation coefficient). The dotted lines represent the 95 % confidence band of the best-fit line.

ranges during CPB. These results indicate that a $PaCO_2$ value is the main factor for stabilizing rSO_2. Therefore, adjusting the $PaCO_2$ values should be the first step toward correcting the rSO_2 value, immediately after an abnormality is detected during CPB. Several reports have demonstrated that $PaCO_2$ or endtidal CO_2 affects cerebral oxygen saturation, and these data support our results.[12-14] During CPB, marked degradation of rSO_2 values is thought to indicate a high probability of cerebral blood flow malperfusion, due to emboli or thrombi. However, when the change in rSO_2 value is within the normal range, intraoperative changes in the rSO_2 value are likely to be a physiological phenomenon caused by changes in cerebral blood flow within the normal range.[15] Blood flow in systemic circulation is commonly considered to be the factor that directly affects cerebral blood flow.[16]

Contrary to expectation, our results revealed that the temperatures and perfusion pressures were significantly different between T1 and T2, but the rates of change for each time point were not significantly correlated with the corresponding rSO_2 values. These results may indicate that the homeostasis and circulatory state were relatively stabilized in terms of the physiological factors we observed at each time point for maintaining rSO_2 values.

We did not find a significant correlation between the percent change in rSO_2 and that in Hb values (data not shown). Single-point measurement of factors during CPB for elucidating the association to rSO_2 might be confounded by various other factors, including individual characteristics. Therefore, two independent time points should be selected for detecting relative changes in order to exclude confounding effects.

Park et al. have reported a strong and significant correlation between changes in $PaCO_2$ and rSO_2 values measured at two time points, namely at the time of full flow after starting CPB and after the first injection of a cardioplegic solution.[9] In our study, the percent change in $PaCO_2$ values showed significant correlation with the percent change in rSO_2 values. In each case, cerebral vascular responsiveness, compared with $PaCO_2$, was probably well maintained during CPB. Therefore, the correlation associated with the percent change was significant.

Conclusions

During the maintenance of hemodynamics and blood gases when using a CPB system, rSO_2 may be affected by changes in the $PaCO_2$ values. In particular, changes in rSO_2 during CPB may indicate autonomic responses of cerebral vessels to $PaCO_2$

Conflict of Interest

The authors declare no conflicts of interest.

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