Changes in cerebral oxygen saturation during pediatric surgery in patients with cyanotic and non-cyanotic congenital heart defects

Nobuhiro Tanaka*1, Hideo Tokuyama*1, Yosuke Uchida*1, Yuji Morimoto*1, Tsuyoshi Tachibana*2

Abstract

The clinical significance of cerebral oxygen saturation (rSO2) measured by near-infrared spectroscopy during pediatric cardiac surgery has not been determined yet. We therefore evaluated the patterns of rSO2 changes during pediatric cardiac surgery in patients with cyanotic and non-cyanotic heart defects and also evaluated the causes of changes from the physiological data.

One hundred eleven children under 6 years old who underwent cardiac surgery with cardiopulmonary bypass (CPB) for congenital heart defects were divided into cyanotic and non-cyanotic groups. rSO2 was measured every 5s throughout the surgery. The values were averaged before, during and after CPB. Intraoperative physiological data were collected at the start of surgery (T1), 5 min after the start of CPB (T2) and 10 min after the end of CPB (T3).

There were 58 patients in the non-cyanotic group and 53 patients in the cyanotic group. In the non-cyanotic group, the average rSO2 during CPB was significantly lower than before and after CPB, and the mean arterial pressure and hemoglobin concentration were significantly lower at T2. In the cyanotic group, there were no significant differences of the average rSO2 among the periods, although the physiological data, including the PaO2 and hemoglobin levels, dramatically changed.

The patterns of rSO2 changes during pediatric cardiac surgery with CPB were different between the cyanotic and non-cyanotic groups. Various changes of physiological data might affect the changes of rSO2. The diversity of rSO2 changes may be one of the causes of the non-establishment of rSO2 monitoring in pediatric cardiac surgery.

Key words: cerebral oxygen saturation, pediatric heart surgery, cyanosis, cardiopulmonary bypass

Introduction

Cerebral oximetry using near-infrared spectroscopy is widely used in cardiac surgery. In adult cardiac surgery, recent reports demonstrated the validity and importance of the monitoring of regional cerebral oxygen saturation (rSO2). In pediatric cardiac surgery, Fenton et al. reported that the values of rSO2 prior to the induction of anesthesia predicted the mortality in 143 infants and children less than 18 years old. MRI evaluation revealed that postoperative cerebral injury was related to lower rSO2 during aortic clamping in 62 neonates with surgery for congenital heart diseases (CHD). On the other hand, another study reported that rSO2 values during surgery were not related to early outcomes such as prism III scores, days intubated and days in the intensive care unit. In a cohort of young infants with CHD, the neurodevelopmental outcomes measured using the Bayley Scales III at 2 years of age were largely influenced by patient-related characteristics, but the predictive values of rSO2 remained unclear. A systemic review of the literature on CHD from 1950 to April 2007 also indicated that the data correlating near-infrared spectroscopy findings with indirect measures of the

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Figure 1 Representative intraoperative changes of rSO$_2$ values during the congenital heart surgery with cardiopulmonary bypass.

**Left:** radical surgery for ventricular septal defect in a 3-year, 5-month-old patient. The rSO$_2$ values dramatically decreased during CPB.

**Right:** radical surgery for atrioventricular septal defect in a 6-month-old patient Distinct changes of rSO$_2$ values were not observed before, during or after CPB and the pattern of changes was clearly different from the one in the non-cyanotic patient.

neurologic outcome and mortality were limited. Thus the clinical significance of this technique in pediatric cardiac surgery has not been determined yet.

We sometimes observe distinct differences in the patterns of rSO$_2$ changes before, during and after cardiopulmonary bypass (CPB) in pediatric cardiac surgery according to the type of CHD, as shown in Fig. 1. We speculated that the patterns of rSO$_2$ changes during pediatric cardiac surgery were different between cyanotic and non-cyanotic CHD patients, and that this difference might contribute to the limited usefulness of rSO$_2$ monitoring. In this study, we therefore evaluated the patterns of rSO$_2$ changes in the cyanotic and non-cyanotic types of CHD during pediatric cardiac surgery with CPB and also evaluated the causes of changes in the intraoperative physiological data.

Patients and Methods

With approval of the Hokkaido University Hospital IRB for clinical research (011–0199), data from a database in Hokkaido University Hospital with 111 children under 6 years old who underwent cardiac surgery with CPB for CHD were retrospectively evaluated. The patients having extracardiac anomalies with more than minor severity or associated cardiovascular anomalies requiring aortic arch reconstruction such as aortic coarctation were excluded. The patients were divided into 2 groups according to whether CHD was cyanotic or non-cyanotic.

Anesthesia was conducted according to our institutional practice. Fentanyl and remifentanil were supplemented with midazolam and sevoflurane as tolerated, and neuromuscular blockade was achieved with rocuronium. Standard monitoring was used, including a femoral artery catheter for measurement of systemic arterial blood pressure and intermittent blood sampling and an internal jugular catheter for measurement of central venous pressure. The bypass circuit was primed with bicarbonate Ringer solution with or without red cell concentrates and/or fresh-frozen plasma. A nonpulsatile roller pump with a membrane oxygenator (Oxia, JMS, Tokyo, Japan) was used at a flow rate of 150 ml/min/kg. An α-stat strategy was used during core cooling. The techniques of deep hypothermic circulatory arrest and regional low-flow cerebral perfusion were not used. Methylprednisolone (25 mg/kg) and mannitol (6 mg/kg) were given to all patients at the initiation of CPB. Conventional ultrafiltration was used during CPB and modified ultrafiltration, after CPB.

The rSO$_2$ was measured with an INVOS 5100B (Somanetics, Troy, MI). After induction of anesthesia, Pediatric SomaSensors® (Somanetics, Troy, MI) were placed on the forehead according to the manufacturer’s guidelines. After an accommodation period, data collection was begun and the data were downloaded to a storage disk every 5s throughout the surgery for further analysis. Average rSO$_2$ values from the start of surgery to the beginning of CPB (pre-CPB), during CPB, and from the end of CPB to the end of surgery (post-CPB) were calculated. The minimum rSO$_2$ value during surgery was recorded and the total duration of rSO$_2$ below 45% was calculated. The cutoff level of 45% for desaturation was decided based on a previous report. Intraoperative physiological data were collected at the start of surgery (T1), 5 min after the start of CPB (T2) and
10 min after the end of CPB (T3). Measurement of systemic arterial blood pressure and blood sampling for blood gas analysis were performed through the femoral artery catheter. Mortality and neurologic complications one month after surgery were evaluated.

Statistical Analysis

Data were analyzed using SPSS (ver.17.0 SPSS Inc., Chicago, IL, USA) and the normality of distribution was evaluated using the Shapiro-Wilk test. Comparisons of perioperative variables and rSO2 values between the groups were made using Fisher’s exact test for categorical variables and the Mann-Whitney U test for continuous variables. P < 0.05 was considered significantly different. Comparisons of rSO2 among the periods and intraoperative physiological variables at each time point were made using the Friedman test. When significance was seen, post hoc analysis with the Wilcoxon signed rank test was conducted with a Bonferroni correction applied, resulting in a significance level of P < 0.017.

Results

There were 58 patients in the non-cyanotic group and 53 patients in the cyanotic group. The names of the congenital heart diseases in each group are listed in Table 1. The patients in the cyanotic group were significantly smaller and had worse risk adjustment for congenital heart surgery (RACHS-1) scores (Table 1). The operation, CPB, and cross-clamp times were significantly longer for the surgery in the cyanotic group (Table 2). There

<table>
<thead>
<tr>
<th>Table 1</th>
<th>Preoperative characteristics</th>
</tr>
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<tbody>
<tr>
<td></td>
<td>non-cyanotic</td>
</tr>
<tr>
<td>Number</td>
<td>58</td>
</tr>
<tr>
<td>Age (m)</td>
<td>20 (4-46.5)</td>
</tr>
<tr>
<td>Body weight (kg)</td>
<td>9.6 (5.9-13.3)</td>
</tr>
<tr>
<td>Sex (%male)</td>
<td>43.1</td>
</tr>
</tbody>
</table>

Name of Congenital heart diseases
- ASD: atrial septal defect
- VSD: ventricular septal defect
- PS: pulmonary stenosis
- AVSD: atrioventricular septal defect
- TOF: tetralogy of Fallot
- PA: pulmonary atresia
- TGA: transposition of great arteries
- TA: tricuspid atresia
- DORV: double outlet right ventricle
- TAPVR: total anomalous pulmonary venous return
- SV: single ventricle
- HLHS: hypoplastic left heart syndrome

RACHS-1
- 1: 16
- 2: 41
- 3: 1
- 4: 12 <0.01*
- 5
- 6: 3

Values are expressed as median (interquartile range). P values were determined using the Mann-Whitney U test for continuous variables and Fisher’s exact test for categorical variables. *: RACHS-1 scores were divided into 2 groups depending on whether the score was more than 3 or not.

physiological data in the non-cyanotic group. The average rSO2 among the periods in the cyanotic group was significantly lower than in the non-cyanotic group. The minimum rSO2 values were not significantly different between the groups, although the duration of desaturation was significantly longer in the cyanotic group (Table 2).

Table 3 shows the changes in average rSO2 in the non-cyanotic and cyanotic groups. The average rSO2 during CPB significantly decreased compared to the pre-CPB values in the non-cyanotic group. After CPB, the average rSO2 increased although it did not return to the pre-CPB values. On the other hand, there were no significant differences in the average rSO2 among the periods in the cyanotic group. Average rSO2 values at pre- and post-CPB in the non-cyanotic group were significantly higher than in the cyanotic group. The minimum rSO2 values were not significantly different between the groups, although the duration of desaturation was significantly longer in the cyanotic group (Table 2).

Table 4 shows the changes in intraoperative physiological data in the non-cyanotic and cyanotic groups. The mean arterial pressure and hemoglobin concentration at T2 were significantly lower than at T1 and T3 in the non-cyanotic group. In the cyanotic group, the median PaO2 value at T1 was 55 Torr, which corresponded to 86% of SaO2. The values of PaO2 increased to the level of around 100% of SaO2 during and after CPB. The hemoglobin concentration at T2 was also significantly lower than at T1 and T3 in the cyanotic group. No patient died or had neurological complications one month after surgery, although one patient in the cyanotic group had seizures 1 and 2 days after surgery.

Discussion

This study demonstrated that changes in average rSO2 values before, during and after CPB in pediatric cardiac surgery for CHD were different between cyanotic and non-cyanotic patients. For
the non-cyanotic group, the average rSO₂ significantly decreased during CPB, whereas no significant changes were observed for the cyanotic group. Average rSO₂ values at pre- and post-CPB in the non-cyanotic group were significantly higher than in the cyanotic group. In addition, the total desaturation time of rSO₂ was longer in the cyanotic group. However, no patient died or had neurological complications one month after surgery in either group.

The cerebral metabolic rate for oxygen (CMRO₂) is calculated as

\[ \text{CMRO}_2 = \frac{\text{CBF} \times (\text{CaO}_2 - \text{CvO}_2)}{\text{SaO}_2} \]

where CBF is cerebral blood flow, and CaO₂ and CvO₂ are the oxygen contents of arterial blood and cerebral venous blood, respectively.

Because oxygen content \((= 1.34 \times \text{Hb} \times \text{SO}_2 + 0.0003 \times \text{PO}_2)\) can be approximated as \(1.34 \times \text{Hb} \times \text{SO}_2\), \(\text{CMRO}_2 = 1.34 \times \text{Hb} \times \text{CBF} \times (\text{SaO}_2 - \text{SvO}_2)\) where Hb is hemoglobin concentration.

\[ \text{SvO}_2 = \text{SaO}_2 - \text{CMRO}_2 / (1.34 \times \text{Hb} \times \text{CBF}) \]

Assuming that 25% and 75% of blood components in the brain exist in the cerebral arterial and cerebral venous vascular beds, respectively, \(r\text{SO}_2 = 0.25 \times \text{SaO}_2 + 0.75 \times \text{SvO}_2 = \text{SaO}_2 - 0.56 \times \text{CMRO}_2 / (\text{Hb} \times \text{CBF})\). Therefore, \(r\text{SO}_2\) can be expressed as a function of SaO₂, CMRO₂, Hb, and CBF.

In the non-cyanotic group, the average rSO₂ significantly decreased during CPB. Similarly, the mean arterial pressure and hemoglobin concentration during CPB were significantly lower. Although the development of cerebral vascular autoregulation is still controversial, it has been reported that rSO₂ can decrease in parallel with decreasing mean arterial pressure throughout cardiac surgery in infants and small children under 4 years old. Accordingly, the decreases in the mean arterial pressure and hemoglobin concentration during CPB might contribute to the decrease in cerebral oxygenation. Moreover, the changes in the average rSO₂ in the patients with non-cyanotic CHD were compatible with those we previously reported.* In that study, changes in cerebral oxygenation were continuously measured in 16 VSD patients by using another type of near-infrared spectrocope (NIRO 500: Hamamatsu Photonics, Hamamatsu, Japan). In 15 patients without complications, similar patterns of changes were observed. That is, brain tissue concentrations of oxyhemoglobin decreased during CPB, whereas there were no significant changes in brain tissue concentrations of deoxyhemoglobin.

Although there were no significant differences in the average rSO₂ among the three periods in the cyanotic group, general physiological data, including PaO₂ and hemoglobin, dramatically changed. Moreover, more than half of the patients were managed under moderate or deep hypothermia during CPB. Some changes might contribute to increased rSO₂, whereas others might decrease rSO₂. Accordingly, these mixed physiological changes might offset the changes in the average rSO₂.

Average rSO₂ values at pre-CPB in the

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**Table 4** Intraoperative physiological data

<table>
<thead>
<tr>
<th></th>
<th>T1</th>
<th>T2</th>
<th>T3</th>
<th>P1</th>
</tr>
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<tbody>
<tr>
<td><strong>Mean arterial pressure (mmHg)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Non-cyanotic</td>
<td>51 (46-59)</td>
<td>39 (30-48)</td>
<td>47 (43-50)</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Cyanotic</td>
<td>47 (43-51)</td>
<td>42 (36-53)</td>
<td>45 (41-52)</td>
<td>0.21</td>
</tr>
<tr>
<td><strong>PaO₂ (Torr)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Non-cyanotic</td>
<td>167 (119-224)</td>
<td>384 (341-446)</td>
<td>368 (244-434)</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Cyanotic</td>
<td>55 (47-73)</td>
<td>384 (359-434)</td>
<td>224 (80-395)</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td><strong>PaCO₂ (Torr)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Non-cyanotic</td>
<td>41 (37-44)</td>
<td>37 (35-41)</td>
<td>46 (40-51)</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Cyanotic</td>
<td>42 (38-49)</td>
<td>36 (32-39)</td>
<td>43 (37-48)</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td><strong>Hemoglobin (g/dl)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Non-cyanotic</td>
<td>10.2 (9.4-10.9)</td>
<td>7.4 (6.5-8.1)</td>
<td>8.6 (7.2-12.9)</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Cyanotic</td>
<td>12.8 (11.4-14.4)</td>
<td>8.5 (8.9-6.6)</td>
<td>12.7 (10.4-14.3)</td>
<td>&lt;0.01</td>
</tr>
</tbody>
</table>

T₁: at the start of surgery, T₂: 5 min after the start of CPB, T₃: 10 min after end of CPB. Values are expressed as median (interquartile range).

P₁ values were determined using the Friedman test for comparison of T₁, T₂, and T₃.

*: significant against T₁ by post-hoc analysis

#: significant against T₂ by post-hoc analysis
non-cyanotic group were significantly higher than in the cyanotic group. Fenton et al. reported that baseline rSO\textsubscript{2} recorded prior to the induction of anesthesia was lower in the L→R shunt without cyanosis than in other types of cardiac physiology\textsuperscript{3}. On the other hand, another study reported that rSO\textsubscript{2} before surgery in VSD patients was similar to that in healthy children and that it was significantly higher than in other types of congenital heart disease\textsuperscript{13}. Our results largely supported the latter findings.

In a study examining the changes in rSO\textsubscript{2} during infant heart surgery for TGA, TOF and VSD, the average rSO\textsubscript{2} during CPB was higher than that at pre- or post-CBP even in VSD patients, as for patients with TGA or TOF\textsuperscript{7}. That result was inconsistent with ours. One reason for the discrepancy may be the difference of temperature management. In that study, even VSD patients were managed under deep hypothermia, whereas mild hypothermia or normothermia was used for more than 90% of the non-cyanotic group in our study. These findings suggest that differences of the CPB management strategy affect the physiological changes, which influence the patterns of rSO\textsubscript{2} changes even if the type of CHD is the same.

One limitation of this study is that many kinds of CHD were included in each group. A prospective study will be necessary to evaluate the changes and their causes by focusing on targeted CHDs. Another one is that the time interval between the average rSO\textsubscript{2} and physiological data was different. Accordingly, there is a possibility that the physiological data did not reflect the changes in average rSO\textsubscript{2} values. However, what we wanted to know most in this study was the patterns of rSO\textsubscript{2} changes before, during and after CPB. The limited rSO\textsubscript{2} values just around the time of physiological examination may not represent the values during the entire phase. To further evaluate the relationship between the rSO\textsubscript{2} changes and physiological data prospectively, the establishment of more time points will be necessary. Third, we evaluated only mortality and neurological complications one month after surgery as outcomes. Thus, further prospective examination of outcomes, including long-term ones, will be necessary to evaluate the efficacy of rSO\textsubscript{2} monitoring.

In conclusion, our study demonstrated that the patterns of rSO\textsubscript{2} changes during pediatric cardiac surgery with CPB were different between cyanotic and non-cyanotic CHD. It is suggested that various changes of physiological data affect the changes of rSO\textsubscript{2}. The diversity of rSO\textsubscript{2} changes may be one of the causes of the non-establishment of rSO\textsubscript{2} monitoring in pediatric cardiac surgery for CHD.

**Conflict of interests:** No

**References**


