Age difference of the relationship between cerebral oxygen saturation and physiological parameters in pediatric cardiac surgery with cardiopulmonary bypass — analysis using the random-effects model

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Abstract

Recently, monitoring of cerebral oxygen saturation (ScO_2) has become widespread in pediatric cardiac surgery. Our previous study reported that mean blood pressure (mBP) was the major contributor to ScO_2 throughout cardiac surgery with cardiopulmonary bypass (CPB) in children weighing under 10kg. We speculated that this result might be attributable to incomplete cerebral autoregulation in such young children. Accordingly, our hypothesis is that the relationship between ScO_2 and the physiological parameters may change according to the growth of the children.

ScO_2 was measured with an INVOS 5100C (Somanetics, Troy, MI). Random-effects analysis was employed with ScO_2 as a dependent variable, and seven physiological parameters (mBP, central venous pressure, nasopharyngeal temperature, SaO_2, hematocrit, $PaCO_2$, and pH) were entered as independent covariates. The analysis was performed during the pre-CPB, CPB and post-CPB periods by dividing the patients into two groups: infants (Infant Group) and children who were more than 1 year old (Child Group).

The Infant and Child Groups consisted of 28 and 21 patients. In the random-effects analysis, mBP was the major contributor to ScO_2 during CPB in both groups. During the

pre-CPB period, the effect of mBP was strongest in the Infant group. However, its effect was second to that of SaO_2 in the Child Group. During the post-CPB period, SaO_2 and mBP still affected ScO_2 in the Infant group. However, the dominant contributors were unclear in the Child Group.

Cerebral autoregulation may be immature in infants. In addition, it may be impaired during CPB even after one year of age.

Key Words: cerebral oxygen saturation; pediatric cardiac surgery; cardiopulmonary bypass; random-effects model; cerebral autoregulation; age

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Introduction

Recently, monitoring of cerebral oxygen saturation (ScO_2) has become widespread in pediatric cardiac surgery because neuronal injury is not necessarily rare even now [1,2]. However, the value of the monitoring seems not to be well established, including that regarding the effectiveness of intraoperative use[3,4]. We hypothesized that one of the reasons why its value is not well established may be that the physiological factors affecting ScO_2 in the perioperative period of pediatric cardiac surgery have not been sufficiently clarified. Accordingly, we performed a study to observe the changes in ScO_2 during cardiac surgery with cardiopulmonary bypass (CPB) in children weighing under 10kg and evaluated the relationship with the physiological parameters by using a random-effects model [5]. We found that systemic blood pressure was the major contributor to ScO_2 throughout the cardiac surgery with CPB in these children. This tendency was seen regardless of the type of congenital heart disease, i.e., the univentricluar or biventricular physiological type. We speculated that this result might be attributable to incomplete cerebral autoregulation in such young children [6]. If so, the relationship between ScO_2 and the physiological parameters may change according to the growth of the children.

Accordingly, in this study, we observed the changes in ScO_2 during cardiac surgery with CPB in children over a wider age range and evaluated the relationship with the physiological parameters by using the random-effects model. For this analysis we divided the children into 2 age groups: infants (0 years old) and children (more than 1 year old).

Patients and Methods

This prospective observational study was approved by Institutional Review Board of the Hokkaido University Hospital (IRB #016-0505) and written informed consent was obtained from the parents of all subjects participating in the trial. The trial was registered at UMIN Clinical Trials Registry prior to patient enrollment (UMIN000028597).

Children who were under 15 years old and who were scheduled for cardiac surgery with CPB were examined. Children with complications of other organs were excluded. Anesthesia and perioperative management, including ICU care, were conducted according to our institutional practices [5,7]. In brief, fentanyl (15-25μg/kg) and remifentanil (0.1-0.5μg/kg/min) were supplemented with midazolam (0.2-0.5mg/kg) and sevoflurane (1-2%) 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 (CVP). In the cardiopulmonary bypass, a nonpulsatile roller pump with a membrane oxygenator (Oxia, JMS, Tokyo, Japan) was used at a flow rate of 150 ml/min/kg. The alpha-stat strategy was used during core cooling.

ScO_2 was measured with an INVOS 5100C (Somanetics, Troy, MI, USA). After induction of anesthesia, SomaSensors® (Somanetics, Troy, MI, USA) were placed on the right side of the forehead. A pediatric sensor (CV-SPFB/INTL) was used for the children whose body weight was from 5 to 40kg and an infant sensor (CV-CNN/SNN) was used for the children who weighed less than 5kg. After an accommodation period, data collection was begun every one minute throughout the surgery. Mean arterial pressure (mBP), CVP, and nasopharyngeal temperature (Tnp) were also obtained every one minute. Arterial blood gases were analyzed at 37°C intermittently and the arterial oxygen saturation (SaO_2), $PaCO_2$, pH and hematocrit (Hct) were obtained. These measurements were linearly interpolated to one-minute intervals.

Statistics

JMP 14 （SAS, Cary, NC, USA） was used for statistical analysis. The main purpose of this study was to examine the relation between the changes of ScO_2 values and physiological parameters according to the growth of children. For this, random-effects analysis was employed for ScO_2 as a dependent variable. In each analysis, seven physiological parameters (mBP, CVP, Trectal, SaO_2, Hct, $PaCO_2$, and pH) were entered as independent covariates. The analysis was done for each infant (Infant Group) and for children who were more than 1 year old (Child Group). It was performed during the pre-

CPB period (from the start of operation to the start of CPB), CPB period and post-CPB period (from the end of CPB to the end of surgery) in each group. The mean regression slope, its confidence interval and p-values were obtained for each parameter. P-values were displayed as negative $\log_{10}$ values because they were so small.

Results

Forty-nine patients were evaluated. The Infant and Child Groups consisted of 28 and 21 patients, respectively. Demographic data are listed in Table 1. During CPB, mild hypothermia and normothermia were used in 18 patients of the Infant Group and 13 patients of the Child Group. In the Infant Group, 7 patients had congenital heart disease with univentricular physiology (PA, HLHS, univentricular heart). Six patients had congenital heart disease with univentricular physiology in the Child Group. Physiological data during pre-CPB, CPB and post-CPB are listed in Table 2. Throughout the whole surgical period, ScO_2 values in the Child Group were higher than those in the Infant Group, although we did not perform statistical analysis of ScO_2 values as we did with other physiological parameters because the comparison of the absolute values was not the purpose of this study.

The results of random-effects analysis for ScO_2 in the Infant Group are listed in Table 3. For the analysis of the pre-CPB period in the Infant Group, 1,2782 data (1,826 1-min records of 7 parameters) were entered. For the analyses of the CPB and post-CPB periods, 27,776 data (3,968 1-min records of 7 parameters) and 12,761 data (1,823 1-min records of 7 parameters) were entered, respectively. During the Pre-CPB and CPB periods, ScO_2

was correlated strongly with mBP. SaO_2 was secondarily related to ScO_2 in the same periods. During the post-CPB period, their order was reversed.

The results of random-effects analysis for ScO_2 in the Child Group are listed in Table 4. For the analysis of the pre-CPB period, 11,620 data (1,660 1-min records of 7 parameters) were entered. For the analyses of the CPB and post-CPB periods, 19,964 data (2,852 1-min records of 7 parameters) and 9,884 data (1,412 1-min records of 7 parameters) were entered, respectively. During the CPB period, ScO_2 was correlated strongly with mBP as in the Infant group. On the other hand, the contribution of mBP was second to that of SaO_2 during the pre-CPB period. The dominant contributors were unclear during the post-CPB period.

Representative cases of simultaneous changes of ScO_2 and mBP over time are shown in Figure 1. The changes in ScO_2 and mBP were almost parallel during the CPB period in a 3-month-old female with AVSD (Fig 1A). On the other hand, ScO_2 and mBP sometimes changed to the opposite direction in a 5-year-old male with VSD during the post-CPB period (Fig 1B).

Discussion

Our study revealed that mBP was the major contributor to ScO_2 during the CPB period in pediatric cardiac surgery with CPB, regardless of any age difference. On the other hand, the contribution of mBP became weak during the pre-CPB and post-CPB periods after one year of age.

During the pre-CPB period, the contribution of mBP was strong in the infant group. However, it became weak after one year of age. Recent findings suggest that term infants have functional autoregulation and vasoreactivity, whereas preterm infants may have anatomically incomplete and underdeveloped cerebral vasculature that cannot yet autoregulate fully[8]. Another study also indicated that static cerebral autoregulation was preserved in infants and children under sevoflurane anesthesia [9]. On the other hand, a recent study reported that term newborns with congenital heart disease showed impaired cerebral autoregulation [10]. Indeed, it was reported that term newborns with congenital heart disease have brains that are smaller and structurally less mature than expected before they undergo cardiac surgery [11,12]. Accordingly, cerebral autoregulation of infants with congenital heart disease may still be immature.

As to the CPB period, mBP was the major contributor to ScO_2 even in the children

more than 1 year old. One study examined the relationships of ScO_2 with physiological parameters in 20 infants with the biventricular physiological type [13]. In that study, ScO_2 showed significant positive correlations with mBP. In another study, the relationship of ScO_2 with physiological parameters during CPB was evaluated in 10 children from 12 days to 9 years old [14]. ScO_2 correlated positively with cerebral perfusion pressure (mBP-CVP) and the partial variance was more than 50%. Accordingly, those previous reports also suggested that the changes in ScO_2 were dependent on mBP changes during CPB. It is well known that cerebral blood flow (CBF) is one of the important determinants of ScO_2 [7]. Accordingly, it is suggested that the changes in CBF were dependent on mBP changes during CPB, possibly due to immature or disturbed cerebral autoregulation.

Cerebral autoregulation during CPB in pediatric cardiac surgery has been evaluated for a long time. One old study evaluated the relationship between mBP and CBF measured by xenon-clearance technique in 67 pediatric patients, aged 1 day–16 years [15]. During moderate-hypothermic CPB (25–32°C), there was no association between CBF and mBP. However, during deep-hypothermic CPB (18–22°C), there was an association between them. Another paper evaluated the relationship between mBP and CBF velocity measured by transcranial Doppler monitor in 25 neonates and infants, aged 3–210 days [16]. A third-order polynomial function showed that cerebral pressure-flow velocity autoregulation

was intact during normothermic CPB (36–37°C). However, cerebral pressure-flow velocity autoregulation became pressure-passive during deep-hypothermic CPB (23–25°C) and profound-hypothermic CPB (14–20°C). These old studies suggested that static cerebral autoregulation was preserved during CPB except under deep hypothermia.

Recently, several studies evaluated dynamic cerebral autoregulation during cardiac operations, including pediatric ones [17,18]. In one study of 54 children undergoing cardiac surgery with CPB, the cerebral oximetry index was calculated as a moving, linear correlation coefficient between slow waves of arterial blood pressure and cerebral oximetry measured with near-infrared spectroscopy [17]. Their mean age was 56 months old and the mean minimum temperature during CPB was 26.9°C. The mean cerebral oximetry index increased during CPB compared to pre-CPB, which indicated impaired cerebral autoregulation. In another study which utilized almost the same methodology, dynamic cerebral autoregulation was impaired during CPB under moderate hypothermia at around 28°C in children whose median age was 2.8 years [18]. On the other hand, there seem to be no data about dynamic cerebral autoregulation under mild hypothermia or normothermia, which our institute mainly adopts. However, in 234 adult patients undergoing coronary artery bypass graft surgery, valvular surgery, or both that required CPB under mild hypothermia at around 35°C, 20% of patients demonstrated impaired

dynamic cerebral autoregulation during CPB using almost the same methodology as described above [19]. Thus, there is possibility that cerebral autoregulation is impaired during CPB under mild hypothermia even in adult patients. Accordingly, cerebral autoregulation may be impaired during CPB under mild hypothermia or normothermia in pediatric cardiac surgery.

During the post-CPB period, the contribution of mBP became weak even in the infants. Moreover, the dominant contributors were unclear in the children. In our previous study, the contribution of mBP also became weak compared to the pre-CPB and CPB periods in patients whose body weight was less than 10kg [5]. On the other hand, it is hard to think that immature cerebral autoregulation became mature after CPB in the infants. During the post-CPB period, cardiovascular agents that affect cerebral blood flow [20] are usually used. In addition, the degree of surgical repair may affect cardiac and respiratory functioning after CPB. Accordingly, such extrinsic factors other than physiological ones may make interpretation difficult.

Throughout the whole surgical period, ScO_2 values in the Child Group were higher than those in the Infant Group, although we did not statistically analyze this. This finding is compatible with recent reports. In one study, ScO_2 values before surgery showed a statistically significant increasing relationship with age in children with VSD younger

than 3 years [21]. In another study, ScO_2 values before and after surgery increased simultaneously with the increase in age between 0 and 7 years in children with non-cyanotic congenital heart disease [22]. If the absolute values are different according to the growth of children, the threshold values of ScO_2 may be different with the difference of age. It is clinically important to clarify the threshold values. The mechanism of the difference of ScO_2 values according to the growth of children should be evaluated as the next step as well the setting of the threshold values by the difference of age.

There are some limitations in our study. First, there were fewer than 10 patients with the univentricular physiological type in each group. Therefore, we could not analyze by dividing the patients into univentricular and biventricular physiological types. However, in our previous study, the tendency was the same for the univentricular and biventricular physiological types, at least in patients weighing under 10kg [5]. Second, 20 of the 21 patients were under 6 years old in the Child Group. Therefore, we could not evaluate school children. Third, as mentioned above, more than half of the patients were managed under mild hypothermia or normothemia during CPB in both groups. When the population managed by moderate or deep hypothermia increases, the effect of body temperature and/or mBP on ScO_2 might be more complicated [23]. Fourth, there are some measurement algorithms utilized in near infrared spectroscopy including the modified

Beer Lambert law (which the INVOS 5100C utilizes), spatially resolved spectroscopy and time-resolved spectroscopy. It was reported that absolute ScO_2 values were different among the different spectroscopic techniques in both adults [24] and infants [25] studies. Moreover, by using a spectroscopic technique that adopts time-resolved spectroscopy, further information such as the absolute values of oxy- and deoxy hemoglobin can be obtained [26]. Thus, it may be necessary to reexamine the findings by using other spectroscopic techniques. Fifth, in this study, we evaluated the relation between ScO_2 and physiological parameters, including mBP. However, to examine whether cerebral autoregulation really exists, continuous analysis of the direct relation between mBP and ScO_2 like the cerebral oximetry index will be necessary [17,18].

In conclusion, mBP was the major contributor to ScO_2 during the CPB period regardless of age in pediatric cardiac surgery. In addition, cerebral autoregulation may be immature in infants. Accordingly, the management of blood pressure in this situation is important in pediatric cardiac surgery.

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References

1 Ghanayem NS, Hoffman GM (2016) Near Infrared Spectroscopy as a Hemodynamic Monitor in Critical Illness. Pediatr Crit Care Med 17: S201-206

2 Zaleski KL, Kussman BD (2020) Near-Infrared Spectroscopy in Pediatric Congenital Heart Disease. J Cardiothorac Vasc Anesth 34: 489-500

3 Andropoulos DB, Hunter JV, Nelson DP, Stayer SA, Stark AR, McKenzie ED, Heinle JS, Graves DE, Fraser CD, Jr. (2010) Brain immaturity is associated with brain injury before and after neonatal cardiac surgery with high-flow bypass and cerebral oxygenation monitoring. J Thorac Cardiovasc Surg 139: 543-556

4 Simons J, Sood ED, Derby CD, Pizarro C (2012) Predictive value of near-infrared spectroscopy on neurodevelopmental outcome after surgery for congenital heart disease in infancy. J Thorac Cardiovasc Surg 143: 118-125

5 Yamamoto M, Mori T, Toki T, Itosu Y, Kubo Y, Yokota I, Morimoto Y (2021) The Relationships of Cerebral and Somatic Oxygen Saturation with Physiological Parameters in Pediatric Cardiac Surgery with Cardiopulmonary Bypass: Analysis Using the Random-Effects Model. Pediatr Cardiol 42: 370-378

6 Hayashida M, Kin N, Tomioka T, Orii R, Sekiyama H, Usui H, Chinzei M,

Hanaoka K (2004) Cerebral ischaemia during cardiac surgery in children detected by combined monitoring of BIS and near-infrared spectroscopy. Br J Anaesth 92: 662-669

7 Yagi Y, Yamamoto M, Saito H, Mori T, Morimoto Y, Oyasu T, Tachibana T, Ito YM (2017) Changes of Cerebral Oxygenation in Sequential Glenn and Fontan Procedures in the Same Children. Pediatr Cardiol 38: 1215-1219

8 Rhee CJ, da Costa CS, Austin T, Brady KM, Czosnyka M, Lee JK (2018) Neonatal cerebrovascular autoregulation. Pediatr Res 84: 602-610

9 Vavilala MS, Lee LA, Lee M, Graham A, Visco E, Lam AM (2003) Cerebral autoregulation in children during sevoflurane anaesthesia. Br J Anaesth 90: 636-641

10 Votava-Smith JK, Statile CJ, Taylor MD, King EC, Pratt JM, Nelson DP, Michelfelder EC (2017) Impaired cerebral autoregulation in preoperative newborn infants with congenital heart disease. J Thorac Cardiovasc Surg 154: 1038-1044

11 Licht DJ, Shera DM, Clancy RR, Wernovsky G, Montenegro LM, Nicolson SC, Zimmerman RA, Spray TL, Gaynor JW, Vossough A (2009) Brain maturation is delayed in infants with complex congenital heart defects. J Thorac Cardiovasc

Surg 137: 529-536

12 Miller SP, McQuillen PS, Hamrick S, Xu D, Glidden DV, Charlton N, Karl T, Azakie A, Ferriero DM, Barkovich AJ, Vigneron DB (2007) Abnormal brain development in newborns with congenital heart disease. N Engl J Med 357: 1928-1938

13 White MC, Edgell D, Li J, Wang J, Holtby H (2009) The relationship between cerebral and somatic oxygenation and superior and inferior vena cava flow, arterial oxygenation and pressure in infants during cardiopulmonary bypass. Anaesthesia 64: 251-258

14 Menke J, Moller G (2014) Cerebral near-infrared spectroscopy correlates to vital parameters during cardiopulmonary bypass surgery in children. Pediatr Cardiol 35: 155-163

15 Greeley WJ, Ungerleider RM, Kern FH, Brusino FG, Smith LR, Reves JG (1989) Effects of cardiopulmonary bypass on cerebral blood flow in neonates, infants, and children. Circulation 80: I209-215

16 Taylor RH, Burrows FA, Bissonnette B (1992) Cerebral pressure-flow velocity relationship during hypothermic cardiopulmonary bypass in neonates and infants. Anesth Analg 74: 636-642

17 Brady KM, Mytar JO, Lee JK, Cameron DE, Vricella LA, Thompson WR, Hogue CW, Easley RB (2010) Monitoring cerebral blood flow pressure autoregulation in pediatric patients during cardiac surgery. Stroke 41: 1957-1962

18 Easley RB, Marino BS, Jennings J, Cassedy AE, Kibler KK, Brady KM, Andropoulos DB, Brunetti M, Hogue CW, Heitmiller ES, Lee JK, Spaeth J, Everett AD (2018) Impaired cerebral autoregulation and elevation in plasma glial fibrillary acidic protein level during cardiopulmonary bypass surgery for CHD. Cardiol Young 28: 55-65

19 Ono M, Joshi B, Brady K, Easley RB, Zheng Y, Brown C, Baumgartner W, Hogue CW (2012) Risks for impaired cerebral autoregulation during cardiopulmonary bypass and postoperative stroke. Br J Anaesth 109: 391-398

20 Patel PM, Drummond JC, Lemkuil BP (2020) Cerebral Physiology and the Effets of Anesthetic Drugs. In: Gropper, M.A. (ed) Miller's Anesthesia. Elsevier, Philadelphia, pp 294-332

21 Cui B, Ou-Yang C, Xie S, Lin D, Ma J (2020) Age-related cerebrovascular carbon dioxide reactivity in children with ventricular septal defect younger than 3 years. Paediatr Anaesth 30: 977-983

22 Sun L, Zhang K, Chen H, Ji W, Huang Y, Zhang M, Zheng J (2021) Age-Related

Changes in Cerebral Hemodynamics in Children Undergoing Congenital Cardiac Surgery: A Prospective Observational Study. J Cardiothorac Vasc Anesth:

23 Smith B, Vu E, Kibler K, Rusin C, Easley RB, Andropoulos D, Heinle J, Czosnyka M, Licht D, Lynch J, Brady K (2017) Does hypothermia impair cerebrovascular autoregulation in neonates during cardiopulmonary bypass? Paediatr Anaesth 27: 905-910

24 Moerman A, Vandenplas G, Bové T, Wouters PF, De Hert SG (2013) Relation between mixed venous oxygen saturation and cerebral oxygen saturation measured by absolute and relative near-infrared spectroscopy during off-pump coronary artery bypass grafting. Br J Anaesth 110: 258-265

25 Schneider A, Minnich B, Hofstätter E, Weisser C, Hattinger-Jürgenssen E, Wald M (2014) Comparison of four near-infrared spectroscopy devices shows that they are only suitable for monitoring cerebral oxygenation trends in preterm infants. Acta Paediatr 103: 934-938

26 Tanaka N, Yamamoto M, Abe T, Osawa T, Matsumoto R, Shinohara N, Saito H, Uchida Y, Morimoto Y (2019) Changes of Cerebral Blood Volume During Robot-Assisted Laparoscopic Radical Prostatectomy: Observational Prospective Study Using Near-Infrared Time-Resolved Spectroscopy. J Endourol 33: 995-1001

Figure legend

Figure 1 Representative cases of simultaneous changes of ScO_2 and mBP over time

(A) during the CPB period in a 3-month-old female with AVSD

(B) during the post-CPB period in a 5-year-old male with VSD

Circles indicate changes in ScO_2 and squares indicate changes in mBP. Time indicates minutes after the start of CPB (A) and after the end of CPB (B).

Table 1 Demographic data of the patients

	Infants Group	Children Group
Male/female	14/14	15/6
Age	118 (85-165) days	30 (24-46) months
Body weight (kg)	4.5 (2.5-8.4)	12 (8.1-22.5)
Surgical time (min)	254 (101-369)	211 (132-511)
CPB time (min)	176 (52-243)	158 (41-329)
Management of body temperature during CPB		
Normothermia (<35℃)	7	10
Mild hypothermia (32-34.9℃)	11	3
Moderate hypothermia (28-31.9℃)	6	5
Deep hypothermia (27.9℃)	4	3
Diagnosis		
ASD	0	4
VSD	2	0
VSD with ASD	3	1
AVSD	5	0
TOF	4	4
TGA	2	2
DOLV	1	2
PA	1	1
HLHS	5	3
Univentricular Heart	1	2
Others	4	2

Data are expressed as medians (interquartile range).

ASD; atrial septal defect, VSD; ventricular septal defect, AVSD; atrioventricular septal defect, TOF; tetralogy of Fallot, TGA; transposition of the great arteries, DOLV; double outlet right ventricle, PA; pulmonary atresia, HLHS; hypoplastic left heart syndrome

Table 2 Physiological data during pre-CPB, CPB and post-CPB periods

	Pre-CPB	CPB	post-CPB
ScO_2 (%)			
Infants Group	56.7 ± 16.2	61.8 ± 14.8	61.2 ± 18.0
Children Group	76.0 ± 11.7	70.2 ± 10.5	80.5 ± 9.7
mBP (mmHg)			
Infants Group	45.3 ± 8.6	44.9 ± 12.6	56.2 ± 10.7
Children Group	53.0 ± 9.2	39.7 ± 12.6	51.7 ± 8.9
CVP (mmHg)			
Infants Group	7.9 ± 3.4	5.6 ± 6.3	13.1 ± 5.3
Children Group	9.7 ± 3.5	6.0 ± 5.6	12.3 ± 4.5
Tnp (°C)			
Infants Group	37.2 ± 1.1	34.1 ± 2.4	36.3 ± 1.0
Children Group	37.5 ± 0.8	34.2 ± 2.9	36.6 ± 1.1
SaO_2 (%)			
Infants Group	88.5 ± 8.3	98.6 ± 3.5	90.1 ± 9.6
Children Group	90.5 ± 7.5	98.7 ± 2.9	97.8± 3.0
pH			
Infants Group	7.35 ± 0.05	7.31 ± 0.06	7.31 ± 0.05
Children Group	7.35 ± 0.04	7.29 ± 0.06	7.30 ± 0.06
PCO_2 (mmHg)			
Infants Group	44 ± 8	45 ± 8	43 ± 7
Children Group	38± 4	43 ± 8	42 ± 5
Hct (%)			
Infants Group	38.6 ±6.4	36.1 ± 5.4	41.7 ± 4.9
Children Group	38.4 ± 5.2	33.0 ± 5.3	37.4 ± 6.5

ScO_2, mBP, CVP and Trnp values obtained every one minute were averaged during each

term. SaO_2, $PaCO_2$, pH and Hct values, which were obtained intermittently and linearly interpolated to minute intervals, were averaged during each term.
The data are expressed as mean ± standard deviation.

Table 3 Relations of ScO_2 with physiological parameters in the Infant Group

pre-CPB

Parameters	Random-effects model for ScO_2 (pre CPB period)	
	Mean regression slope (95% CI)	$-\log_{10}$ (p value)
mBP	0.48 (0.44, 0.52)	115.2
SaO_2	0.35 (0.26, 0.43)	14.6
CVP	-0.50 (-0.62, -0.37)	13.7
pH	90.8 (50.5, 131.0)	5.0
$PaCO_2$	0.56 (0.21, 0.92)	2.8
Tnp	1.41 (0.49, 2.32)	2.6
Hct	0.55 (0.04, 1.06)	1.4

CPB

Parameters	Random-effects model for ScO_2 (CPB period)	
	Mean regression slope (95% CI)	$-\log_{10}$ (p value)
mBP	0.26 (0.24, 0.29)	103.8
SaO_2	0.61 (0.54, 0.68)	64.2
$PaCO_2$	0.54 (0.47, 0.62)	44.9
pH	66.1 (56.6, 75.5)	41.2
Hct	0.38 (0.30, 0.45)	21.8
Tnp	-0.26(-0.38, -0.13)	4.1
CVP	-0.03 (-0.09 to 0.02)	0.6

post-CPB

Parameters	Random-effects model for ScO_2 (post CPB period)	
	Mean regression slope (95% CI)	$-\log_{10}$ (p value)
SaO_2	0.34 (0.25, 0.43)	12.4
mBP	0.10 (0.07, 0.13)	8.9
Hct	-0.21 (-0.29, -0.14)	7.3
pH	-26.7 (-39.4, -14.0)	4.4
Tnp	1.04 (0.51, 1.56)	4.0
CVP	0.14(0.05, 0.23)	2.8
$PaCO_2$	-0.02 (-0.11, 0.06)	0.2

Table4 Relations of ScO_2 with physiological parameters in the Children Group

pre-CPB

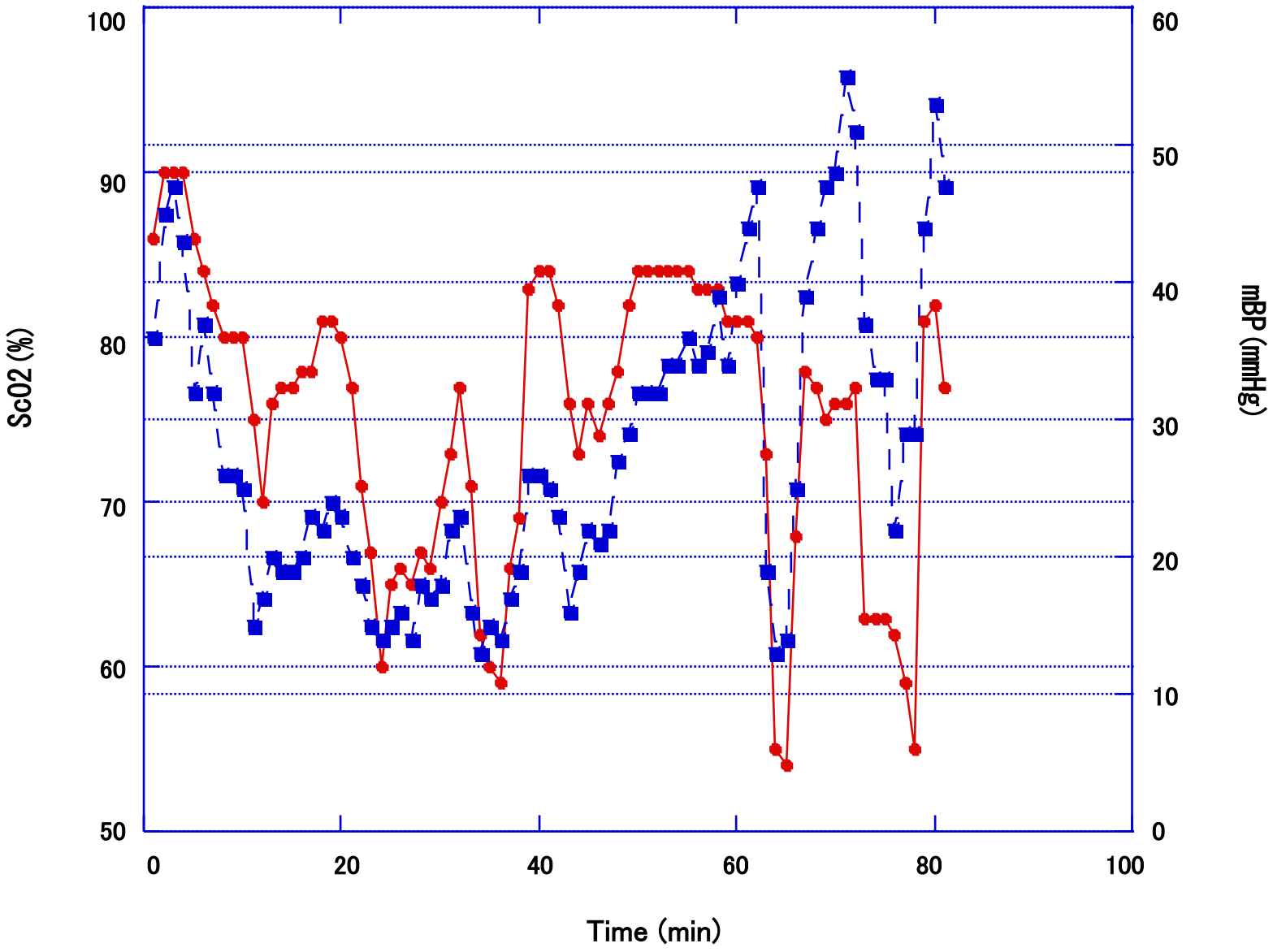
Parameters	Random-effects model for ScO_2 (pre CPB period)	
	Mean regression slope (95% CI)	$-\log_{10}$ (p value)
SaO_2	0.92 (0.79, 1.04)	41.6
mBP	0.20 (0.16, 0.24)	23.6
CVP	-0.34 (-0.44, -0.23)	9.3
pH	47.7 (26.5, 68.8)	5.0
Tnp	-0.90(-1.71, -0.09)	1.5
Hct	-0.25 (-0.63, 0.13)	0.7
$PaCO_2$	0.55 (0.04, 1.06)	0.1

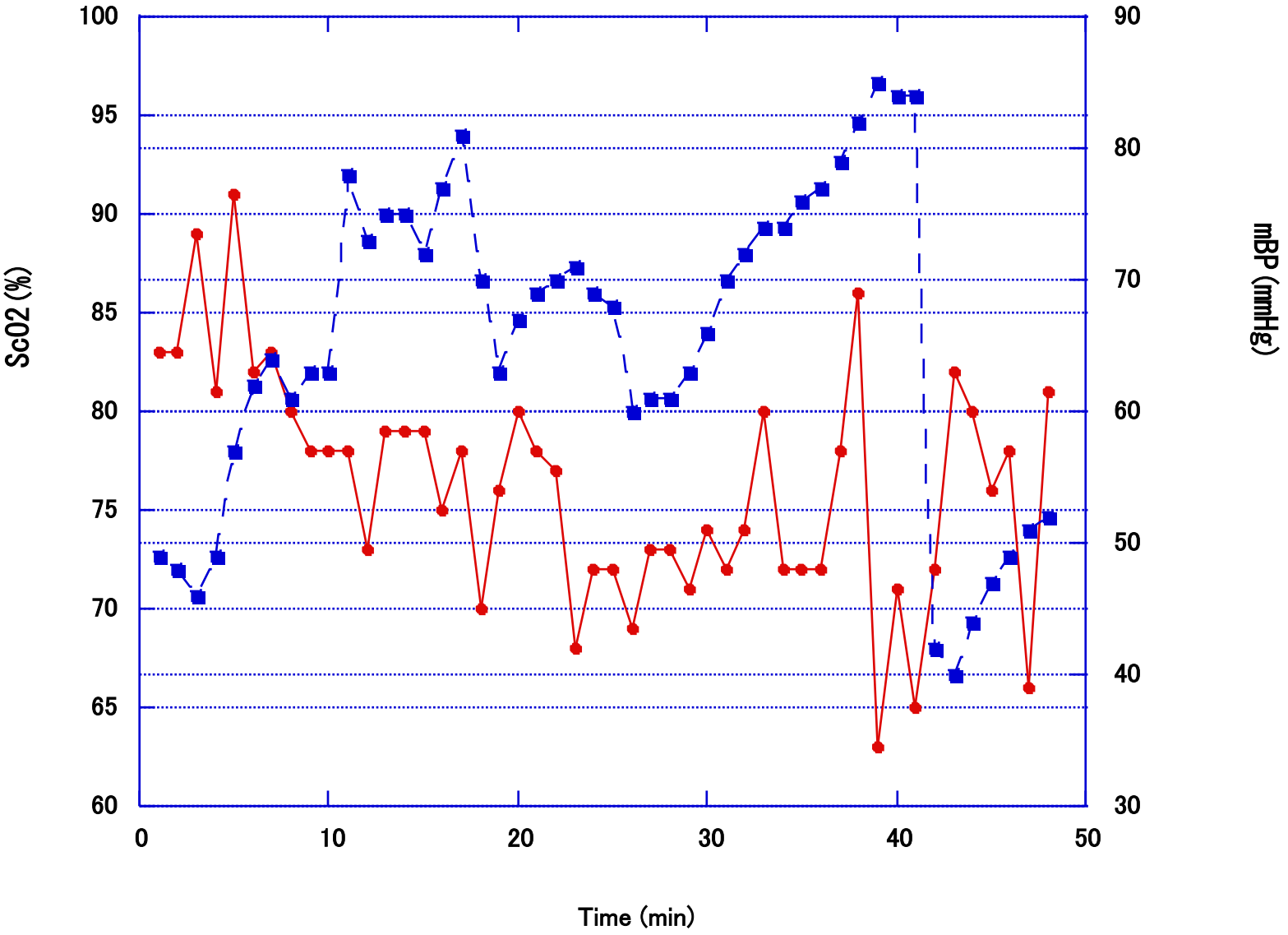
CPB

Parameters	Random-effects model for ScO_2 (CPB period)	
	Mean regression slope (95% CI)	$-\log_{10}$ (p value)
mBP	0.37 (0.33, 0.41)	68.4
CVP	0.53 (0.43, 0.62)	27.6
SaO_2	0.49 (0.39, 0.59)	22.0
Hct	0.25 (0.17,0.34)	9.0
Tnp	0.42 (0.26, 0.59)	6.3
pH	-17.7(-30.4, -5.1)	2.2
$PaCO_2$	-0.09 (-0.20, 0.01)	1.1

post-CPB

Parameters	Random-effects model for ScO_2 (post CPB period)	
	Mean regression slope (95% CI)	$-\log_{10}$ (p value)
Tnp	-0.76 (-1.19, -0.34)	3.4
CVP	0.20 (0.09, 032)	3.4
pH	-23.0 (-35.8, -10.3)	3.4
$PaCO_2$	0.16 (0.03, 0.28)	1.8
SaO_2	-0.19 (-0.40, 0.02)	1.1
Hct	-0.10 (-0.21, 0.02)	1.0
mBP	-0.01 (-001, 0.04)	0.2


100
90
80
70
60
50
ScO2 (%)
60
50
40
30
20
10
0
mBP (mmHg)
0
20
40
60
80
100
Time (min)


100
95
90
85
80
75
70
65
60
ScO2 (%)
90
80
70
60
50
40
30
mBP (mmHg)
0
10
20
30
40
50
Time (min)