HOKKAIDO UNIVERSITY

Title	Changes in cerebral hemodynamics during pediatric cardiac surgery with cardiopulmonary bypass for congenital heart disease
Author(s)	Takeda, Yoshifumi; Hoshino, Koji; Yamamoto, Masataka et al.
Citation	Pediatric cardiology, 47(1), 74-83 https://doi.org/10.1007/s00246-024-03727-y
Issue Date	2024-12-11
Doc URL	https://hdl.handle.net/2115/97332
Rights	This version of the article has been accepted for publication, after peer review (when applicable) and is subject to Springer Nature's AM terms of use, but is not the Version of Record and does not reflect post-acceptance improvements, or any corrections. The Version of Record is available online at: http://dx.doi.org/10.1007/s00246-024-03727-y
Type	journal article
File Information	manuscript.pdf

Hokkaido University Collection of Scholarly and Academic Papers : HUSCAP

Changes in cerebral hemodynamics during pediatric cardiac surgery with cardiopulmonary bypass for congenital heart disease

The names of the authors

Yoshifumi Takeda, MD, Koji Hoshino, MD, PhD, Masataka Yamamoto, MD, PhD, Yuji Morimoto, MD, PhD

The affiliations of the authors:

Department of Anesthesiology and Critical Care Medicine, Hokkaido University Graduate School of Medicine, N15 W7, Sapporo, 0608638 Japan

Corresponding Author:

Yuji Morimoto, MD, PhD: morim2@med.hokudai.ac.jp

ORCID: 0000-0001-8160-6829

Authors' contributions

Conceptualization: [Masataka Yamamoto, Yuji Morimoto]; Methodology: [Masataka Yamamoto, Yuji Morimoto]; Formal analysis and investigation: [Yoshifumi Takeda,

Masataka Yamamoto, Yuji Morimoto]; Writing – original draft preparation: [Yoshifumi Takeda, Yuji Morimoto]; Writing – review and editing: [Koji Hoshino]

Abstract

During pediatric cardiac surgery with cardiopulmonary bypass (CPB) for congenital heart disease, systemic hemodynamics dramatically change, which also causes changes in the cerebral hemodynamics. One of the representative methods in bedside monitoring for the estimation of cerebral hemodynamics during pediatric cardiac surgery is transcranial Doppler ultrasonography (TCD). However, there seem to be few reports on the changes in TCD findings in such operations, especially in cyanotic children. Accordingly, we examined the changes in TCD indices during these procedures in cyanotic children as well as non-cyanotic children.

In the post hoc analysis of a previous prospective observational study, TCD indices of the middle cerebral artery at the start and end of surgery in patients aged 6 years or less were compared. The cerebral oxygenation (rSO_2) values were also compared.

For this study, 47 cyanotic children and 49 non-cyanotic children were evaluated. At the end of surgery, cerebral blood flow velocities decreased and cerebrovascular resistance increased significantly compared to the start of surgery in both the cyanotic and non-cyanotic patients. This finding was almost constant regardless of age differences, although cerebral blood flow velocities and the rSO_2 increased until around 20 months after birth. The rSO_2 values did not change between the start and end of surgery.

Thus, the changes in cerebral hemodynamics during pediatric surgery with CPB in cyanotic children were not so different from those in non-cyanotic children. The significance of monitoring of cerebral hemodynamics by TCD and rSO_2 should be evaluated further.

Key Words: pediatric cardiac surgery, congenital heart disease, cardiopulmonary bypass, transcranial Doppler ultrasonography, cerebral oxygen saturation, near-infrared spectroscopy

Introduction

There are many kinds of congenital heart disease and their hemodynamics are very complicated according to each patient's condition [1]. Various radical and palliative procedures using cardiopulmonary bypass (CPB) are performed for the improvement of these pathological conditions. As a result, the systemic hemodynamics of the patients change dramatically after surgery, which also causes changes in cerebral hemodynamics. In addition, CPB induces stress responses including the release of large amounts of metabolic and hormonal substances such as catecholamines, cortisol, growth hormones, prostaglandins, complement, and insulin endorphins that can mediate myocardial damage, systemic and pulmonary hypertension, pulmonary endothelial damage and pulmonary vascular reactivity [1].

One of the representative methods used in bedside monitoring for the estimation of cerebral hemodynamics during pediatric cardiac surgery is transcranial Doppler ultrasonography (TCD) [2,3]. Since before the year 2000, there have been reports on the use of TCD in pediatric cardiac surgery [4]. Recently, we reported the changes in TCD indices such as cerebral blood flow velocities and cerebrovascular resistance in palliative surgery without CPB (systemic pulmonary shunt and pulmonary artery banding) for

congenital heart diseases [5]. However, there seem to be few reports on the changes in TCD findings in pediatric cardiac surgery with CPB [2]. In contrast, there have been many studies evaluating the cerebrovascular resistance in fetuses with congenital heart diseases [6-10]. However, there also seem to be few studies evaluating the changes in cerebrovascular resistance during pediatric cardiac surgery with CPB [11,12].

Recently, a study comparing the TCD indices at the start and end of pediatric surgery with CPB for non-cyanotic children was reported [12]. In this study, cerebral blood flow velocities and cerebrovascular resistance were decreased at the end of surgery compared to the start of surgery and these changes were constant regardless of age differences, although cerebral blood flow velocities increased and cerebrovascular resistance decreased until 18 months from birth [12].

However, whether the same findings occur in cyanotic children is unknown. Accordingly, we examined the changes in TCD indices during pediatric cardiac surgery with CPB in cyanotic children as well as non-cyanotic children by using our previous prospective observational study. We also evaluated the changes in cerebral tissue oxygen saturation (rSO_2) measured by near-infrared spectroscopy.

Patients and Methods

This study is a post hoc analysis of a previous prospective observational study approved by the Institutional Review Board of the Hokkaido University Hospital (IRB #016-0505). Written informed consent for the prospective study was obtained from the parents of all subjects. This post hoc analysis was also approved by the Institutional Review Board of the Hokkaido University Hospital (IRB #022-0040) and we employed the opt-out method to obtain consent. The opportunity to opt-out of the study was provided through the Hokkaido University Hospital website. The study was registered at the UMIN Clinical Trials Registry (UMIN000047805).

The patients aged 6 years or less who underwent operations for congenital heart diseases under CPB during the registration period of the prospective study (2017/8/10-2020/12/30) were examined. Those who had at least 2 examinations of cerebral hemodynamics by TCD, at around the start of surgery and at the around end of surgery, were included. Children with intracranial disorders were excluded. The children were divided into two groups, cyanotic and non-cyanotic, according to Saito's classification [13].

Anesthesia and perioperative management, including ICU care, were conducted according to our institutional practices [14]. In brief, fentanyl (15-25μg/kg) was supplemented with midazolam (0.2-0.5mg/kg) and sevoflurane (1-2%) as tolerated, and neuromuscular blockade was achieved with rocuronium. Remifentanil (0.1-

0.5μg/kg/min) was used in some older children. After weaning of CPB, epinephrine for younger children and dobutamine for older children were mainly used as inotropic drugs. Olprinone was added in many cases.

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 and the infusion of the inotropic drugs. A standard roller pump and membrane oxygenator（Oxia, JMS, Tokyo, Japan）were used to establish nonpulsatile CPB. The circuit was coated with heparin or high molecular weight polymers. CPB flow was maintained at 150ml/min/kg. Arterial blood gas analysis was performed at 30-minute intervals during CPB, maintaining an arterial PaO_2 around 200 mmHg and $PaCO_2$ between 35-45 mmHg at 37°C, following α-stat management. The target for venous oxygen saturation (SvO_2) was set at 70% or higher.

A 2-MHz, range-gated, pulsed-wave transcranial Doppler ultrasonographic probe (Multi-Dop T, DWL Elektronische Systeme GmbH, Sipplingen, Germany) was placed over the right temporal window. As an index of cerebral blood flow (CBF), middle cerebral artery blood flow velocity in the proximal (M1) segment of the middle cerebral artery was measured. To ensure a reproducible window, the signal from the artery was

adjusted to be accompanied by retrograde anterior cerebral artery flow. The sample volume, gain, and power of ultrasound were kept constant for all measurements. Peak systolic, mean, and peak end-diastolic flow velocities（Vs, Vm, Vd) were recorded at around the start of surgery and the end of it. The pulsatility index (PI) and resistance index (RI) were used as qualitative measures of cerebrovascular resistance and calculated according to the formula: PI=[Vs-Vd]/Vm, RI=[Vs-Vd]/Vs .

In the former part of the experimental period, rSO_2 was measured with an INVOS 5100C (Somanetics, Troy, MI, USA). In the latter part of 2018, the spectroscope was temporarily changed to a ForeSight Elite（CASMED, Irvine, CA, USA). Finally, the spectroscope was changed to a NIRO 200NX (Hamamatsu Photonics, Hamamatsu, Japan). Following the induction of anesthesia, the sensor was placed on the right side of the forehead. After an accommodation period, data collection was begun every one minute throughout the surgery.

Statistics

The primary outcome in this study was to compare the changes in indices of TCD (Vs, Vm, Vd, PI, and RI) between the start and end of surgery in both cyanotic and non-cyanotic patients by Wilcoxon signed-rank sum test.

The secondary outcome was to compare the rSO_2 values between the start and end of surgery in cyanotic and non-cyanotic patients using the Wilcoxon signed-rank sum test. After that, these values were evaluated for each of the three spectroscopes. Those values were also compared among the three spectroscopes at the start and end of surgery by the Kruskal-Wallis test. When significant differences were found, the Steel-Dwass test was used for multiple comparison.

Lastly, scatter plots were obtained between the age and the TCD indices and the rSO_2 values. When differences were seen by age, comparison of the changes in TCD indices and rSO_2 values between the start and end of surgery was performed by classifying the patients by age.

As physiological values, mean arterial pressure, central venous pressure, body temperature, and FiO_2 at the TCD measurement points were compared using the Wilcoxon signed-rank sum test. Arterial blood gas values (SaO_2, $PaCO_2$, and Hct) at the nearest points of TCD measurement were also compared with the Wilcoxon signed-rank sum test. All data are expressed as medians (minimum value, maximum value). Statistical analysis was performed using EZR [15]. A P-value of <0.05 was considered statistically significant.

Results

During the study period, there were 104 children aged 6 years old or less who underwent surgery for congenital heart diseases under CPB. Among them, 96 children had at least 2 TCD measurements at around the start and end of surgery; 47 were cyanotic and 49 were non-cyanotic. Demographics and physiological data of the patients are listed in Tables 1 and 2. There were no patients who had new neurologic disorders within one month after surgery.

The results of the changes in indices of TCD between the start and end of surgery in cyanotic and non-cyanotic patients are shown in Table 3 and Figure 1. Cerebral blood flow velocities (Vs, Vm and Vd) decreased at the end of surgery in both groups. PI significantly increased in the cyanotic patients, whereas PI and RI increased significantly in the non-cyanotic patients.

The rSO_2 values did not change significantly in either cyanotic or non-cyanotic patients (Table 3 and Figure 1). In the comparison of the spectroscopes, the values obtained using INVOS 5100C increased and the values with the NIRO 200MX decreased although there were no significant changes (Table 4). In Fig. 2, the comparison among the three spectroscopes is shown. In the non-cyanotic patients, the values of NIRO 200NX were

significantly lower than those of the ForeSight Elite at both the start and end of surgery.

In Figure 3, scatter plots for age, the TCD indices and the rSO_2 values are shown. Cerebral flow velocities and the rSO_2 values increased until around 20 months after birth and reached a plateau after that in both cyanotic and non-cyanotic patients. Cerebrovascular resistance values decreased until around 20 months of age and reached a plateau after that, especially in the cyanotic patients. These findings were almost the same as in Sun's report, in which the turning points were seen at 18 months of age [12], Accordingly, we divided the patients into two age groups (18 months old and younger and 19 or more months old) and compared their TCD indices and the rSO_2 values at the start and end of surgery. As shown in Table 5, the tendency was the same in both groups regardless of age differences except for cerebrovascular resistance in younger cyanotic children.

Discussion

In both cyanotic and non-cyanotic patients aged 6 years old or less who underwent surgery for congenital heart diseases under CPB, cerebral blood flow velocities decreased and cerebrovascular resistance were increased at the end of surgery compared to the start of surgery. This finding was almost constant regardless of age differences, although cerebral blood flow velocities increased until around 20 months after birth. The rSO_2 values did not change between the start and end of surgery.

In surgical procedures for congenital heart diseases under CPB, cerebral blood flow velocities at the end of the procedures decreased compared to the beginning in both cyanotic and non-cyanotic patients. On the other hand, our previous report demonstrated that cerebral blood flow velocities did not change between the start and end of surgery in palliative surgery for congenital heart diseases without CPB [5]. As with Sun's report in which cerebral blood flow velocities decreased after CPB in non-cyanotic children [12], another report demonstrated that cerebral blood flow velocities decreased after CPB mainly in non-cyanotic infants, regardless of whether pump flow was pulsatile or non-pulsatile [16]. In our study, cerebral blood flow velocities decreased after CPB even in the cyanotic patients. Considering these findings, CPB itself may cause a decrease in CBF in pediatric cardiac surgery with CPB.

Another plausible mechanism other than the effect of CPB is the increase in hematocrit [17]. When hematocrit increases, cerebrovascular resistance increases and CBF decreases. In our study, hematocrit increased in both groups after CPB. Cerebrovascular resistance increased in both groups. In Wang's report, cerebrovascular resistance also increased although there was no information on hematocrit [16]. However, cerebrovascular resistance decreased in Sun's report (there was also no information of hematocrit) [12]. Unfortunately, we could not clarify the reason for the difference of changes in cerebrovascular resistance among these studies.

There were no significant changes in rSO_2 in either group. This means that cerebral oxygenation was maintained even if the CBF decreased in both cyanotic and non-cyanotic children during surgery with CPB. However, differences of rSO_2 values among the different spectroscopes were seen in the non-cyanotic children. The changes were not constant according to the type of spectroscope, although significant differences were not seen. In our recent study, rSO_2 values in children without cerebral and cardiac disorders were rather different according to the type of spectroscope [18]. A recent review indicated that adverse outcomes have not been consistently associated with low perioperative rSO_2 [19]. The significance of rSO_2 monitoring in pediatric cardiac surgery should be evaluated more in future.

Cerebral flow velocities increased until around 20 months of age and reached a plateau after that in both cyanotic and non-cyanotic patients. This was almost the same as in Sun's report, in which the turning points were seen at 18 months of age in the non-cyanotic patients [12]. In the children without congenital heart disease, cerebral blood flow velocities increased after birth and reached a plateau at around 1-3 years of age [4]. Therefore, the changes in children with congenital heart disease may not be so different from those in children without disease. Regardless of age differences, the differences in the TCD indices between before and after surgery were almost the same, which indicated that the effects of surgery or CPB on cerebral hemodynamics were constant. The rSO_2 values increased with growth, which is also the same finding as in Sun's report [12]. Our recent report indicated that the rSO_2 values in toddlers without cerebral or cardiac diseases were higher than in infants without them [18]. Therefore, this is also the same finding as for those healthy children.

As one of the limitations of this study, the evaluation of cerebral hemodynamics was performed at only two points; at the start and end of surgery. In fact, we measured them during CPB. However, because the timing of the measurements was not constant, we could not include these data. One previous report indicated that differences of the temperature management during CPB may affect the cerebral blood flow velocities after

CPB [11]. However, in our study, the major management of temperature during CPB was in mild to moderate ranges in both groups. In addition, we did not perform preanesthetic evaluation of cerebral hemodynamics and general physiological condition. Accordingly, the awake status of these conditions was unknown. That is, the changes due to anesthetic management (mechanical ventilation, anesthetics and so on) were unknown, Next, we used olprinone in many cases in both groups. Olprinone has the effect of cerebral vascular dilation[20] and then induces an increase in cerebral blood flow [21,22]. In our study, the cerebrovascular resistance increased and cerebral blood flow velocities decreased at the end of surgery, is spite of its use. These results would likely have been even more pronounced had oloprinone not been employed. As another limitation, we did not estimate the relationship between the indices of cerebral hemodynamics and the neurologic outcomes. One previous study indicated that cerebral blood flow velocities at 18 hours post-CPB in surgery for biventricular repair such as D-transposition of the great arteries was related to early postoperative and neurodevelopmental outcomes at 1 year of age [23]. In another study on fetuses with single ventricular anomalies, lower cerebrovascular resistance was associated with impaired neurodevelopment assessed by the Bayler Scales of Infant Development II at 14 months after birth [9]. In our study, there were no patients who had a new neurologic disorder within one month after surgery. Therefore, our study

may be an analysis of children with good early neurologic outcomes. The changes in cerebral hemodynamics measured by TCD showed a constant tendency to some extent in both cyanotic and non-cyanotic patients. In other words, unusual changes in TCD indices may indicate abnormal symptoms. Thus, further study will be necessary to elucidate the relationships between TCD indices and neurologic outcomes [2].

In conclusion, cerebral blood flow velocities at the end of surgery decreased compared to the start of surgery in both cyanotic and non-cyanotic children aged 6 years old or younger who underwent surgery for congenital heart diseases with CPB. This finding was constant in both groups regardless of age differences, although cerebral blood flow velocities increased until around 20 months after birth. The rSO_2 values did not significantly change between the start and end of surgery in either group. Thus, the changes in cerebral hemodynamics during the pediatric surgery with CPB in the cyanotic children are not so different from those in non-cyanotic children. The significance of monitoring of cerebral hemodynamics, including TCD and rSO_2, needs to be further evaluated.

Statements and Declarations:

This was a retrospective observational study approved by the Institutional Review Board of our University Hospital (IRB #022-0040) in accordance with the ethical principles outlined in 1964 Declaration of Helsinki and Good Clinical Practice.

Competing Interests and Funding: No funds, grants, or other support was received.

Data availability

The data are available from the corresponding author upon reasonable request.

References

1 Jooste EH, Machovec KA, Greeley WJ (2020) Anesthesia for pediatric cardiac surgery. In: Gropper, M.A. (ed) Miller's Anesthesia. Elsevier, Philadelphia, pp 2459-2512

2 Finucane E, Jooste E, Machovec KA (2020) Neuromonitoring Modalities in Pediatric Cardiac Anesthesia: A Review of the Literature. J Cardiothorac Vasc Anesth 34: 3420-3428

3 Milne B, Gilbey T, Gautel L, Kunst G (2022) Neuromonitoring and Neurocognitive Outcomes in Cardiac Surgery: A Narrative Review. J Cardiothorac Vasc Anesth 36: 2098-2113

4 Polito A, Ricci Z, Di Chiara L, Giorni C, Iacoella C, Sanders SP, Picardo S (2006) Cerebral blood flow during cardiopulmonary bypass in pediatric cardiac surgery: the role of transcranial Doppler--a systematic review of the literature. Cardiovasc Ultrasound 4: 47

5 Takeda Y, Yamamoto M, Hoshino K, Ito YM, Kato N, Wakasa S, Morimoto Y (2023) Changes in Cerebral Hemodynamics During Systemic Pulmonary Shunt and Pulmonary Artery Banding in Infants with Congenital Heart Disease. Pediatr

Cardiol 44: 695-701

6 Grzyb A, Szymkiewicz-Dangel J (2023) Cerebroplacental hemodynamics in fetuses with transposition of the great arteries and usefulness in predicting neonatal condition. Ultrasound Obstet Gynecol 62: 414-421

7 Kaltman JR, Di H, Tian Z, Rychik J (2005) Impact of congenital heart disease on cerebrovascular blood flow dynamics in the fetus. Ultrasound Obstet Gynecol 25: 32-36

8 Man T, He Y, Zhao Y, Sun L, Liu X, Ge S (2017) Cerebrovascular hemodynamics in fetuses with congenital heart disease. Echocardiography 34: 1867-1871

9 Williams IA, Fifer C, Jaeggi E, Levine JC, Michelfelder EC, Szwast AL (2013) The association of fetal cerebrovascular resistance with early neurodevelopment in single ventricle congenital heart disease. Am Heart J 165: 544-550.e541

10 Wójtowicz A, Ochoda-Mazur A, Mroczek T, Huras H, Włoch A (2022) Near-Term Cerebroplacental Doppler, Heart Morphology, and Neonatal Biometry in Hypoplastic Left Heart Syndrome. J Ultrasound Med 41: 2087-2096

11 Abdul-Khaliq H, Uhlig R, Böttcher W, Ewert P, Alexi-Meskishvili V, Lange PE (2002) Factors influencing the change in cerebral hemodynamics in pediatric patients during and after corrective cardiac surgery of congenital heart diseases

by means of full-flow cardiopulmonary bypass. Perfusion 17: 179-185

12 Sun L, Zhang K, Chen H, Ji W, Huang Y, Zhang M, Zheng J (2022) Age-Related Changes in Cerebral Hemodynamics in Children Undergoing Congenital Cardiac Surgery: A Prospective Observational Study. J Cardiothorac Vasc Anesth 36: 1617-1624

13 Saito J, Takekawa D, Kawaguchi J, Suganuma T, Konno M, Noguchi S, Tokita T, Hashiba E, Hirota K (2019) Preoperative cerebral and renal oxygen saturation and clinical outcomes in pediatric patients with congenital heart disease. J Clin Monit Comput 33: 1015-1022

14 Yamamoto M, Toki T, Kubo Y, Hoshino K, Morimoto Y (2022) 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. Pediatr Cardiol 43: 1606-1614

15 Kanda Y (2013) Investigation of the freely available easy-to-use software 'EZR' for medical statistics. Bone Marrow Transplant 48: 452-458

16 Wang W, Bai SY, Zhang HB, Bai J, Zhang SJ, Zhu DM (2010) Pulsatile flow improves cerebral blood flow in pediatric cardiopulmonary bypass. Artif Organs 34: 874-878

17 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

18 Kubo Y, Itosu Y, Kubo T, Saito H, Okada K, Ito YM, Morimoto Y (2024) Cerebral oxygenation saturation in childhood: difference by age and comparison of two cerebral oximetry algorithms. J Clin Monit Comput 38: 639-648

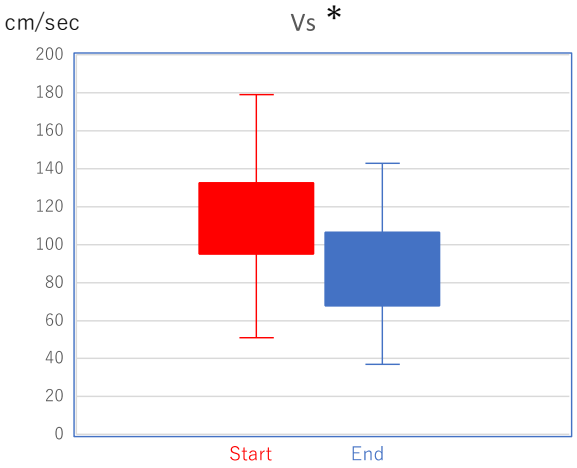
19 Zaleski KL, Kussman BD (2020) Near-Infrared Spectroscopy in Pediatric Congenital Heart Disease. J Cardiothorac Vasc Anesth 34: 489-500

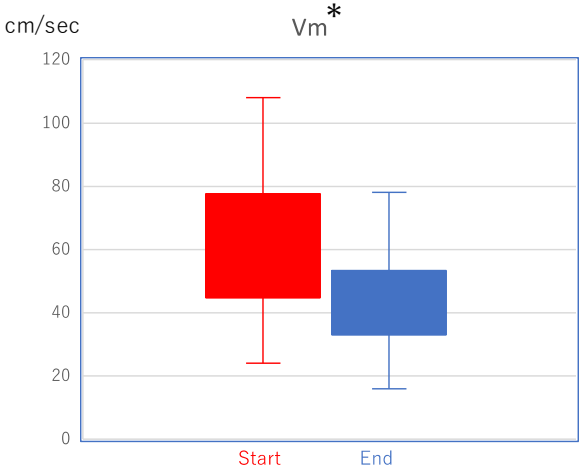
20 Ueda T, Mizushige K, Yukiiri K, Nishiyama Y, Kohno M (2004) The cerebrovascular dilatation effects of olprinone, a phosphodiesterase III inhibitor, in comparison with acetazolamide--a pilot study. Clin Neurol Neurosurg 106: 284-288

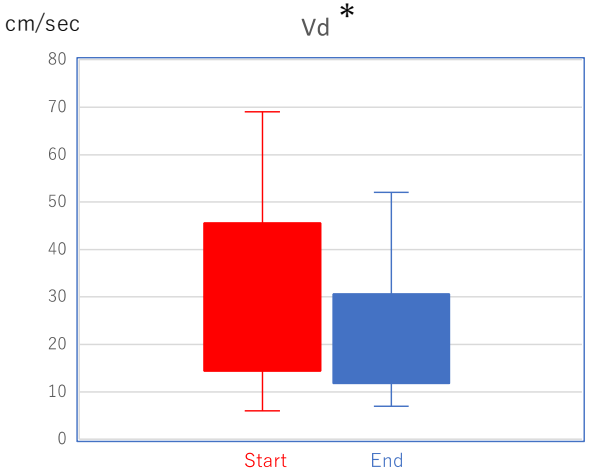
21 Mazzon E, Esposito E, Di Paola R, Impellizzeri D, Bramanti P, Cuzzocrea S (2011) Olprinone, a specific phosphodiesterase (PDE)-III inhibitor, reduces the development of multiple organ dysfunction syndrome in mice. Pharmacol Res 64: 68-79

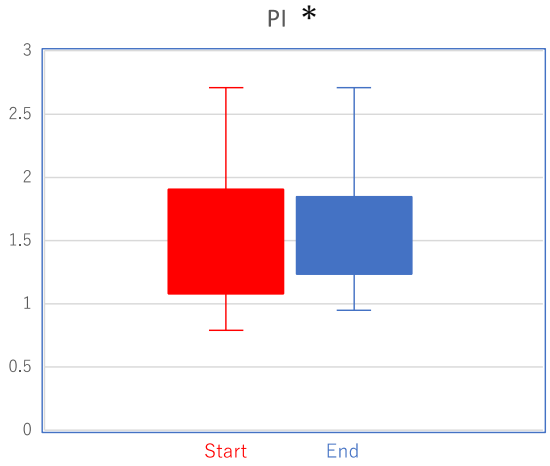
22 Ueda T, Mizushige K (2006) The effects of olprinone, a phosphodiesterase 3 inhibitor, on systemic and cerebral circulation. Curr Vasc Pharmacol 4: 1-7

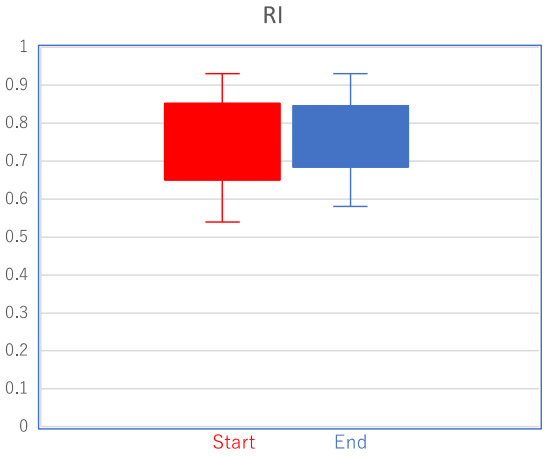
23 Cheng HH, Wypij D, Laussen PC, Bellinger DC, Stopp CD, Soul JS, Newburger JW, Kussman BD (2014) Cerebral blood flow velocity and neurodevelopmental outcome in infants undergoing surgery for congenital heart disease. Ann Thorac Surg 98: 125-132


cm/sec
Vs *
200
180
160
140
120
100
80
60
40
20
0
Start
End


cm/sec
Vm *
120
100
80
60
40
20
0
Start
End


cm/sec
Vd *
80
70
60
50
40
30
20
10
0
Start
End


PI *
3
2.5
2
1.5
1
0.5
0
Start
End


RI
1
0.9
0.8
0.7
0.6
0.5
0.4
0.3
0.2
0.1
0
Start
End

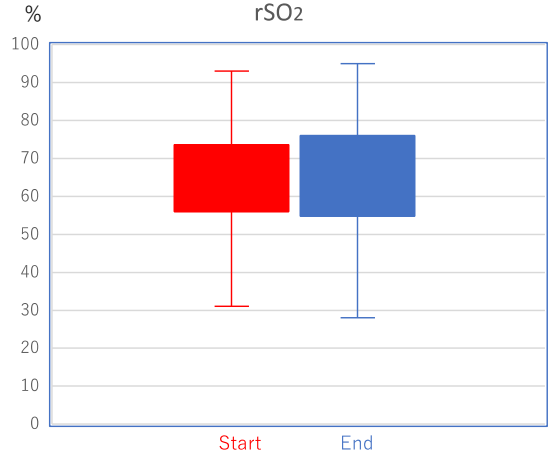

%
rSO2
100
90
80
70
60
50
40
30
20
10
0
Start
End

Figure 1a-1

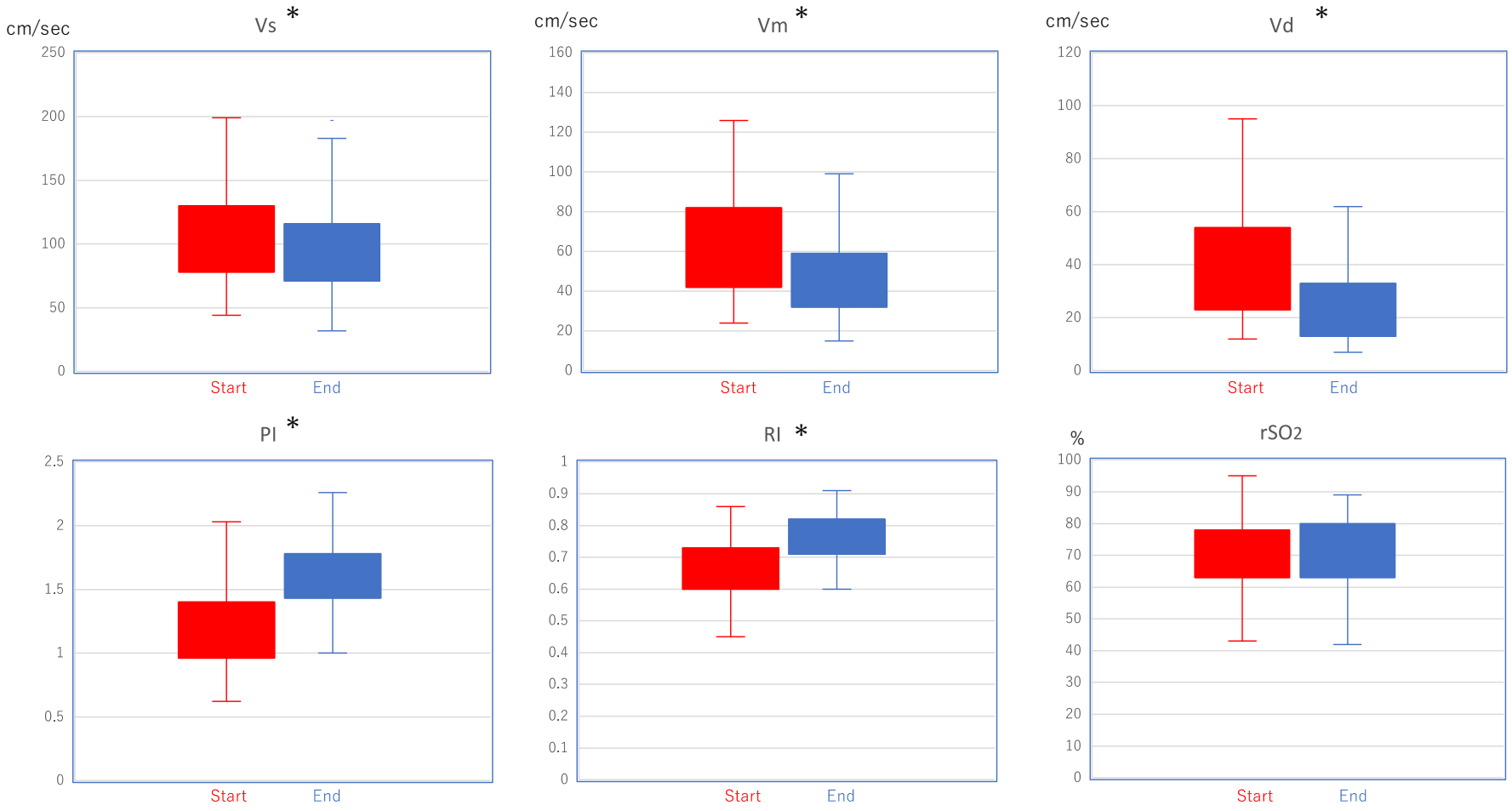

cm/sec
Vs *
250
200
150
100
50
0
Start
End
cm/sec
Vm *
160
140
120
100
80
60
40
20
0
Start
End
cm/sec
Vd *
120
100
80
60
40
20
0
Start
End
PI *
2.5
2
1.5
1
0.5
0
Start
End
RI *
1
0.9
0.8
0.7
0.6
0.5
0.4
0.3
0.2
0.1
0
Start
End
%
rSO2
100
90
80
70
60
50
40
30
20
10
0
Start
End

Figure 1b-1

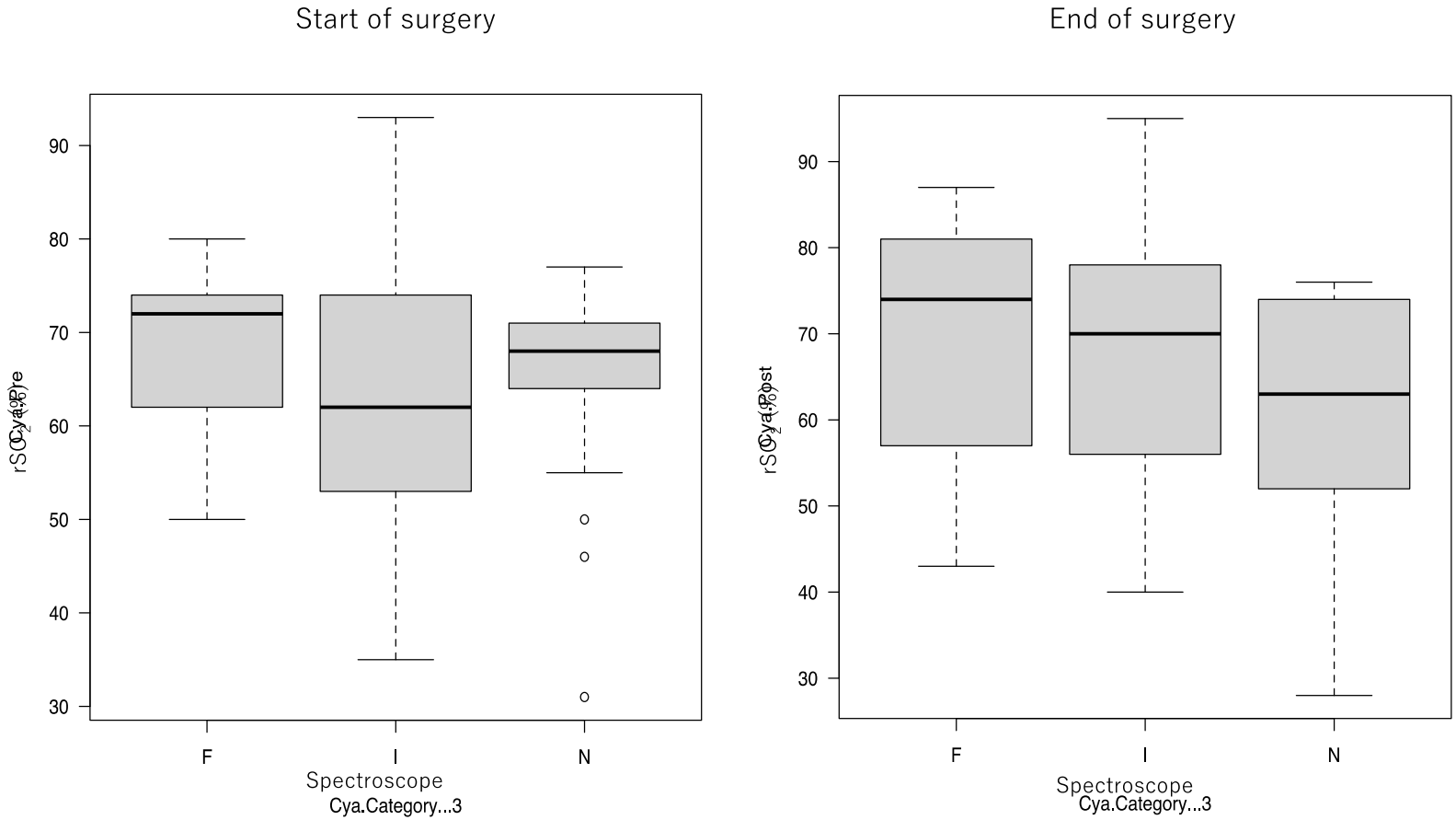
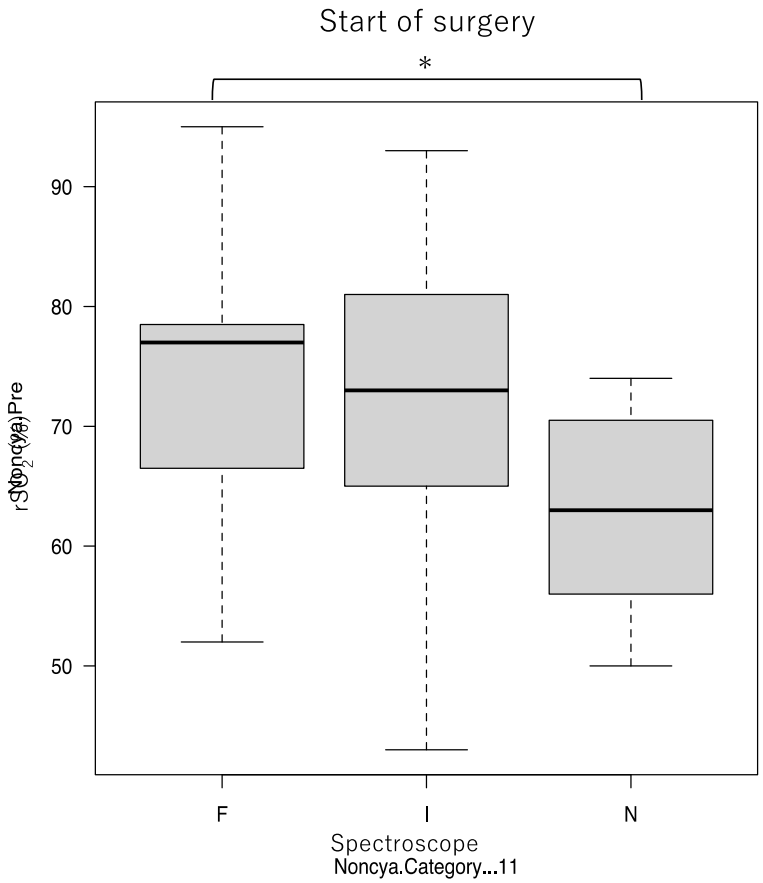

Start of surgery
End of surgery
90
80
70
60
50
40
30
F
I
N
Spectroscope
Cya.Category...3

Figure 2a-1


Start of surgery
*
90
80
70
60
50
F
I
N
Spectroscope
Noncya.Category...11

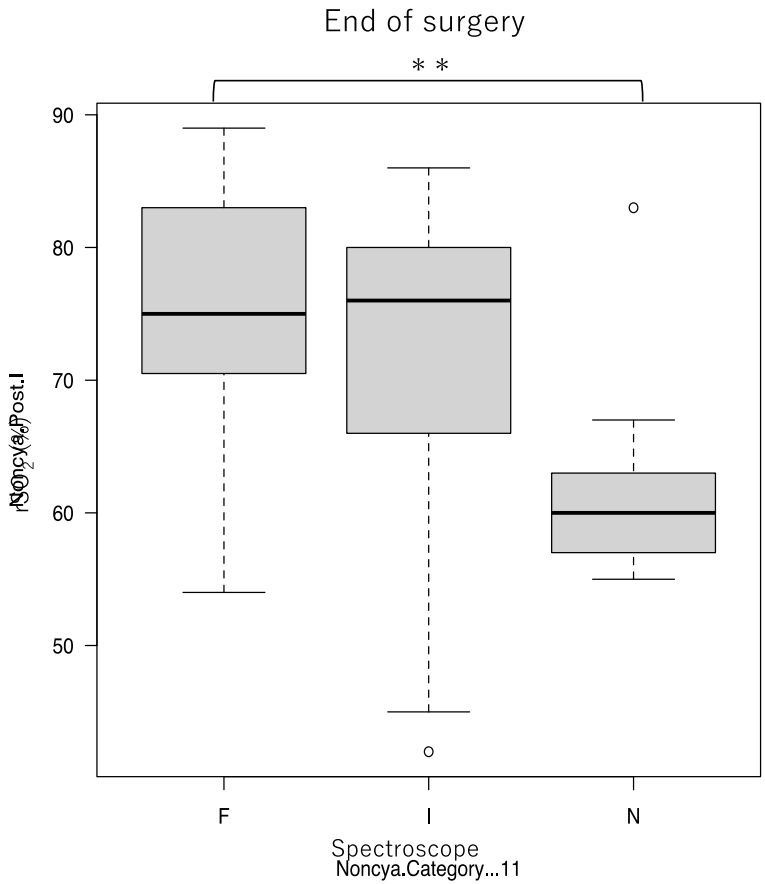

End of surgery
* *
90
80
70
60
50
F
I
N
Spectroscope
Noncya.Category...11

Figure 2b-1

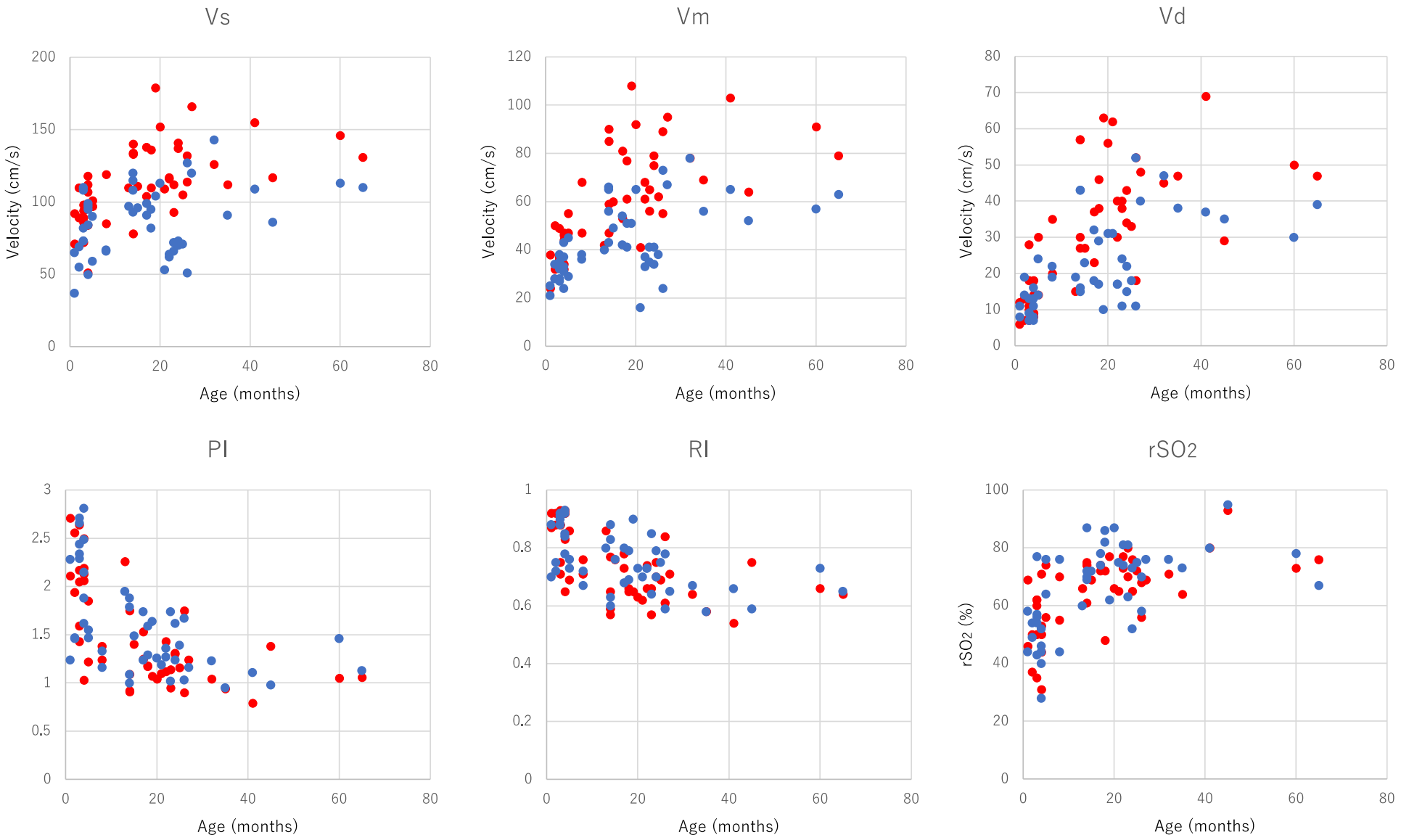

Vs
Velocity (cm/s)
Age (months)
Vm
Velocity (cm/s)
Age (months)
Vd
Velocity (cm/s)
Age (months)
PI
Age (months)
RI
Age (months)
rSO2
rSO2 (%)
Age (months)

Figure 3a-1

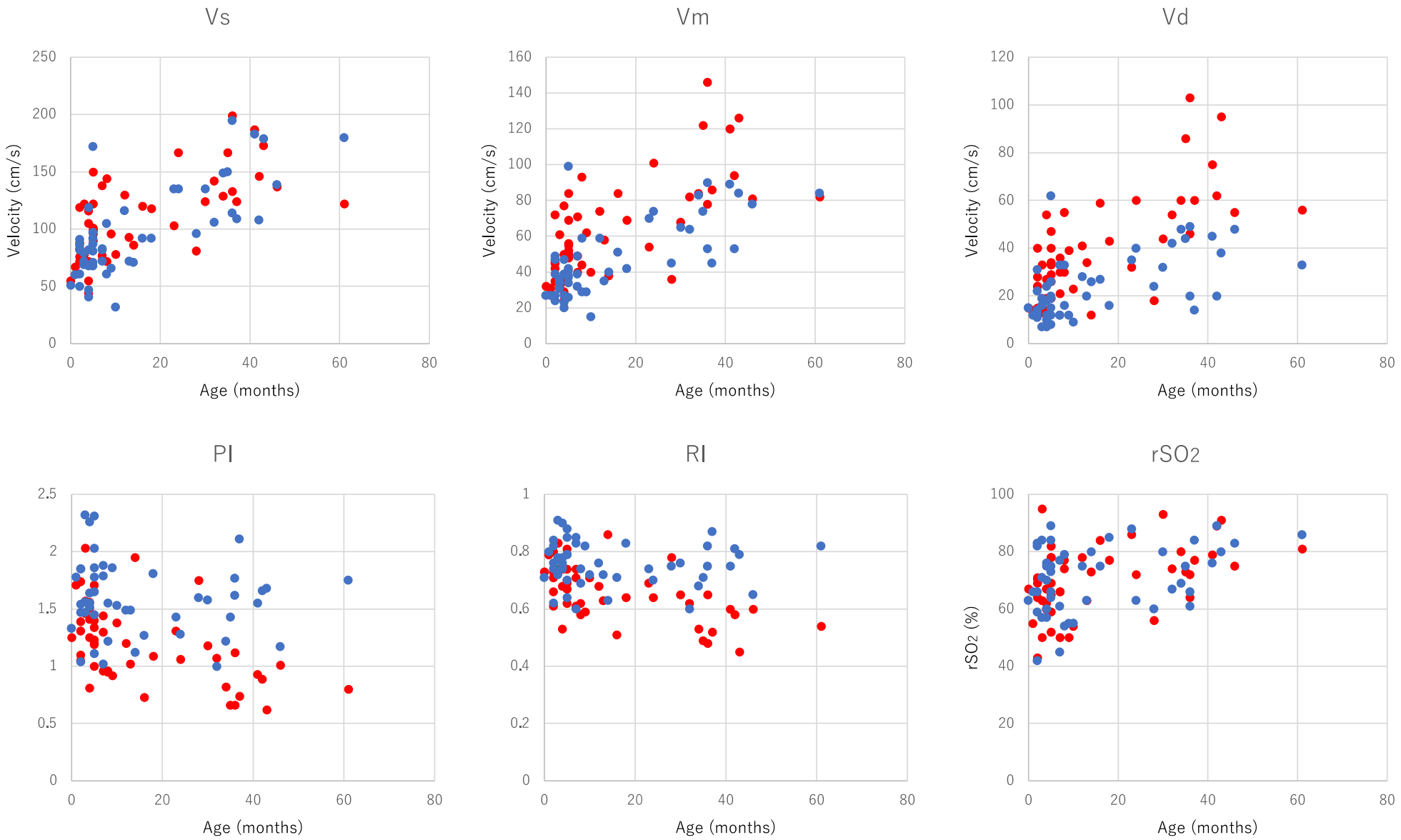

Vs
Velocity (cm/s)
250
200
150
100
50
0
0
20
40
60
80
Age (months)
Vm
Velocity (cm/s)
160
140
120
100
80
60
40
20
0
0
20
40
60
80
Age (months)
Vd
Velocity (cm/s)
120
100
80
60
40
20
0
0
20
40
60
80
Age (months)
PI
2.5
2
1.5
1
0.5
0
0
20
40
60
80
Age (months)
RI
1
0.8
0.6
0.4
0.2
0
0
20
40
60
80
Age (months)
rSO2
rSO2 (%)
100
80
60
40
20
0
0
20
40
60
80
Age (months)

Figure 3b-1

Table 1 Demographic data of the patients

	Cyanotic	Non-cyanotic
Patient number	47	49
Age (months)	15 (4, 24)	7 (4, 28)
Weight (kg)	8.8 (5.3, 10.9)	6.7 (5.0, 11.2)
Male:female	29:18	28:21
Surgery time (min)	277 (226, 369)	177 (151, 235)
Anesthesia time (min)	426 (352, 488)	299 (264, 364)
CPB time (min)	149 (105, 192)	96 (72, 133)
Aorta clamp time (min)	33 (0, 78)	55 (35, 82)
Management of body temperature during CPB		
>36℃	4	8
33.0 - 35.9℃	23	26
28.0 – 32.9℃	16	12
<27.9℃	4	3
Diagnosis		
Abnormal origin of coronary artery	0	2
Atrial septal defect	0	14
Atrioventricular septal defect	0	12
Coarctation complex	0	1
Double outlet right ventricle	6	0
Ebstein's anomaly	3	0
Hypoplastic left heart syndrome	3	0
Mitral stenosis	0	1
Mitral regurgitation	0	1
Partial anomalous pulmonary venous connection	0	1
Pulmonary artery stenosis	0	1
Pulmonary atresia	12	0
Single left ventricle	3	0
Tetralogy of Fallot	9	0
Transposition of great arteries	6	0
Truncus arteriosus communis	1	0
Tricuspid arteriosus	4	0
Ventricle septal defect	0	16
Near infrared spectroscope used		
ForeSight Elite	13	23
INVOS 5100S	17	13
NIRO 200NX	17	13

Table 2 Physiological data of the patients

	Start of surgery	End of surgery	P value
Cyanotic			
Mean arterial pressure (mmHg)	48 (44, 55)	53 (48, 58)	<0.05
Central venous pressure (mmHg)	7 (5, 9)	12 (9, 15)	<0.05
Body temperature (℃)	36.9 (36.4, 37.2)	36.8 (36.4, 37.5)	0.70
$PaCO_2$ (mmHg)	38 (37, 42)	40 (37, 42)	0.86
SaO_2 (%)	89 (82.9, 93.1)	99.2 (84, 99.6)	<0.05
FiO_2	0.58 (0.39, 0.61)	0.95 (0.86, 0.98)	<0.05
Hct (%)	37.9 (35.3, 43.3)	41 (38.6, 45.78)	<0.05
Non-cyanotic			
Mean arterial pressure (mmHg)	51 (48, 60)	57 (53, 64)	0.06
Central venous pressure (mmHg) (n=49)	6 (4, 9)	7 (5, 10)	<0.05
Body temperature (℃)	36.6 (36.1, 37.0)	36.9 (36.5, 37.2)	<0.05
$PaCO_2$ (mmHg)	39 (37, 43)	39 (37, 42)	0.35
SaO_2 (%)	98.7 (97.0, 99.4)	99.3 (98.9, 99.8)	<0.05
FiO_2	0.29 (0.23, 0.46)	0.90 (0.60, 0.98)	<0.05
Hct (%)	33.8 (31.5, 36.3)	39.3 (38.3, 41.7)	0.06

P values comparing the start and end of surgery were obtained using the Wilcoxon signed-rank sum test.

Table 3 Comparison of TCD indices and rSO_2 values at the start and end of surgery

	Start of surgery	End of surgery	*P* value
Cyanotic			
Vs	112 (96, 133)	90 (68, 106)	<0.05
Vm	59 (45, 78)	40 (33, 53)	<0.05
Vd	30 (15, 46)	18 (12, 31)	<0.05
PI	1.3 (1.08, 1.9)	1.47 (1.24, 1.86)	<0.05
RI	0.71 (0.65, 0.85)	0.75 (0.69, 0.85)	0.16
rSO_2	69 (56, 74)	70 (55, 76)	0.45
Non-cyanotic			
Vs	103 (78, 130)	87 (71, 116)	<0.05
Vm	58 (42, 82)	42 (32, 59)	<0.05
Vd	34 (23, 54)	20 (13, 33)	<0.05
PI	1.19 (0.96, 1.40)	1.55 (1.43, 1.78)	<0.05
RI	0.67 (0.60, 0.73)	0.76 (0.71, 0.82)	<0.05
rSO_2	71 (63, 78)	73 (63, 80)	0.51

P values comparing the start and end of surgery were obtained using the Wilcoxon signed-rank sum test.

Table 4 Comparison of rSO_2 values at the start and end of surgery by spectroscope

	Start of surgery	End of surgery	P value
Cyanotic			
ForeSight Elite	72 (62, 74)	74 (57, 81)	0.58
INVOS 5100S	62 (53, 74)	70 (56, 78)	0.14
NIRO 200NX	68 (64, 71)	63 (52, 74)	0.37
Non-cyanotic			
ForeSight Elite	77 (67, 78)	75 (71, 83)	0.31
INVOS 5100S	73(65, 81)	76 (66, 80)	0.67
NIRO 200NX	63 (56, 70.5)	60 (57, 63)	0.72

P values comparing the start and end of surgery were obtained using the Wilcoxon signed-rank sum test.

Table 5 Comparison of TCD indices and rSO_2 values at the start and end of surgery according to age differences

	Start of surgery	End of surgery	P value
Cyanotic			
≤ 18 months old (n=28)			
Vs	101 (88, 114)	90 (69, 98)	<0.05
Vm	47 (37, 59)	37 (31, 44)	<0.05
Vd	18 (11, 30)	16 (11, 20)	<0.05
PI	1.59 (1.24, 2.14)	1.62 (1.43, 2.28)	0.37
RI	0.78 (0.71, 0.88)	0.79 (0.72, 0.88)	0.83
rSO_2	62 (50, 71)	58 (48, 75)	0.82
19–72 months old (n=19)			
Vs	126 (113, 144)	86 (68, 112)	<0.05
Vm	75 (63, 90)	51 (36, 64)	<0.05
Vd	45 (36, 51)	30 (17, 38)	<0.05
PI	1.10 (1.04, 1.27)	1.24 (1.12, 1.43)	<0.05
RI	0.66 (0.63, 0.71)	0.70 (0.65, 0.74)	<0.05
rSO_2	72 (67, 77)	75 (69, 79)	0.34
Non-cyanotic			
≤ 18 months old (n=34)			
Vs	92 (75, 118)	76 (67, 90)	<0.05
Vm	50 (39, 67)	37 (28, 42)	<0.05
Vd	29 (19, 38)	16 (12, 24)	<0.05
PI	1.28 (1.06, 1.46)	1.55 (1.47, 1.84)	<0.05
RI	0.71 (0.63, 0.74)	0.76 (0.72, 0.82)	<0.05
rSO_2	67 (60, 74)	71 (60, 76.8)	0.13
19–72 months old (n=15)			
Vs	137 (124, 167)	135 (112, 165)	0.74
Vm	84 (80, 111)	74 (59, 84)	<0.05
Vd	60 (50, 69)	38 (28, 44.5)	<0.05
PI	0.93 (0.77, 1.10)	1.58 (1.36, 1.67)	<0.05
RI	0.6 (0.53, 0.65)	0.75 (0.71, 0.80)	<0.05
rSO_2	77 (73, 84)	76 (67, 84)	0.20

The patients were divided into two age groups (≤ 18 months old and ≥ 19 months old).
P values comparing the start and end of surgery were obtained using the Wilcoxon signed-rank sum test.