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ARTICLE

Dynamic Changes in Left and Right Cerebral Oxygen Saturation during Selective Cerebral Perfusion in Young Infants

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ABSTRACT

Objectives: We investigated whether the selective cerebral perfusion (SCP) technique causes differences in changes in cerebral perfusion between both hemispheres in young infants, using cerebral oxygen saturation (ScO_2) as an index. Further, we determined the association between the discrepancy in ScO_2 and cerebral perfusion pressure during SCP. **Methods:** The difference in ScO_2 between the left and right cerebral hemispheres ($\Delta ScO_{2\ Rt\text{-}Lt}$) was calculated during clamping of the innominate artery (IA) and during SCP. **Results:** In 25 infants (aged 2 to 78 days), the left and right ScO_2 were well maintained (median 63.2% and 60.9% during IA clamping, respectively; 64.0% and 65.6% during SCP, respectively). During IA clamping, right and left ScO_2 decreased (median −1.4% and −1.0%, respectively). During SCP, right ΔScO_2 was higher compared to left ΔScO_2 (median 1.5% *vs.* 0.6%; $p < 0.001$). Eight patients had a higher right ΔScO_2 than left ΔScO_2 throughout SCP. They had lower $\Delta ScO_{2\ Rt\text{-}Lt}$ during IA clamping (median −3.2% *vs.* 0.0%; $p < 0.001$) and higher $\Delta ScO_{2\ Rt\text{-}Lt}$ during SCP than others (median 5.0% *vs.* −0.8%; $p < 0.001$). During and after SCP, the correlation coefficient between right ΔScO_2 and change in the mean arterial pressure was higher in patients with a discrepancy than in others ($r = 0.731$ *vs.* $r = 0.519$; $p < 0.001$). **Conclusions:** This study suggests that SCP permits adequate bilateral cerebral perfusion. However, the unilateral cerebral perfusion technique may cause a difference in cerebral perfusion between both hemispheres in young infants; this may depend on the perfusion pressure.

KEYWORDS

Cerebral circulation; congenital; heart defects; monitoring; near-infrared spectroscopy

1 Introduction

Selective antegrade cerebral perfusion (SCP) is performed to save the brain from neurological injury during aortic arch surgery requiring cardiopulmonary bypass [1–3]. During interrupted blood flow to the left carotid and vertebral arteries due to clamping of the aortic arch, SCP ensures sustained cerebral perfusion in both hemispheres through the collateral vessels of the brain. Unfortunately, an investigation using magnetic resonance angiography recently revealed that the completion rate of the circle of Willis was only 40% in neonates and infants [4]. Moreover, infants, especially neonates, are more vulnerable to brain hypoxia during aortic arch surgery since they are still in the process of development [5]. Prolonged hypoxic and ischemic injury leads to cellular necrosis, apoptosis, and excitotoxicity, especially in the basal ganglia, brain stem, and sensory cortex of neonates [5]. Fluctuations in cerebral blood flow can worsen neurodevelopmental outcomes, especially during aortic arch repair [6].

Assessment of the adequacy of cerebral perfusion can be investigated during SCP for aortic arch surgery using transcranial doppler, electroencephalography, and near-infrared spectroscopy (NIRS) [7]. There are few studies on whether cerebral perfusion is adequately maintained through unilateral SCP [8,9]. Although SCP is generally believed to be safer than deep hypothermic circulatory arrest, whether unilateral cerebral perfusion results in an even distribution of blood to both hemispheres remains unresolved. In other words, cerebral blood flow to the right side may be more than that to the left side in a perfusion pressure-dependent manner [10].

Therefore, we investigated whether there is a difference between changes in left and right cerebral perfusion based on the SCP technique used during aortic arch surgery in young infants, using continuous monitoring of cerebral oxygen saturation (ScO_2) in both hemispheres. In addition, we also determined whether the difference between changes in left and right cerebral oxygen saturation is associated with the perfusion pressure during SCP.

2 Methods

2.1 Patients

This retrospective study was performed using the electronic medical records and database of patients who underwent aortic arch surgery for conditions including coarctation of aorta (CoA), hypoplastic left heart syndrome (HLHS), and interruption of aortic arch (IAA). All patients underwent arch reconstruction with cardiopulmonary bypass (CPB). Of 150 patients younger than 3 months from February 2017 to March 2022, 125 patients were excluded. 124 either lacked ScO_2 data on one side or had incomplete medical records. One patient was excluded due to undergoing deep hyperthermic circulatory arrest. All included patients underwent antegrade SCP during arch reconstruction.

2.2 General Anesthesia and Monitoring

All patients were operated under general anesthesia, maintained by continuous infusion of midazolam 0.1–0.2 mg/kg/hr, remifentanil 0.1–0.2 μg/kg/min, and rocuronium 1 mg/kg/hr. Invasive arterial blood pressure monitoring was performed simultaneously at the radial and femoral arteries, and central venous catheterization was performed for central venous pressure monitoring and the infusion of vasoactive and inotropic agents. All intraoperative variables, including arterial blood pressure, central venous pressure, body temperature, oxygen saturation (SpO_2; measured using a pulse oximeter), end-tidal carbon dioxide concentration, and electrocardiographic data, were obtained from a prospectively established database by real-time recording using Vital Recorder [11].

2.3 Surgical Procedures

The surgical procedures were performed according to our institutional protocol of pediatric cardiac surgery [12]. For the SCP, a 3.5-mm polytetrafluoroethylene prosthetic graft (WL Gore & Associates, Inc., Flagstaff, AZ) was connected end-to-side to the innominate artery (IA). The right brachiocephalic circulation had to be transiently interrupted because the IA was clamped during the anastomosis. Following this, an 8-Fr arterial cannula was inserted into the IA via the prosthetic graft. Under moderate hypothermia (27°C–28°C), SCP was initiated through the right IA cannulation, at a flow rate of 50–70 ml/kg/min. During arch repair with aorta cross-clamping, only the brain and right arm received perfusion. Depending on the surgeon's discretion, selective myocardial perfusion was done if necessary. After completion of the arch repair, the full flow rate of the CPB was restored.

2.4 Measurement and Analysis of ScO_2

Using near-infrared spectroscopy (O3® Regional Oximeter, Masimo, Irvine, CA), ScO_2 was measured in both hemispheres by neonatal sensors placed on the forehead. ScO_2 was also recorded bilaterally at time intervals of 2 s simultaneously with other intraoperative variables and stored in the Vital Recorder database. The ScO_2 data of each side of the cerebral hemisphere were extracted and averaged at 30-s intervals, and divided into the following four periods: 1) 10 min immediately after the IA was clamped for arterial cannulation 2) 10 min immediately after declamping of the IA 3) 20 min during the SCP for arch reconstruction 4) 10 min after full CPB flow was restored (Fig. 1).

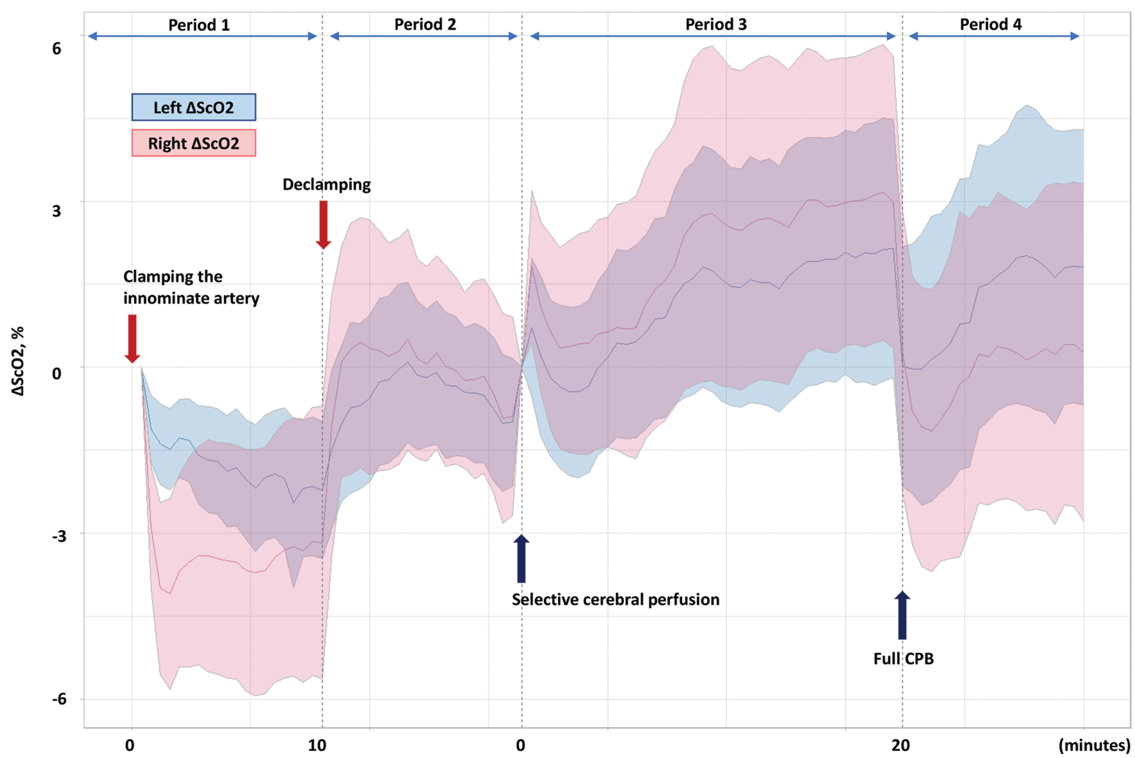

Figure 1: Changes in cerebral oxygen saturation (ΔScO_2) of left (light blue) and right (pink) hemispheres. Lines represent median ScO_2 values measured throughout each period and shading around the median ScO_2 lines indicates 95% confidence intervals

The changes in ScO_2 in each hemisphere and mean radial arterial pressure (ΔScO_2 and ΔMAP, respectively) were calculated: ΔScO_2 (ΔMAP) = the mean ScO_2 (MAP) measured throughout each period-the reference value of the ScO_2 (MAP) of each period. The reference values of the ScO_2 (MAP) were defined as the mean ScO_2 (MAP) for 1 min before IA clamping (periods 1 and 2) and 1 min before starting SCP (periods 3 and 4), respectively (Fig. 1). The MAP was measured from the femoral artery during IA clamping and from the radial artery during the SCP.

To identify patients at risk of higher right brain than left brain perfusion, patients were classified into 2 groups: 1) those with a difference in ScO_2 between the left and right hemispheres ($\Delta ScO_{2\ Rt\text{-}Lt}$), defined as higher right ΔScO_2 than left ΔScO_2 throughout the SCP period, and 2) others.

2.5 Statistical Analysis

All data are presented as mean (SD, standard deviation), median (IQR, interquartile range), and number (%). Difference between right and left ScO_2 parameters were analyzed using Wilcoxon signed rank test.

Comparison between the two groups based on whether the patient had a difference in ScO_2 between both sides was performed using the Mann-Whitney test. A Linear regression was performed to investigate the relationship between ΔScO_2 and ΔMAP. Fisher's z-transformation test was performed to compare correlation coefficients between patients with and without any ScO_2 discrepancy. A *p*-value below 0.05 was considered statistically significant. R 4.2.0 (http://www.r-project.org) was used for all statistical analysis.

3 Results

In this study, the data of 25 patients were finally analyzed: 15 had CoA, 7 had HLHS, and 3 had IAA. The median age of HLHS patients (median 30 days [IQR 18–48 days]) was higher compared to those with CoA (median 7 days [IQR 6–9 days]) and IAA (median 6 days [IQR 6–15 days]) ($p = 0.011$). Among the patients with CoA or IAA, 13 had a concomitant ventricular septal defect (VSD). Of these, 11 underwent VSD closure, while 2 underwent pulmonary artery banding following arch reconstruction. The median duration of aortic cross-clamping was 54 min [IQR 24–64 min].

Before CPB, the median left ScO_2 was 64.4% (IQR 58.7%–67.5%), and the median right ScO_2 was 64.0% (IQR 60%–67.5%). Throughout the surgical procedures, the absolute values of ScO_2 in both sides were within normal range (Table 1). While there was no difference in left ScO_2 based on each period of surgery, right ScO_2 significantly differed between clamping and declamping of the IA and between SCP and post-SCP periods ($p < 0.001$ in both cases) (Table 1).

Table 1: Cerebral oxygen saturation (ScO_2) according to the surgical periods related to selective cerebral perfusion (SCP)

	Left ScO_2			Right ScO_2			Difference between left and right ScO_2		
	Total	Without discrepancy	With discrepancy	Total	Without discrepancy	With discrepancy	Total	Without discrepancy	With discrepancy
Clamping IA	63.2 [58.8–69.2]	65.4 [60.8–73.0]	59.5 [50.0–65.5]†	60.9 [56.0–67.9]*‡	62.0 [58.0–68.0]	58.1 [48.8–64.2]c	−2.6 [−6.5–1.7]‡	−3.0 [−6.6–(−1.2)]	0.4 [−6.5–5.6]†
Declamping IA	63.3 [60.0–71.2]	66.0 [61.7–73.6]	61.2 [49.8–63.7]†	64.0 [59.0–69.0]*	64.0 [59.4–68.8]	63.0 [52.6–72.2]	−2.0 [−5.8–2.2]	−2.5 [−6.0–(−0.9)]	3.4 [−3.7–10.2]†
SCP	64.0 [59.5–69.2]	67.0 [61.5–73.0]	59.4 [52.0–63.0]†	65.6 [59.0–69.0]*‡	65.0 [58.0–67.4]	67.0 [62.9–75.8]†	−1.0 [−5.0–7.1]‡	−3.2 [−6.0–0.0]	7.9 [4.0–15.0]†
After SCP	64.0 [59.7–69.3]	66.8 [63.0–71.4]	58.0 [53.0–62.7]†	64.0 [58.3–67.2]*	64.3 [58.2–67.0]	63.2 [59.0–68.0]	−1.5 [−5.3–3.1]	−4.2 [−6.4–(−1.0)]	4.3 [0.0–8.7]†

Note: * left *vs*. right; Wilcoxon signed rank test $p < 0.05$.
† with *vs*. without discrepancy; Wilcoxon signed rank test $p < 0.05$.
‡ clamping *vs*. declamping the innominate artery (IA) or SCP *vs*. after SCP; Wilcoxon signed rank test $p < 0.05$.

While the IA was clamped for arterial cannulation (median duration of 14 min [IQR 12–16 min]), the decrease in right ΔScO_2 was more pronounced than that of left ΔScO_2, reaching a median nadir of −4.1% at two min after clamping. Following the declamping of the IA, both left and right ΔScO_2 showed transient overshoot and returned to baseline levels. With starting SCP (median duration of 28 min [IQR 22–31 min]), the ΔScO_2 in both sides increased; in particular, the right ΔScO_2 was higher than the left ΔScO_2. After cessation of SCP and full CPB flow, the decrease in right ΔScO_2 was greater than that of the left ΔScO_2 (Table 2 and Fig. 1).

Eight patients consistently showed higher right ΔScO_2 than left ΔScO_2 throughout SCP (Fig. 2), indicating a discrepancy in $\Delta ScO_{2\ Rt\text{-}Lt}$. $\Delta ScO_{2\ Rt\text{-}Lt}$ during SCP was higher in patients with this discrepancy than in others (median 5.0% [IQR 2.8%–6.9 %] *vs*. −0.8% [−2.0%–0.5%]; $p < 0.001$).

Table 2: Changes in cerebral oxygen saturation (ΔScO_2) according to the surgical periods related to selective cerebral perfusion (SCP)

	Left ΔScO_2, %			Right ΔScO_2, %			$\Delta ScO_{2Rt\text{-}Lt}$, %		
	Total	Without discrepancy	With discrepancy	Total	Without discrepancy	With discrepancy	Total	Without discrepancy	With discrepancy
Clamping IA	−1.0 [−2.7; 0.0]‡	−1.0 [−2.1;– 0.0]	−1.5 [−5.0; 0.0]†	−1.4 [−5.4; 0.0]*‡	−1.0 [−2.4; 0.3]	−6.0 [−8.6; −3.0]†	−0.4 [−3.2; 0.8]‡	0.0 [−1.6– 1.2]	−3.2 [−5.4– (−1.6)]†
Declamping IA	−0.3 [−2.5; 1.1]	−0.4 [−2.1; 0.7]	0.3 [−3.7; 2.6]	−0.0 [−2.6; 2.0]	0.3 [−1.4; 1.8]	−2.9 [−5.8; 4.0]†	0.8 [−0.7; 2.0]	0.9 [0.0; 2.0]	−0.5 [−4.2; 2.5]†
SCP	0.6 [−2.0; 3.6]	0.0 [−2.4; 3.2]	1.7 [−1.3; 3.8]†	1.5 [−1.8; 5.0]*‡	−0.2 [−3.6; 1.7]	5.4 [3.5; 8.4]†	0.4 [−1.5; 2.8]‡	−0.8 [−2.0– 0.5]	5.0 [2.8– 6.9]†
After SCP	2.0 [−2.2; 5.6]	1.5 [−3.0; 4.8]	4.5 [−1.4; 7.0]†	0.0 [−3.6; 3.2]*	−1.2 [−4.1; 2.0]	4.7 [−1.8; 7.8]†	−1.7 [−3.5; 0.2]	−2.6 [−3.8; −0.1]	−0.4 [−1.8; 3.9]†

Note: * left *vs*. right; Wilcoxon signed rank test $p < 0.05$.
† with *vs*. without discrepancy; Wilcoxon signed rank test $p < 0.05$.
‡ clamping *vs*. declamping the innominate artery (IA) or SCP *vs*. After SCP; Wilcoxon signed rank test $p < 0.05$.

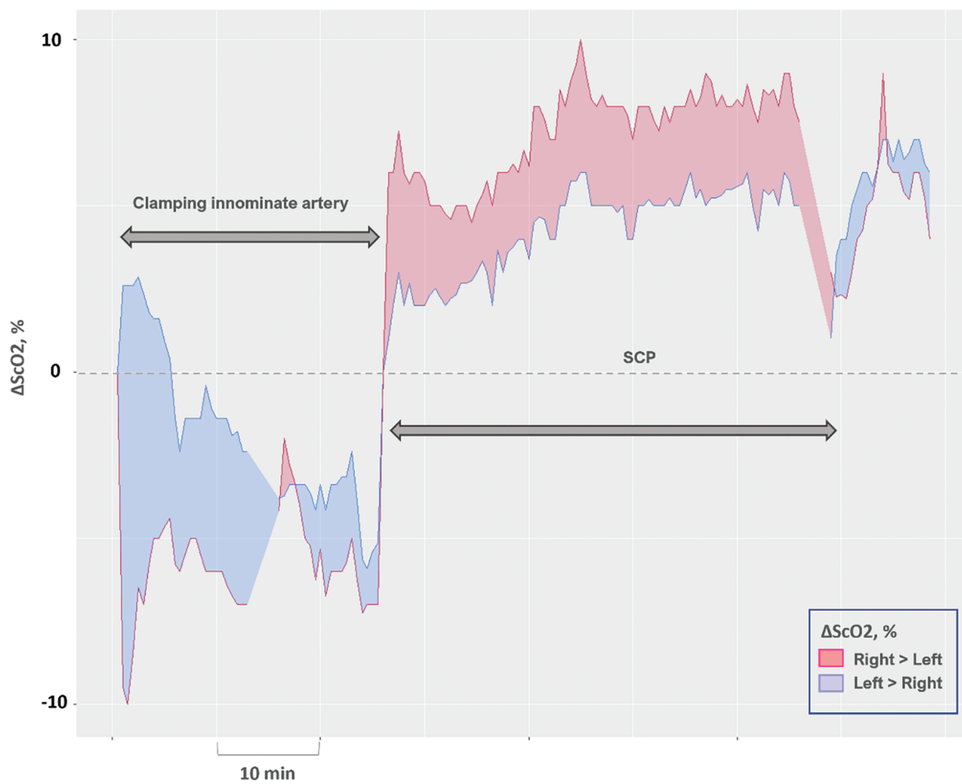

Figure 2: A representative plot tracking the changes in cerebral oxygen saturation in the left and right hemispheres, simultaneously recorded during surgical periods related to selective cerebral perfusion (SCP). This patient has a higher right ΔScO_2 than left ΔScO_2 throughout the SCP period

Patients with a difference in ΔScO_2 had significantly lower right ΔScO_2 during IA clamping than others (median −6.0% [IQR −8.6%–−3.0%] *vs*. −1.0% [−2.4%–0.3%]; $p < 0.001$). Moreover, patients with a difference in ΔScO_2 exhibited a significantly higher correlation coefficient of linear regression between right ΔScO_2 and ΔMAP compared to others (r = 0.735 *vs*. r = 0.510, Fisher's Z = 6.53; $p < 0.001$) (Fig. 3).

Figure 3: Correlations between changes in cerebral oxygen saturation (ΔScO_2) in the right hemisphere and changes in mean arterial pressure (ΔMAP). Patients with a difference in ΔScO_2 had a significantly higher correlation coefficient of linear regression than those without discrepancy

4 Discussion

This study demonstrates that ScO_2 fluctuated during the procedure based on SCP during aortic arch surgery in young infants. Moreover, changes in ScO_2 showed the difference between the left and right hemispheres depending on the cessation and resumption of unilateral cerebral perfusion by surgical techniques. 32% of infants exhibited consistently higher right ΔScO_2 than left ΔScO_2 throughout the SCP period. Interestingly, in these patients with discrepancies in ΔScO_2 during SCP, IA clamping for cannulation resulted in a greater decrease in right ScO_2 than in left ScO_2. We also observed that ΔScO_2 in the right hemispheres supplied by direct unilateral SCP, was dependent on the perfusion pressure, especially in patients with discrepancies in ΔScO_2.

The SCP is a mainstream procedure during aortic arch surgery in children to improve neurologic morbidity and mortality by ensuring continuous cerebral circulation [1,2,13]. A few studies investigating ScO_2 in neonates and young infants undergoing SCP reported that there is no significant difference between left and right ScO_2 during SCP, suggesting that SCP can provide efficient cerebral perfusion [9,14]. In this study, ScO_2 was also well maintained in both hemispheres throughout the surgery; however, the ScO_2 of each side significantly changed depending on the dynamics of the cerebral perfusion technique. During IA clamping for arterial cannulation, a sudden cessation of right cerebral blood flow resulted in decreased ScO_2 in the right brain. In contrast, unilateral selective perfusion via the right IA directly increases the right ScO_2. Even if sufficient cerebral circulation is achieved by unilateral SCP, we obviously observed that fluctuations in ScO_2 differed between the left and right brain.

An imbalance of cerebral circulation between the left and right hemispheres can lead to hyperemia in the perfused hemisphere and hypoperfusion in the contralateral side. In most studies investigating ScO_2 during the SCP, cerebral ScO_2 increases compared to the pre-SCP value [10,15]. Important factors affecting cerebral circulation are perfusion flow and pressure [16,17]. In this study, the degree of right ΔScO_2 was highly correlated with the unilateral perfusion pressure, especially in patients with a discrepancy of $\Delta ScO_{2\ Rt\text{-}Lt}$, which indicates the risk of hyperperfusion in the right side when unilateral perfusion is performed. However, how much flow and pressure are optimal for preventing both hypoperfusion and hyperperfusion in a hypothermic state in neonates remains unresolved. Currently, a flow of 20–150 ml/kg/min at a perfusion pressure of 20–60 mmHg is recommended for regional SCP, which has very wide ranges [1,5,9,10]. Therefore, to avoid significant differences between the hemispheres, unilateral perfusion pressure, and flow rate should be prudently adjusted based on monitoring of bilateral cerebral circulation.

The integrity of bilateral cerebral circulation during the SCP varies based on the completion of the circle of Willis. Unfortunately, the completion rate of the circle of Willis is reported to be 56.1% in the pediatric population, while the young infant population has the lowest completion rate of approximately 40% [4]. The present study showed that the right ScO_2 in 32% of patients increased more than the left ScO_2 throughout SCP. Regarding the immaturity of cerebral collaterals, this result suggests that SCP may not always ensure uniformity of circulation across both cerebral hemispheres in neonates and young infants. Notably, right ScO_2 was significantly decreased compared to left ScO_2 during IA clamping in patients with a discrepancy in $\Delta ScO_{2\ Rt\text{-}Lt}$, which was opposite to the change during SCP. We hypothesize that the incompleteness of the circle of Willis may have caused the unevenness of changes in the ScO_2 on both sides during 'left' unilateral perfusion apart from SCP. We infer that the decrease in right ScO_2 following IA clamping may precede the rise in right ScO_2 during SCP.

We also found that both ScO_2 instantaneously reduced with the transition from SCP to restoration of full CPB. Immediately after declamping the IA, both ScO_2 suddenly increased, in contrast to the change observed during SCP. In addition, the degree of the change in ScO_2 was greater in the right hemisphere than in the left. Considering that cerebral autoregulation is operational in term infants, a persistent increase in the MAP associated with SCP may induce a rise in cerebrovascular resistance as a protective mechanism against excessive cerebral blood flow [18]. It is believed that cerebral vasoconstriction by static autoregulation during SCP results in a temporal decrease in cerebral blood flow, represented by the change in ScO_2 [18]. The reverse could occur with a sudden overshoot of ScO_2 immediately after declamping the IA. However, cerebral autoregulation functions below capacity during CPB and hypothermia in infants [19,20]. Besides the immaturity of cerebrovascular collaterals, impaired autoregulation could contribute to hypoperfusion or hyperperfusion when the MAP varies according to the SCP procedure.

As a method of cerebral monitoring during SCP, ScO_2 estimates the cerebral blood flow based on the concept of balance between oxygen delivery and consumption in the brain [21]. Measurement of ScO_2 using NIRS is limited by being an indirect estimate of cerebral blood flow and cellular metabolism. However, NIRS provides continuous real-time trends in cerebral oxygen delivery given a constant oxygen consumption during hypothermic CPB [7]. The present study is valuable because ScO_2 was analyzed in each hemisphere using visualization with dynamic tracking of changes in ScO_2 from the baseline value, which was defined as the value of 1-min before IA clamping and SCP. We observed that the distribution of cerebral blood flow can be changed according to an abrupt increase in unilateral cerebral perfusion pressure and sudden interruptions in blood flow during the clamping IA. This highlights the importance of separately measuring left and right ScO_2 and the need for vigilant monitoring of changes in relation to surgical steps associated with SCP.

This study has some limitations. First, this study was a retrospective observational study with a small number of patients. Unfortunately, due to the limitations of a retrospective study in our research, a substantial number of cases (124) were excluded from data analysis due to incomplete data collection. Since our center employs SCP as the standard approach for aortic arch surgery in young infants, one of the exclusion criteria, circulatory arrest, was present in only one out of the 150 cases. Therefore, we believe that the 25 cases used for analysis in our study can be considered representative of routine surgical procedures. Second, we could not determine the association between the discrepancy in $\Delta ScO_{2\ Rt\text{-}Lt}$ and neurologic complications related to SCP. In addition, the completeness of the circle of Willis was not evaluated to determine its effect on changes in bilateral cerebral circulation. Third, as mentioned above, NIRS reflects, but cannot directly measure, cerebral blood flow and oxygen delivery. Key physiologic variables, including hematocrit, temperature, carbon dioxide tension, and pH also influence cerebral blood flow, however, their effects may not be significant during CPB [16,17]. Moreover, relative changes in ScO_2 from the baseline value were used for analysis rather than absolute values in an individual patient.

In conclusion, this study showed that SCP in young infants permits the maintenance of ScO_2 indicating adequate bilateral cerebral perfusion. However, differences in cerebral circulation between both hemispheres can be affected by SCP and are related to the technique used, especially in the immature brain with incomplete cerebral collaterals; this may depend on the perfusion pressure. Further studies to elucidate which individual characteristics affect the distribution of cerebral circulation during aortic arch surgery with SCP in young infants are required.

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Availability of Data and Materials: The datasets generated during and/or analyzed during the current study are available from the corresponding author on reasonable request.

Ethics Approval: All study protocols were approved and written informed consent was waived by the Asan Medical Center institutional review board (protocol number, 2022-0964). The study was performed in accordance with the ethical standards of the 1964 Declaration of Helsinki and its amendments.

Conflicts of Interest: The authors declare that they have no conflicts of interest to report regarding the present study.

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