

Correlation between Mean Arterial Pressure and Regional Cerebral Oxygen Saturation on Cardiopulmonary Bypass in Pediatric Cardiac Surgery

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Some pediatric cardiac patients might experience low regional cerebral oxygen saturation (rSO₂) during surgery. We investigated whether a pediatric patient's mean arterial pressure (MAP) can affect the rSO₂ value during cardiopulmonary bypass (CPB). We retrospectively analyzed the cases of the pediatric patients who underwent cardiac surgery at our hospital (Jan. -Dec. 2019; n=141). At each MAP stage, we constructed line charts through the mean of the rSO₂ values corresponding to each MAP and then calculated the correlation coefficients. We next divided the patients into age subgroups (neonates, infants, children) and into cyanotic congenital heart disease (CHD) and acyanotic CHD groups and analyzed these groups in the same way. The analyses of all 141 patients revealed that during CPB the rSO₂ value increased with an increase in MAP ($r=0.1626$). There was a correlation between rSO₂ and MAP in the children ($r=0.2720$) but not in the neonates ($r=0.06626$) or infants ($r=0.05260$). Cyanotic CHD or acyanotic CHD did not have a significant effect on the rSO₂/MAP correlation. Our analysis demonstrated different patterns of a correlation between MAP and rSO₂ in pediatric cardiac surgery patients, depending on age. MAP was positively correlated with rSO₂ typically in children but not in neonate or infant patients.

Key words: mean arterial pressure, cerebral oxygen saturation

The past few decades have provided tremendous progress in the diagnosis and management of congenital heart disease (CHD). Neonatal patients are a special group, and the regional cerebral oxygen saturation (rSO₂) levels in newborns are different from those in older patients [1]. Neonatal rSO₂ levels can indicate the cardiac output status or signal perfusion [2]. The clinical outcomes of children with cyanotic CHD have been shown to be worse than those of children with acyanotic CHD [3,4]. Although it is clear that compared to acyanotic CHD, cyanotic CHD is associated with lower SpO₂, there has been no compar-

ison of the rSO₂ values in pediatric patients with cyanotic CHD and acyanotic CHD during cardiopulmonary bypass (CPB) surgery, and we do not know whether the rSO₂ values and the correlation between mean arterial pressure (MAP) and rSO₂ are the same in these patients. Moreover, children of different ages with CHD were shown to have different levels of behavioral function after surgery [5]. Thus, the patient's age and the type of their heart disease are factors that affect the success rate of pediatric cardiac surgery. In addition, some pediatric cardiac patients might have a low rSO₂ level during the surgery that results in postoperative neurological complications [6].

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Near-infrared spectroscopy (NIRS) is a noninvasive method to continuously monitor rSO_2 at the bedside. It has been reported that the rSO_2 gradually decreases during surgery, indicating that the longer the surgical time is, the higher the risk of hypoxic brain injury is [7]. MAP has been shown to affect the fluctuation of rSO_2 during a surgery [8]. A combined monitoring of a patient's rSO_2 and MAP is one method for estimating cerebral autoregulation and the ability to maintain stable cerebral perfusion and oxygenation during fluctuations in MAP. However, the correlation between rSO_2 and MAP in infants with CHD has not been reported. We thus conducted the present study of pediatric cardiac surgery patients and analyzed the correlation between MAP and rSO_2 during the patients' CPB surgeries. We hypothesized that (i) changes in MAP may lead to changes in rSO_2 during CPB in pediatric cardiac surgery, and (ii) the age of the patient and the type of heart disease may affect the correlation between rSO_2 and MAP.

Patients and Methods

Study design. This study was a retrospective investigation conducted at Okayama University Hospital in Japan; the Institutional Review Board waived informed consent (2106-047). We analyzed the cases of the pediatric patients who underwent cardiac surgery with CPB during the period from January 2019 to December 2019 at our hospital. We selected the cases of the patients with continuous data for MAP and rSO_2 during their CPB surgery. Our patient inclusion criteria were age <18 years and surgery for congenital heart disease. We excluded patients with missing rSO_2 and/or MAP data.

Variables. The rSO_2 during the CPB of each patient was measured; the O3 regional oximetry device (Masimo Corp, Irvine, CA, USA) was used for rSO_2 measurements. Data for rSO_2 were obtained from the patients' electronic anesthesia records. We obtained the data for rSO_2 during the first 120 min of each CPB. A line chart with the time course was used to evaluate changes in rSO_2 during the first 120 min of the CPB. The records included rSO_2 values recorded every 1 min, and we obtained the data for the rSO_2 values recorded every 1 min from the start of the CPB to the end of the CPB. We also obtained the MAP data by the same method. The patients' MAP was usually measured with

the use of an invasive arterial cannula, and the data were stored in the electronic anesthesia records. Patients with incomplete monitoring of MAP and rSO_2 values were excluded from the analyses. Information on patient demographics including age, gender, body weight, type of disease, and type of surgery was obtained from the electronic medical records system.

CPB strategy. All patients included this study were received CPB during surgery. Our basic CPB strategy is as follows. First, aortic cannula is inserted into the ascending aorta. If the patients receive arch reconstruction which needs isolated cerebral perfusion, aortic cannula is inserted into the innominate artery using Gore-Tex artificial graft. Then venous cannula is inserted into superior vena cava. And then, start CPB and increase flow rate in stages. Total CPB flow is achieved after adding a venous cannula to the inferior vena cava. During CPB, arterial blood gas analysis is performed every 30 min and hematocrit is basically maintained at around 30%. Target body temperature during CPB is determined by each kind of surgery. Body temperature is gradually lowered after the start of CPB and maintained at the target temperature.

General intervention strategy for MAP and rSO_2 during CPB. The MAP control strategy at our hospital is as follows: for neonate patients, we control MAP at around 30-45 mmHg; for infant patients, we control MAP at ~35-50 mmHg, and for child patients, we control MAP at ~35-55 mmHg. The rSO_2 is maintained at >50% for all patients.

Outcomes. The study's primary outcome was the correlation between MAP and rSO_2 during CPB in pediatric patients. Secondary outcomes were whether the patient's age and the type of CHD affected the correlation between MAP and rSO_2 .

Subgroups according to age and type of CHD. To determine whether age is a factor that affects the correlation between rSO_2 and MAP, we divided the patients into three age groups: neonates <1 month old, infants aged 1 month to 1 year, and children >1 year old. We also divided the patients into a cyanotic CHD group and acyanotic CHD group.

MAP groups. To investigate the trends in MAP and rSO_2 , we put all MAP values of all patients together and divided them into six groups: <20 mmHg (MAP1), 20-30 mmHg (MAP2), 30-40 mmHg (MAP3), 40-50 mmHg (MAP4), 50-60 mmHg (MAP5) and >60 mmHg (MAP6). We investigated the changes in

rSO₂ in these different MAP groups.

Statistical analyses. The demographic and outcome data are presented as the mean ± standard deviation or the median and interquartile range (IQR). We obtained the line chart with the time course of MAP and rSO₂ values for the first 120 min of CPB with 95% confidence intervals (95% CIs). We also constructed line graphs of rSO₂ and MAP data using means with 95% CIs. The line chart was used to determine the correlation between MAP and rSO₂. We also conducted Pearson's correlation analysis of the MAP and rSO₂ values.

Results

Patients' demographic information. Among the 209 patients screened, we excluded 68 patients including 45 patients in whom rSO₂ or MAP was not monitored and 23 patients in whom rSO₂ or MAP was not fully monitored during CPB (Fig. 1). As shown in Table 1, the cases of 141 patients including 79 male patients (56.1%) and 62 female patients (43.9%) were enrolled. The patients' mean height was 81.59 ± 29.47 cm; their mean weight was 11.62 ± 10.11 kg, and the mean body mass index (BMI) was 14.63 ± 2.07. The patient series was comprised of 54.7% child patients, 36.1% infants, and 9.2% neonates. There were 83 cyanotic CHD patients (58.9%) and 58 acyanotic CHD patients (41.1%).

The mean duration of the surgeries was 215.28 ± 68.98 min; that of anesthesia was 310.09 ± 72.89 min, and that of the CPBs was 103.21 ± 50.85 min. The duration of stay in the intensive care unit (ICU) was 6 (3,9) days, and 72.3% of the patients received mechanical

ventilation in the ICU. The types of main congenital heart malformation in the 141 patients are shown in Table 2: 22.6% of the patients had a ventricular septal defect, 13.4% of the patients had tetralogy of Fallot, and 10.6% of the patients had an atrial septal defect.

Changes in MAP and rSO₂ during the first 120 min of CPB.

The patients' MAP first fluctuated greatly in the first 25 min and then gradually stabilized (Fig. 2A). We divided the patients into the three groups of neonates (<1 month of age), infants (1 month to 1 year of age) and children (>1 year of age) and analyzed the changes in MAP during the first 120 min of CPB in the different age groups. As shown in Fig. 2B, the MAP values in the neonate group fluctuated greatly, indicating that the surgery can cause dramatic changes in MAP

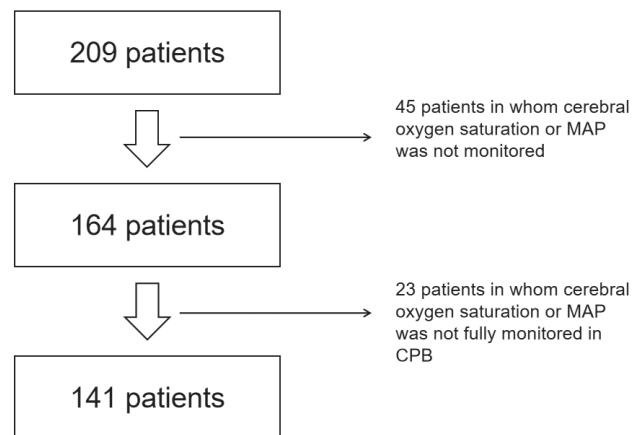


Fig. 1 Flow chart of the patients.

Table 1 Clinical characteristics of the patients

Characteristics	Patients (N = 141)
Gender	
Male. n (%)	79 (56.1%)
Female. n (%)	62 (43.9%)
Age	
Neonate patients. N (%), day	13 (9.2%) 12.15 ± 7.97
Infant patients. N (%), month	51 (36.1%) 5.03 ± 2.77
Child patients. N (%), year	77 (54.7%) 4.79 ± 3.74
Cyanotic CHD patients. N (%)	83 (58.9%)
Acyanotic CHD patients. N (%)	58 (41.1%)
Others	
Height. cm	81.59 ± 29.47
Weight. kg	11.62 ± 10.11
BMI	14.63 ± 2.07
Time of surgery. minutes	215.28 ± 68.98
Time of anesthesia. minutes	310.09 ± 72.89
Time of CPB. minutes	103.21 ± 50.85
ICU stay, days	6 (3,9)
Mechanical ventilation. N (%)	102 (72.3%)

Table 2 Types of the main congenital heart malformation in the 141 patients

Diagnosis	Patients (N = 141)
Ventricular septal defect	32 (22.6%)
Tetralogy of Fallot	19 (13.4%)
Atrial septal defect	15 (10.6%)
Hypoplastic left heart syndrome	9 (6.3%)
Complete atrioventricular septal defect	8 (5.6%)
Double outlet right ventricle	6 (4.2%)
Pulmonary atresia	5 (3.5%)
Others	47 (33.8%)

in a neonate patient. In the infant and child groups, the MAP changed greatly in the first 25 min and during the last 25 min and was relatively stable at other times (Fig. 2C).

The patients were also divided into acyanotic CHD and cyanotic CHD groups. The MAP in the cyanotic CHD group fluctuated greatly in the first 25 min and then gradually stabilized. In the acyanotic CHD group, the MAP changed markedly during the first 25 min and during the last 25 min. We also evaluated the changes

in rSO_2 during the first 120 min of CPB by obtaining the line chart with time course. As shown in Fig. 3A, the patients' rSO_2 values were highest at the beginning and then gradually decreased. After 25 min, the rSO_2 values stabilized. We then analyzed the changes in rSO_2 in during the first 120 min of CPB in the different age groups, and as shown in Fig. 3B, the rSO_2 values in the neonate group fluctuated greatly, suggesting that this surgery can cause dramatic changes in rSO_2 in neonates. In the infant and child groups, the rSO_2 was relatively

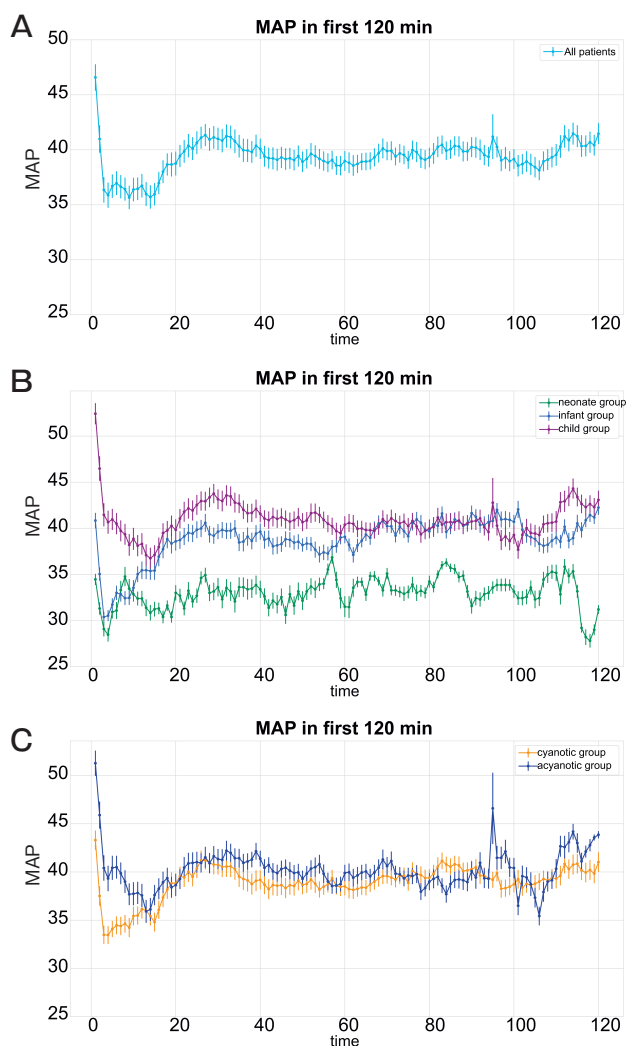


Fig. 2 Changes in the mean arterial pressure (MAP) during the pediatric patients' cardiopulmonary bypass (CPB) surgeries. **A**, All patients (n=141); **B**, The different age groups. *Green line*: Neonates (n=13). *Blue line*: Infants (n=51). *Purple line*: Children (n=77); **C**, The different types of surgery. *Orange line*: Cyanotic group (n=83). *Blue line*: Acyanotic group (n=58).

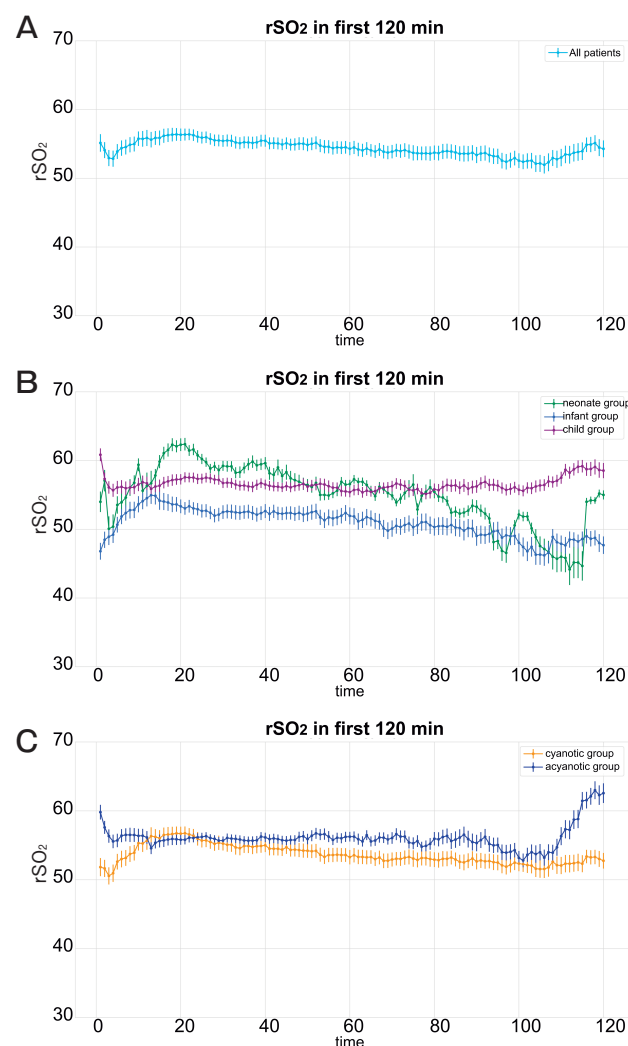


Fig. 3 Changes in the regional cerebral oxygen saturation (rSO_2) of the pediatric patients during their CPB surgeries. **A**, All patients (n=141); **B**, The different age groups. *Green line*: Neonates (n=13). *Blue line*: Infants (n=51). *Purple line*: Children (n=77); **C**, The different types of surgery. *Orange line*: Cyanotic group (n=83). *Blue line*: Acyanotic group (n=58).

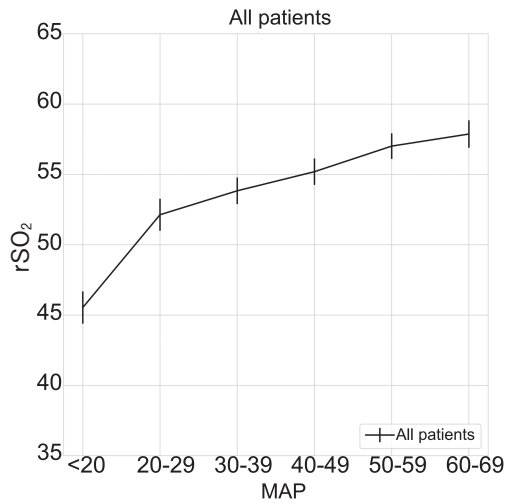


Fig. 4 The relationship between MAP and rSO₂ in all patients (n=141).

stable. The rSO₂ values in the cyanotic CHD and acyanotic CHD groups are depicted in Fig. 3C. The rSO₂ was relatively stable in the patients with cyanotic CHD but changed drastically during the last 25 min of surgery in the acyanotic CHD group.

Correlation between MAP and rSO₂ in all patients.

A line chart showing the correlation between MAP and rSO₂ is presented in Fig. 4. The rSO₂ value is the mean value of all of the patients for each MAP interval. As shown in Fig. 4, the value of rSO₂ increased with the increase in MAP ($r=0.1626$).

Effect of age on the correlation between MAP and rSO₂.

We obtained additional line charts to determine the effect of age on the correlation between MAP and rSO₂. As shown in Fig. 5A, B, the MAP in the neonate patients was almost <50 mmHg, and there was no correlation between MAP and rSO₂ in the neonates ($r=0.06626$) or infants ($r=0.05260$). As shown in

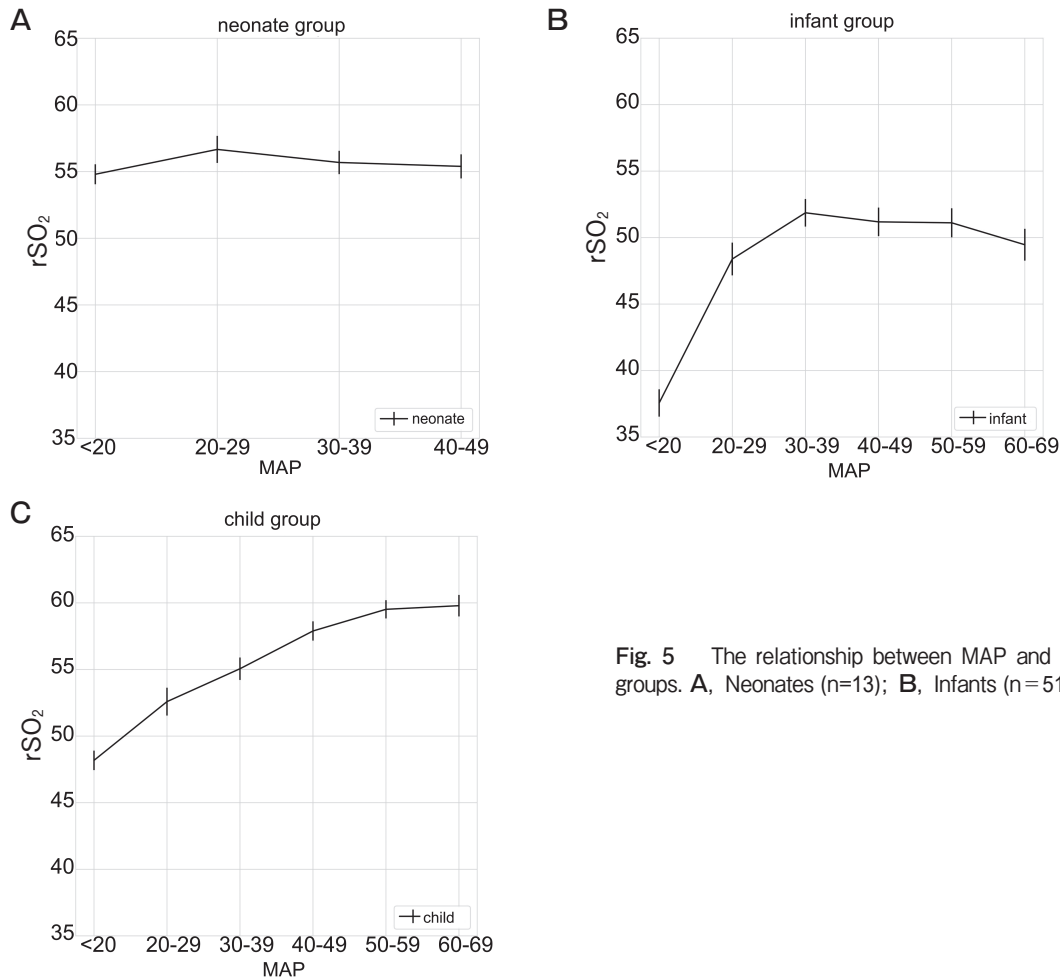


Fig. 5 The relationship between MAP and rSO₂ in the different age groups. A, Neonates (n=13); B, Infants (n=51); C, Children (n=77).

Fig. 5C, there was a positive correlation between MAP and rSO_2 only in the child patients ($r=0.2720$). The rSO_2 values in the infant group were smaller than the values in the neonate and child groups. Thus, to ensure a normal rSO_2 value in infant patients, the MAP should be maintained at >30 mmHg, and to ensure a normal rSO_2 value in neonatal and child patients the MAP should be maintained at >20 mmHg.

Effect of cyanotic CHD on the correlation between MAP and rSO_2 . To determine the effect of cyanotic CHD on the correlation between MAP and rSO_2 , we divided the patients into a cyanotic CHD group and an acyanotic CHD group. As shown in Fig. 6A, B, there

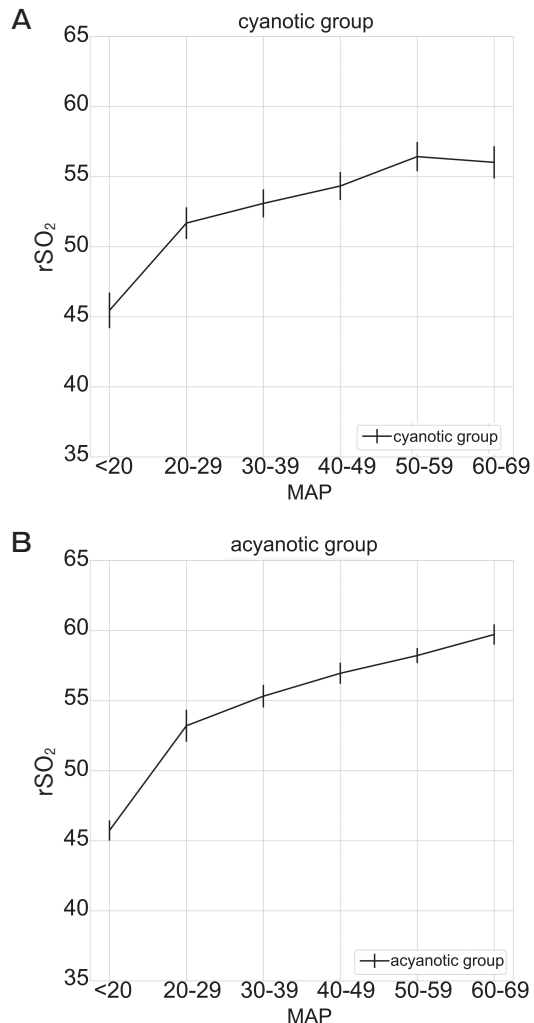


Fig. 6 The relationship between MAP and rSO_2 in different types of surgery. **A**, Cyanotic CHD patients ($n=83$); **B**, Acyanotic CHD patients ($n=58$).

were positive correlations between MAP and rSO_2 in both the cyanotic CHD and acyanotic CHD groups ($r=0.1378$ and $r=0.2149$, respectively). When the patients' MAP values were at the same level, the rSO_2 value in the cyanotic CHD group was higher than that in the acyanotic CHD group, especially when the MAP was >20 mmHg.

Discussion

We conducted a retrospective analysis to assess the relationship between MAP and rSO_2 values during CPB in pediatric cardiac surgery. The results confirmed that after an initial drop, the patients' MAP was almost stable around 40 mmHg but was lowest in neonates (around 30 mmHg). The patients' rSO_2 changed only in the range from 50% to 60% during the CPB, with the lowest values in infants. Our results also demonstrated that higher MAP was associated with higher rSO_2 , but the trends were different in the three age subgroups. There was almost no difference between the cyanotic CHD and acyanotic CHD groups.

An earlier study showed that the MAP values in pediatric patients undergoing a CPB were 30-45 mmHg in neonates, 45-50 mmHg in infants and >50 mmHg in children, indicating that different age groups have different ranges of MAP [9]. Our present findings are consistent with these results, and we believe that the MAP values in our patients of different ages are reasonable. For neonate patients, blood pressure itself poorly represents systemic blood flow, especially when the fetal channels are open and the developmentally regulated vital organ assignment may not have been completed [10]. Our observation of the lowest blood pressure in the neonate patients may thus be reasonable.

In our patient series, the rSO_2 did not change much during the CPBs (only in the range of 50-60%). Other studies indicated that an rSO_2 value $>50\%$ is normal [11] and that the rSO_2 in children should not be lower than 50% [12]. Although there were small differences among the age subgroups in our present investigation, the overall stability was between 50% and 60%. Our results suggest that the patient's age and the type of heart disease do not affect the rSO_2 . Moreover, abnormal changes in rSO_2 can affect neurological parameters such as neurodevelopment, communication and cognitive impairment, and IQ. Hoffman *et al.* reported that $rSO_2 <45\%$ as shown by NIRS in neonate patients was asso-

ciated with impairment of neurodevelopment, indicating that efforts should be made to avoid cerebral hypoxia in order to improve outcomes in this high-risk population [13]. Simons *et al.* reported that rSO₂ < 20% demonstrated by NIRS in infant patients with CHD was related to communication abnormality [14]. The study of neonates by Sood *et al.* indicated that the use of perioperative NIRS can affect cognitive, communication, and motor function [15]. Hasen *et al.* reported that preoperative NIRS showing rSO₂ < 40-45% in infant patients was correlated with IQ [16]. The rSO₂ value around 50-60% in our patients therefore seems to be a reasonable value during CPB in pediatric cardiac surgery.

Changes in MAP can result in a fluctuation of rSO₂ during surgery for CHD [17, 18]. However, it was also shown that MAP and rSO₂ were not correlated in neonatal and infant patients [19]. We also observed that higher MAP was associated with higher rSO₂, but the trends were different among the age subgroups. In the neonate group, rSO₂ values remained stable regardless of MAP. In the children, MAP and rSO₂ were positively correlated. A suggested reason for this difference is that neonates are more tolerant to lower blood pressure, which allows them to autoregulate cerebral blood flow and maintain NIRS even at a low blood pressure [19-21]. Our results indicate that attention should be paid to the patient's age for the management of blood pressure and cerebral blood flow during CPB, with consideration of the patient's physiologic development.

Cyanotic CHD or acyanotic CHD did not greatly affect the patients' MAP and rSO₂ in our series. Another investigation found no significant difference between the MAP values of cyanotic CHD and acyanotic CHD patients during pediatric surgery [19], and it was reported that patients with cyanotic CHD had lower preoperative SpO₂ compared to patients with acyanotic CHD [19, 22]. It is well known that the SpO₂ should be low in patients with cyanotic CHD, but that does not mean that the rSO₂ is also low during surgery. Our present findings indicate that values of rSO₂ in both cyanotic CHD and acyanotic CHD patients seem to be consistent at approx. 50-60% during a CPB in pediatric cardiac surgery.

Study limitations. Our study has several limitations. The retrospective nature of the study may include selection bias. We can discuss only the relationship between MAP and rSO₂ during CPB in pediatric cardiac

surgery. We were unable to accurately predict correlations prior to the study, and we were unable to obtain patient information factors that could potentially affect rSO₂. We therefore could not control for some additional factors affecting the results. Second, this was a physiologic study, not an outcome study. We focused on physiological outcomes rather than important clinical outcomes. The clinical importance of our study thus remains unclear. However, the management of MAP and rSO₂ is important during CPB, and an understanding of their relationship would be useful for their management. Third, our patients' rSO₂ values were determined by a combination of various variables including the depth of anesthesia, intraoperative ventilation, drug-induced systemic vasodilation, ejection fraction, blood, carbon dioxide concentration, and more. We did not rule out the influence of these factors on rSO₂. Differences between cyanotic CHD and acyanotic CHD patients might be affected by the hemoglobin concentration and collateral arteries. However, we did not include these factors in the present analysis, which may have had some influence on the results.

Lastly, the proportion of newborns in this study was small (9%), and since the physiological mechanisms and our CPB management in neonates are different from those in other patients, it is crucial to investigate the relationship between MAP and rSO₂ in different neonates' patients group. The results of this study would be more persuasive if the proportion of newborns had been higher.

In conclusion, the rSO₂ of pediatric cardiac surgery patients was positively correlated with their MAP values. However, the correlations differed among age subgroups and did not differ depending on cyanotic versus acyanotic CHD.

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