# **Cerebral Oxymeter Changes and Clinical Outcomes at Different Hypothermic Levels During Cardiopulmonary Bypass in Pediatric Patients**

#### Tanıl Özer, Hakan Ceyran

University of Health Sciences, Kartal Koşuyolu High Specialization Health Application and Research Center, Clinic of Cardiovascular Surgery, İstanbul, Turkey

## ABSTRACT

**Introduction:** Cardiopulmonary bypass (CPB) may not provide sufficient tissue perfusion. Hypothermia is used to protect the organs, especially the brain and heart, from this perfusion insufficiency. We investigated the effect of different hypothermic levels on cerebral oxygenation during CPB by using a cerebral oxymeter.

**Patients and Methods:** The study included 30 consecutive pediatric patients with congenital heart disease who were planned to be operated on in the year 2012. The mean age was  $41.83 \pm 39.96$  months (2-156 months), with 19 males. Children were divided into three groups by different hypothermic levels at CPB (32°C, 30°C, and 28°C). The measurements were made five times: before anesthesia induction (baseline values), during cooling (34°C), at the coldest value (first group 32°C, second group 30°C, third group 28°C), during rewarming (34°C), and at the end of rewarming (37°C-38°C). Cerebral-oxygen saturation, arterial oxygen saturation, arterial carbon dioxide pressure, mean arterial pressure, pH, lactate, base excess, and hematocrit measurements were made for all patients, and mean values were calculated for each group.

**Results:** There were no significant differences between the 32°C, 30°C, and 28°C groups (p> 0.05). When comparing change in cerebral-oxygen saturation values with the other parameters' changes between the periods, mean arterial pressure, and hematocrit changes showed noteworthy similarities. However, no relationship had been found between the other parameters and cerebral-oxygen saturation.

**Conclusion:** In our study, it was observed that cerebral oxygenation had not changed significantly at different hypothermic degrees of moderate levels during CPB. The highest temperature level of moderate hypothermic degrees (32°C instead of 28°C) was secure enough. This might be more advantageous to avoid the possible negative effects of hypothermia. Close monitoring of the cerebral oxygenation with cerebral oximetry may play an important role in ensuring patients' safety.

Key Words: Cardiopulmonary bypass; cerebral oxymeter; near-infrared spectroscopy; hypothermia; cerebral perfusion

# Pediatrik Hastalarda Kardiyopulmoner Baypas Sırasında Farklı Hipotermik Seviyelerinde Serebral Oksimetri Değişimi ve Klinik Sonuçları

## ÖZET

**Giriş:** Kardiyopulmoner baypas (KPB) yeterli doku perfüzyonu sağlayamayabilir. Organları bu perfüzyon yetersizliğinden korumak için hipotermi kullanılır. Biz çalışmamızda farklı hipotermik seviyelerin serebral oksijenasyona etkisini serebral oksimetre kullanarak araştırmayı amaçladık.

Hastalar ve Yöntem: Çalışmaya konjenital kalp cerrahisi uygulanan 30 pediatrik hasta dahil edildi. Ortalama yaş 41.83  $\pm$  39.96 ay (2-156 ay), 19 erkek. Hastalar KPB'deki farklı hipotermik seviyelere göre üç gruba ayrıldı. Ölçümler beş farklı aşamada yapıldı: anestezi indüksiyonu öncesi, soğuma aşamasında (34°C), en son soğuma değerinde (1. Grup 32°C, 2. Grup 30°C, 3. Grup 28°C), ısınma aşamasında (34°C), ısınmanın sonunda (37-38°C). Her hasta için serebral oksijen satürasyonu, arteriyel oksijen satürasyonu, arteriyel karbondioksit basıncı, ortalama arter basıncı, pH, laktat, baz fazlası, hematokrit ölçümleri yapıldı ve ortalama değerler her grup için hesaplandı.

**Bulgular:** Kaydedilen değerlerin karşılaştırıldığında 32°C, 30°C ve 28°C gruplarında anlamlı fark yoktu (p> 0.05). Serebral oksijen satürasyonundaki değişim ile diğer parametrelerdeki değişimler ile ortalama arter basıncı ve hematokrit değerlerindeki değişimler kayda değer benzerlik göstermekteydi. Bununla beraber, serebral oksijen satürasyonu ile diğer parametreler arasında ilişki bulunamadı.

**Sonuç:** Serebral oksijenasyonun farklı hipotermik seviyelerde değişmediği göz önüne alındığında, sıcaklık seviyesini mümkün olduğunca korumanın hipoterminin olası negatif etkilerinden korumada önemli olduğunu düşünmekteyiz. Ayrıca serebral oksijenasyonun serebral oksimetre ile yakın monitörizasyonu hastanın güvenliğini sağlamada önemli rol oynayabilir.

Anahtar Kelimeler: Kardiyopulmoner baypas; serebral oksimetri; kızıl ötesi spektroskopi; hipotermi; serebral perfüzyon



#### Correspondence

# Tanıl Özer

E-mail: drtanilozer@gmail.com Submitted: 20.06.2018 Accepted: 08.09.2018

© Copyright 2018 by Koşuyolu Heart Journal. Available on-line at www.kosuyoluheartjournal.com

#### INTRODUCTION

Increasing the flow speed to provide perfusion to the tissues not only increases the physical side effects but also fills the operating area with blood, making the surgeon's task much more difficult. Reducing the perfusion also makes it harder for the tissues to supply oxygen. Therefore, full-body hypothermia is used to reduce the need for oxygen by the tissues and at the same time to curb the inflammatory effects of cardiopulmonary bypass (CPB).

Reducing the body temperature in line with the planned procedure is a frequently used method in cardiac surgery. In this way, the safe intervals of perfusion pressure can be expanded, and the pump flow can also be reduced at that same interval and even be stopped for a period. Especially for pediatric patients, an average hypothermia level (32°C-28°C) is preferred. Deep hypothermia is used more in cases when there is a need for circulatory arrest<sup>(1,2)</sup>.

During CPB, using measures that provide information regarding full-body perfusion, such as monitoring blood pressure, examining arterial blood gas, and measuring oxygen saturation, are routinely used. However, in centers that specialize in congenital heart surgery, additional methods are used to monitor specific tissue perfusion<sup>(3-7)</sup>.

As use during cardiac surgery, the wealth of information provided by the cerebral oxymeter (near-infrared spectroscopy, or NIRS) allows physicians to have instant information regarding cerebral perfusion. As a result, it allows for the surgical team to intervene before it is too late in cases of hypoperfusion<sup>(5,6)</sup>.

In this study, we attempted to gauge the probable relationship between cerebral oxygenation and body temperature at different temperatures in medium-degree hypothermia, which is frequently used in congenital cardiac surgery. In this study, we employed the cerebral oxymeter method routinely used in our congenital cardiac-surgery clinic.

#### **PATIENTS and METHODS**

With the approval of our hospital ethics committee and patients' parents, we compiled the data from our patients in our routine surgical program. During the surgical planning and application phase, no special medications were used, and no changes were made at our routine practice.

We included 30 pediatric patients from our hospital. These patients were diagnosed with congenital cardiac anomalies and were operated on via open-heart surgery using a cardiopulmonary bypass procedure. These patients' status was stable, and they did not exhibit any growth or developmental retardation. The average age was  $41.83 \pm 39.96$  months [(2-156 months), 19 boys (63.3%), 11 girls (36.7%)] (Table 1).

The patients were divided into three groups according to the level of hypothermia they were subjected to (32°C, 30°C, and 28°C). The groups were randomly chosen and included ten patients.

Five measurement were taken for each child at different intervals; 1- prior to the induction of anesthesia (basal value), 2- during cooling under CPB ( $34^{\circ}$ C), 3- the lowest cooling level ( $32^{\circ}$ C for the first group,  $30^{\circ}$ C for the second group, and  $28^{\circ}$ C for the third group), 4- during rewarming ( $34^{\circ}$ C) and postwarming ( $37^{\circ}$ C- $38^{\circ}$ C), 5- before CPB was completed. The parameters for the measurements included: cerebral-oxygen saturation (rSO<sub>2</sub>), arterial-oxygen saturation (SaO<sub>2</sub>), arterial carbon dioxide pressure (PaCO<sub>2</sub>), mean arterial pressure (MAP), pH, lactate, base excess, and hematocrit (Hct).

The nasopharyngeal temperature of the patients in the first group was cooled to 32°C, 30°C for the second group, and 28°C for the third group. After the desired cooling was achieved, the cooling was stopped and the body temperatures were kept constant. After the surgical intervention, the bodies were rewarmed to 37°C-38°C.

The pump flow was set to the hypothermic level and body surface area (BSA) as a systemic arterial pressure control, as per Table 2. For the acid-base balance control, the  $\alpha$ -stat method was used during all the phases of cardiopulmonary bypass (CPB).

#### **Statistical Analysis**

In analyzing the findings of the study, the SPSS (Statistical Package for Social Sciences) for Windows 15.0 program was used. In analyzing the data, we used the statistical methods (mean, standard deviation, frequency) and the one-way Anova test to measure the quantitative data comparisons among the different groups, which show the normal distribution parameters. We used the Tukey HDS test for the group that showed a difference. To conduct a data comparison among the different groups for the parameters that do not show a normal curve, we used the Kruskal-Wallis test and the Mann-Whitney U test for the group that showed a difference. For a comparison of the data within a group that does not show a normal distribution we used the paired sample t test. To compare the qualitative data, we used the Ki-Square test. To measure the relationship between the parameters, we used the Spearman's rho correlation analysis. The statistical significance was at the p < 0.05 level.

#### RESULTS

Of the 30 pediatric patients having undergone open-heart surgery, 6 (20%) were cyanotic and 24 (80%) were acyanotic. The distribution of cyanotic and acyanotic patients among the groups was homogenous. All the patients who did not show any signs of growth or developmental retardation were hemodynamically stable. The demographic characteristics and distribution according to groups is provided in Table 1. We could find no significant statistical difference between the children's average ages, weights, and genders among the different groups (p> 0.05). The distribution of the diagnoses for the different

		32°C (n= 10)	<b>30°</b> C ( <b>n= 10</b> )	28°C (n= 10)	
		Mean ± SD (Median)	Mean ± SD (Median)	Mean ± SD (Median)	*р
Age (month)		41.40 ± 38.83 (27)	40.60 ± 44.75 (33)	43.50 ± 40.35 (23.5)	0.954
Weight		12.29 ± 6.70 (10.3)	16.20 ± 15.73 (12.5)	14.30 ± 8.62 (11.0)	0.890
		n (%)	n (%)	n (%)	**p
Gender	Male	6 (60.0%)	7 (70.0%)	6 (60.0%)	0.866
	Female	4 (40.0%)	3 (30.0%)	4 (40.0%)	

\* Tukey HDS. \*\* Kruskal-Wallis test.

Table 2. Flow management due to bod	ly temperature
37°C-34°C	(BSA x 2400) mL/m <sup>2</sup> .min
34°C-32°C	(BSA x 2200) mL/m <sup>2</sup> .min
32°C-30°C	(BSA x 2000) mL/m <sup>2</sup> .min
30°C-26°C	(BSA x 1800) mL/m <sup>2</sup> .min

Table 3. Distribution	Table 3. Distribution of the diagnoses			
	32°C	30°C	28°C	Total
Diagnose	n (%)	n (%)	n (%)	n (%)
ALCAPA syndrome	0 (0.0%)	0 (0.0%)	1 (10.0%)	1 (3.3%)
ASD	2 (20.0%)	3 (30.0%)	3 (30.0%)	8 (26.7%)
AVCD	0 (0.0%)	1 (10.0%)	1 (10.0%)	2 (6.7%)
Hemitruncus arteriosus	1 (10.0%)	0 (0.0%)	0 (0.0%)	1 (3.3%)
Mitral insufficiency/ stenosis	1 (10.0%)	0 (0.0%)	0 (0.0%)	1 (3.3%)
TOF	1 (10.0%)	2 (20.0%)	2 (20.0%)	5 (16.7%)
Tricuspid hypoplasia	1 (10.0%)	0 (0.0%)	0 (0.0%)	1 (3.3%)
VSD	5 (50.0%)	6 (60.0%)	5 (50.0%)	16 (53.3%)
ASD: Atrial septal defect fallot, VSD: Ventricular		oventricular ca	nal defect, TO	F: Tetralogy of

groups can be found in Table 3. The study included a maximum of 16 (53.3%) of patients diagnosed with ventricular septal defect (VSD), 8 (26.7%) of atrial septal defect (ASD), and 5 (16.7%) with tetralogy of fallout. The diagnoses were either isolated or mixed type.

# **Cerebral and Peripheral Arterial-Oxygen Saturation**

Figures 1 and 2 show the mean cerebral and peripheral oxygen-saturation levels of the groups before the induction of anesthesia, during cooling, at the lowest cooling level, during warming, and after the warming phase. There were no significant statistical differences found (p > 0.05).

The cerebral oxygen saturation of the groups taken during the different phases of the monitoring showed no significant statistical difference between the groups (p>0.05).

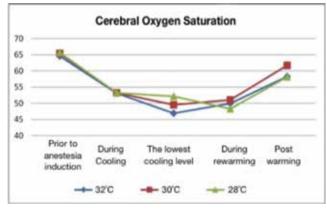


Figure 1. Mean cerebral-oxygen saturation.

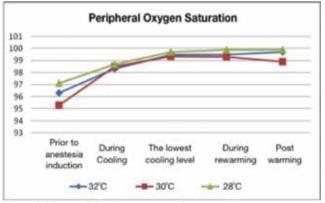


Figure 2. Mean peripheral oxygen saturation.

The peripheral oxygen saturation of the groups taken during the different phases of the monitoring showed no significant statistical difference between the groups (p> 0.05).

## Peripheral Arterial Carbondioxic Pressure

There was a significant statistical difference in the PaCO<sub>2</sub> levels before the induction of anesthesia between the groups (p< 0.05) (Table 4). Before induction of anesthesia, the 32°C group's PaCO<sub>2</sub> levels were significantly higher than the 28°C group's (p< 0.05). The other groups showed no significant differences in PaCO<sub>2</sub> levels before the induction of anesthesia (p> 0.05).

There was a significant statistical difference in the  $PaCO_2$  levels during the cooling phase (34°C) for the groups (p< 0.05).

Table 4. Post hoc test results		
PaCO <sub>2</sub>	During Cooling-The Lowest Cooling Level	
32°C/30°C	0.013*	
32°C/28°C	0.016*	
30°C/28°C	0.226	
Mann-Whitney U t	est, * p< 0.05.	

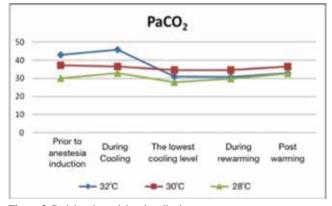


Figure 3. Peripheral arterial carbondioxic pressure.

The 32°C group's  $PaCO_2$  levels during the cooling phase were significantly higher than the 28°C group's (p< 0.05). The other groups showed no significant differences in  $PaCO_2$  levels during the cooling phase (p> 0.05).

There was a significant statistical difference in the PaCO<sub>2</sub> levels during the warming phase (34°C) for the groups (p<0.05). The 30°C group's PaCO<sub>2</sub> levels during the warming phase were significantly higher than the 28°C group's (p<0.05). The other groups showed no significant differences in PaCO<sub>2</sub> levels during the warming phase (p>0.05).

There was a significant statistical difference in the average  $PaCO_2$  levels during the coolest phase for the groups (32°C for the first group, 30°C for the second group, and 28°C for the third group) and after warming (37°C-38°C) (p> 0.05).

There was a significant statistical difference in the PaCO<sub>2</sub> levels between the groups during the cooling phase. The PaCO<sub>2</sub> levels that dropped the most were (first group 32°C, second group 30°C, and third group 28°C). The reduction in the PaCO<sub>2</sub> levels was highest in the 32°C group and was also significantly higher than the 30°C and 28°C groups (p>0.05) (Figure 3).

### Mean Arterial Pressure

There was no significant statistical difference in the average arterial pressure between the groups before the induction of anesthesia, during cooling, at the coolest phase, during warmup, and postwarmup (p > 0.05).

There was a significant statistical difference in the average arterial pressure between the groups during the coolest phase and during warmup (p < 0.05). While there was an increase in

the average arterial pressure for the 32°C group during warmup when compared to the coolest phase, there was a decrease in the arterial pressure for the 28°C group, and this difference was found to be significant (Table 5). There was no significant statistical difference in the average arterial pressure between the other groups from the coolest phase to the warmup phase (Figure 4).

# PH Level

There was no significant statistical difference in the average pH levels between the groups before the induction of anesthesia, during cooling, at the coolest phase, during warmup, and after warmup (p > 0.05).

There was no significant statistical difference in the changes in the pH levels during monitoring of the three groups (p> 0.05) (Figure 5).

	The coolest phase-	
MAP	During warming	
32°C/30°C	0.095	
32°C/28°C	0.012*	
30°C/28°C	0.183	

Mann-Whitney U test, \* p< 0.05.

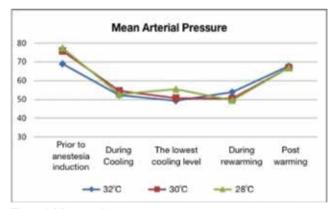


Figure 4. Mean arterial pressure.

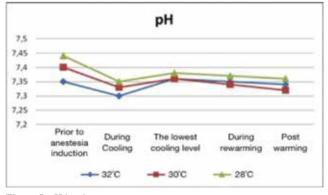


Figure 5. pH level.

# Lactate Level

There was no significant statistical difference in the average lactate levels between the groups before the induction of anesthesia, during cooling, at the coolest phase, during warmup, and after warmup (p > 0.05).

There was no significant statistical difference in the changes in the lactate levels during the monitoring of the three groups (p > 0.05) (Figure 6).

#### **Base-Deficit Level**

There was a significant statistical difference in the basedeficit levels between the groups before the induction of anesthesia (p> 0.05). The base-deficit levels of the 28°C group before the induction of anesthesia were significantly higher than the 30°C group (p: 0.016; p< 0.05).

There was no significant statistical difference in the basedeficit levels between the other groups before the induction of anesthesia (p > 0.05).

There was no significant statistical difference in the average base-deficit levels between the groups during the cooling phase (34°C), during the coolest phase (32°C for the first group, 30°C for the second group, and 28°C for the third group), during the warming phase (34°C), and postwarmup (37°C-8°C) (p> 0.05) (Figure 7).

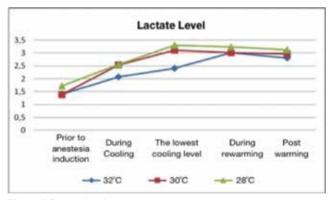


Figure 6. Lactate level.

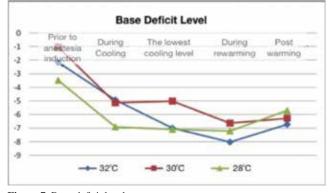


Figure 7. Base-deficit level.

### Hematocrit Level

There was no significant statistical difference in the average hematocrit levels between the groups before the induction of anesthesia, during cooling, at the coolest phase, during warmup, and after warmup (p > 0.05).

There was no significant statistical difference in the drop of average hematocrit levels between the groups before the induction of anesthesia compared to the cooling phase (p>0.05).

There was no significant statistical difference in the drop of hematocrit levels between the groups from before the induction of the anesthesia phase to the coolest phase ( $32^{\circ}$ C for the first group,  $30^{\circ}$ C for the second group, and  $28^{\circ}$ C for the third group) (p> 0.05).

There was no significant statistical difference in the increase of hematocrit levels between the groups before the induction of the anesthesia phase and postwarmup phase (p > 0.05).

There was no significant statistical difference in the drop of hematocrit levels between the group's cooling phase and coolest phase (p > 0.05).

There was a significant statistical difference in the increase of hematocrit levels between the group's coolest phase (32°C for the first group, 30°C for the second group, and 28°C for the third group) and the warmup phase (p< 0.05). The increase in hematocrit levels for the 28°C group from the coolest phase to the warmup phase was significantly less than those recorded for the 32°C and 30°C groups (p< 0.05). There was no significant statistical difference in the increase in hematocrit levels between the 32°C and 30°C groups from the coolest phase to the warmup phase (p> 0.05).

There was no significant statistical difference in the increase of hematocrit levels between the group's warmup phase and postwarmup phase (p>0.05) (Figure 8).

## Analysis of the Postoperative Results

There was no significant statistical difference in the patients' waking up from anesthesia, extubation time, or in the length of ICU and hospital stays between the groups (p>0.05) (Table 6).

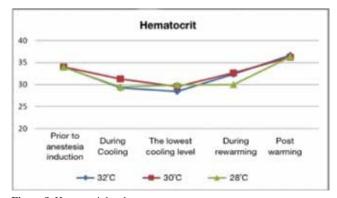


Figure 8. Hematocrit level.

	32°C (n= 10)	30°C (n= 10)	28°C (n=10)	
	Mean ± SD (Median)	Mean ± SD (Median)	Mean ± SD (Median)	*p
Waking up (minute)	90.00 ± 61.64 (60.0)	69.00 ± 40.12 (60.0)	$77.00 \pm 45.71$ (60.0)	0.786
Extubation (hour)	$17.55 \pm 13.24$ (18.5)	13.70 ± 7.68 (13.0)	23.40 ± 34.50 (13.0)	0.974
ICU (day)	$3.20 \pm 2.89$ (2.00)	$2.10 \pm 1.66$ (1.50)	$2.50 \pm 1.90$ (2.0)	0.407
Hospital (day)	$9.20 \pm 3.48$ (8.50)	$8.10 \pm 4.53$ (6.50)	$7.40 \pm 2.17$ (7.0)	0.516

\* Kruskal-Wallis test.

\*\* Ki-square test.

#### DISCUSSION

Open-heart surgery has shown significant progress since CPB was first implemented in the 1950s. CPB gave surgeons the opportunity to stop a constantly beating heart filled with blood, making the heart blood-free and thereby making it much easier to open the heart and operate. This procedure, while very significant for cardiac surgery, has been a popular topic to help shed light on the reason behind some of the negative effects of CPB in order to develop precautionary measures.

The unhindered blood flow, which reaches surfaces outside of the body, stimulates the cellular and humoral inflammation mechanisms, leading to unwanted coagulation or hemostasis defects, and causes cytological and chemical changes, which negatively affect organ and tissue function<sup>(8)</sup>. In addition, it adds to the physical traumas associated with CPB, like hemodilution, the vacuum and pumping ability, and the difference in the diameter and structure of the cannula<sup>(9,10)</sup>.

During open-heart surgery, to minimize the effects of CPB, it is not always the best approach to maintain the homeostasis of the tissues and organs close to the physiological borders. Rather, it is important to set the safety intervals and monitoring of the tissues and organs according to the momentary conditions. When compared to adult patients, this momentary monitoring is much more critical for patients in the pediatric group.

In order to counter the effects of CPB, it is important to reduce the perfusion to the lowest level possible. To increase the body's tolerance to hipoperfusion, an intervention must be made. Among such interventions, full-body hypothermia tops the list.

During a CPB procedure, the most affected organ is the brain. In the cases of low hypoxia tolerance and damage, there can be very dramatic clinical results. Therefore, methods to monitor the brain's perfusion and to protect the brain are gaining importance<sup>(11,12)</sup>.

Varying levels of hypothermia during open-heart surgery is a commonly used method. Systemic hypothermia is used to lower systemic and particularly cerebral oxygen consumption and to support myocardial hypothermia during the aortal clamp. Cerebral hypothermia reduces the negative effects of low perfusion pressure and hematocrit levels and extends the safety period for low-flow CPB and circulatory arrest.

Hypothermia also has the negative effect of hindering the central nervous system's protective function and impeding the coagulation system, causing wound infection and neurocognitive problems<sup>(13)</sup>.

During CPB, parameters like MAP, oxygen saturation  $(SaO_2)$ , partial alveolar carbon dioxide pressure  $(PaCO_2)$ , acidbase balance (pH), hematocrit (Hct), and body temperature have effects on cerebral perfusion<sup>(14-16)</sup>.

In the study of Ehrlich et. al. conducted on pigs, they found that at the 37°C baseline level, the speed of cerebral blood flow, and cerebral metabolism dropped during medium hypothermia (28°C) and deep hypothermia (18°C) but increased during very deep hypothermia (8°C)<sup>(17)</sup>.

In the same study, they found that at 18°C (the assumed level for cerebral metabolism to stop), the brain's basal metabolism continued, and although cerebral protection increased, it was not complete. For cerebral metabolism to stop completely, they recommended more cooling.

We noted in our study that normal body temperature (36°C-37°C), taken as first measurement value and cerebral oxygenation-saturation values during the stable hemodynamic phase (rSO<sub>2</sub>) (baseline) in the cooling phase (34°C), dropped in the coolest phase (first group 32°C, second group 30°C, and third group 28°C). We noted that aside from the third group (28°C group), during the warmup phase (34°C), the rSO<sub>2</sub> values started to increase again. Postwarmup, before the end of CPB, during the (37°C-38°C) phase, we noticed that the rSO<sub>2</sub> values for all three groups continued to rise. When we analyzed all the patients, the change between the first measurement and the other measurements was found to be statistically significant (p< 0.05; p< 0.01). When we compared the groups, however, the change between the groups was not found to be statistically significant (p> 0.05).

In their 2009 article, Murphy et al. discussed optimal perfusion during CPB<sup>(18)</sup>. These researchers examined various cases where certain parameters were effective in cerebral perfusion and oxygenation. According to these cases, there is no specific view on the MAP level during CPB, but for most clinics, it is at the 50- to 60-mm Hg level and in deep hypothermia, the lower limit could drop to as low as 20-30 mmHg. Furthermore, they mentioned that keeping the MAP low could have positive effects, like less blood-cell trauma and less collateral backflow for a heart in diastolic arrest.

Sungurtekin et al. argued that for safe cerebral perfusion during CPB, instead of pump-flow speed, MAP was effective, and that if pump flow was to be thought of as independent from MAP, then cerebral perfusion was not effective<sup>(19)</sup>. In our study, we did not see any significant differences between the groups in MAP levels during the rSO<sub>2</sub> measurement phases. Furthermore, when we looked at the changes in MAP levels within the groups, there was significant change between the first measurement and the second, third, and fourth measurements (a drop in the 32°C and 30°C groups and an increase in the 28°C group) (p<0.05; p<0.01), but there was no real change observed during the fifth measurement (p>0.05). The change graph, when examined together with the rSO<sub>2</sub> change graph, depicts that MAP and rSO<sub>2</sub> showed a similar change.

Alexander Gersten, in his study, listed cerebral-perfusion pressure, partial arterial-oxygen pressure  $(PaO_2)$ , cerebral metabolism, partial arterial carbon dioxide pressure  $(PaCO_2)$ , and cardiac output as the major factors in the control of cerebral blood flow<sup>(20)</sup>. He stated that  $PaCO_2$ , independent of the cerebral blood-flow autoregulation mechanism, increased cerebral blood flow by cerebral vascular dilation.

In our study, we also measured patients' arterial blood-gas levels when we were measuring cerebral oxygen saturation (rSO<sub>2</sub>). In the periods when we were measuring PaCO<sub>2</sub> values and the changes in these values, there was a change within the groups and between the groups, but no correlation between the changes in rSO<sub>2</sub> values. There was no significant statistical difference in the arterial oxygen-saturation values in the different measurement periods or between the groups (p> 0.05). At the same time, we could find no correlation between these changes and rSO<sub>2</sub>.

Moura Luz and colleagues, in their studies comparing acidbase balance during normothermy (37°C) and light/medium hypothermia (35°C-33°C), examined parameters like pH, arterial bicarbonate, and base deficit, and could not find a significant statistical change in those parameters<sup>(21)</sup>.

We also measured pH, lactate, and base-deficit values as indirect gauges of patients' full-body perfusion when looking at cerebral perfusion. To control the acid-base balance in our clinic, we use the  $\alpha$ -stat method, and during base deficit increases alongside acidosis, we use bicarbonate infusions. There was no significant change in patients' pH values from the first measurement and the other measurements, aside from a few measurements (p> 0.05). There was no significant change in the pH values between the groups and measurement periods (p> 0.05). However, there was a significant increase in the lactate levels between the first measurement and the other measurements (p< 0.05; p< 0.01). In addition, there was no statistical difference between the groups in the measurement levels and measurement periods between the groups (p> 0.05).

There was a significant increase in the base-deficit values of the patients from the first measurement and the other measurements (p< 0.05; p< 0.01). When these changes were compared between the groups, the largest increase was seen in the 28°C group, and this difference was statistically significant (p< 0.05). There was no difference between the other groups (p> 0.05). When these changes were examined in line with the changes in rSO<sub>2</sub>, there was no correlation between them.

One of the inevitable results of the CPB procedure, especially in pediatric patients, is hemodilution. Even though at first, it seemed positive that there is a lessening in the physical effects of the hypothermia-related increase in blood viscosity and blood trauma and an increase in microcirculation, in later studies it was shown that there were oxygenation defects in three organs. These later studies also showed that there was an increase in mortality/ morbidity and an increase in the length of hospitalization<sup>(22-24)</sup>.

Despite the fact that hemodilution increase the flow of cerebral blood, because of its reduction in oxygen, it does not provide any benefits for cerebral oxygenation, and there are studies that show it even hinders cerebral oxygenation<sup>(25,26)</sup>, In our study, hematocrit levels were recorded at the same measurement intervals. The hematocrit levels recorded during our study fell consecutively in line with the cooling but did not demonstrate a significant difference (p> 0.05) at the coolest levels except for the 28°C group. In the other groups, there was a significant drop compared to the first measurement (p< 0.05). In the warming phase, there was an increase once more in the hematocrit levels of all the patients. When examined graphically, there is a graphical similarity with the change recorded in the rSO<sub>2</sub> graph.

#### **Study Limitations**

This study has a number of limitations. First, this is a retrospective and nonrandomized study. Therefore, it is likely to have selection bias. However, the study attempted to select the patients consecutively. The second limitation is number of patients. Although the number of patients is small, this study may be a preliminary study for further studies. The third limitation is the operative-approach difference. The operations mentioned in this study were performed by different surgical teams. This situation is inevitable while choosing patients consecutively in a retrospective study.

# CONCLUSION

There may be some methodological differences between clinics while conducting a CPB procedure during open-heart surgery. However, mild and medium systemic hypothermia is more often preferred to achieve surgical comfort and ensure patients' safety.

If the general medical principle should be "Primum, non nocere" ("First do not harm"), any physical intervention should be well specified, and a decision should be made accordingly. We believe that if there are no real benefits for the patient, the patient's physical boundaries should not be altered.

When we analyzed the results of our study, we concluded that monitoring a patient's arterial and central venous pressure, blood gas, urine output, and selective organ perfusion will give us useful information about a patient's simultaneous condition during a CPB procedure. In particular, in order to monitor brain perfusion, the oxymeter method can help us intervene quickly if there are perfusion defects and also can prevent the practitioner from taking unnecessary approaches.

NIRS showed us that the MAP was the most important parameter that affects the cerebral perfusion, even though the hypothermic level had been chosen.

In order to achieve cerebral oxygenation, there is no difference between the hypothermic levels in medium-level hypothermia. Moreover, it is unnecessary to further lower body temperature (to 28°C from 32°C). Furthermore, we believe that using a method like NIRS in cerebral-perfusion monitoring could be beneficial in enhancing patient safety.

# **CONFLICT of INTEREST**

The authors reported no conflict of interest related to this article.

### AUTHORSHIP CONTRIBUTIONS

Concept/Design: TÖ Analysis/Interpretation: TÖ, HC Data Acquisition: TÖ Writting: TÖ Critical Revision: HC Final Approval: All of authors

## REFERENCES

- Mault JR, Ohtake S, Klingensmith ME, Heinle JS, Greeley WJ, Ungerleider RM. Cerebral metabolism and circulatory arrest: effects of duration and strategies for protection. Ann Thorac Surg 1993;55:57-63.
- McCullough JN, Zhang N, Reich DL, Juvonen TS, Klein JJ, Spielvogel D, et al. Cerebral metabolic suppression during hypothermic circulatory arrest in humans. Ann Thorac Surg 1999;67:1895-9.
- Edmonds H, Rodriguez R, Audenaert S, Austin EH, Pollock SB, Ganzel BL. The role of neuromonitoring in cardiovascular surgery. J Cardiothorac Vasc Anesth 1996;10:15-23.
- Tekin S, Soybir N, Arat S. Pediyatrik kardiyak anestezi. Kalp-damar cerrahisi. Kısım: Pediyatrik kalp cerrahisi. Paç M (ed). Ankara: MN Medikal ve Nobel Tıp Yayınları, 2012; 5:11-3.
- Clark JB, Barnes ML, Undar A, Myers JL. Multimodality neuromonitoring for pediatric cardiac surgery: our approach and a critical appraisal of the available evidence. World J Pediatr Congenit Heart Surg 2012;3:87-95.
- Hu Z, Xu L, Zhu Z, Seal R, McQuillan PM. Effects of hypothermic cardiopulmonary bypass on internal jugular bulb venous oxygen saturation, cerebral oxygen saturation, and bispectral index in pediatric patients undergoing cardiac surgery: a prospective study. Medicine (Baltimore) 2016;95:e2483.

- Austin EH, Edmonds HL, Auden SM, Seremet V, Niznik G, Sehic A, et al. Benefit of neurophysiologic monitoring for pediatric cardiac surgery. J Thorac Cardiovasc Surg 1997;114:707-15, 717.
- Çelebioğlu B, Özer E. Kardiyopulmoner by-pass ve sistemik inflamatuvar yanıt. Hacettepe Tıp Dergisi 2004;35:18-26.
- Yalçınbaş YK, Sarıoğlu T. Pediyatrik kardiyopulmoner bypass ve miyokard korunması. Paç M (ed). Kalp-damar cerrahisi kitabı. 2012.
- Edmunds LH, Hessel EA, Colman RW, Menasche P, Hammon JW. Extracorporeal circulation. In: Edmunds LH, Cohn LH (ed). Cardiac surgery in the adult. New York: McGraw-Hill Companies, 2003:315-87.
- Cook DJ. Neurologic effects. In: Gravlee GP, Davis RF, Kurusz M, Utley J (eds). Cardiopulmonary bypass principles and practice. 2<sup>nd</sup> ed. Lippincott Williams & Wilkins, 2000:403-31.
- Schell RM, Kern FH, Greeley WJ, Schulman SR, Frasco PE, Croughwell ND, et al. Cerebral blood flow and metabolism during cardiopulmonary bypass. Aneth Analg 1993;76:849.
- Chong SY, Chow MY, Kang DS, Sin YK, Sim EK, Ti LK. Deep hypothermic circulatory arrest in adults undergoing aortic surgery: local experience. Ann Acad Med Singapore 2004:33;289-93.
- Badner NH, Murkin JM, Lock P. Difference in pH management and pulsatil/nonpulsatil perfusion during cardiopulmonary bypass do not influence renal function. Anesth Analg 1992;75:696.
- 15. Mauroudis C. To pulse or not to pulse. Ann Thorac Surg 1978;25:259.
- Grossi EA, Connolly MW, Krieger KH. Quantification of pulsatil flow during cardiopulmonary bypass to permit direct comparison of the effectiveness of various types of pulsatil and nonpulsatil flow. Surgery 1985;98:547.
- Ehrlich MP, McCullough JN, Zhang N, Weisz DJ, Juvonen T, Bodian CA, et al. Effect of Hypothermia on cerebral blood flow and metabolism in the pig. Ann Thorac Surg 2002;73:191-7.
- Murphy GS, Hessel EA, Groom RC. Optimal perfusion during cardiopulmonary bypass: an evidence-based approach. Anesth Analg 2009;108:1394-417.
- Sungurtekin H, Boston US, Cook DJ. Bypass flow, mean arterial pressure, and cerebral perfusion during cardiopulmonary bypass in dogs. J Cardiothorac Vasc Anesth 2000;14:25-8.
- Gersten A. Peculiarities of brain's blood flow: role of carbon dioxide. arXiv preprint arXiv 2011;1103.5491.
- Luz HL, Auler Junior JO. Temperature and acid-base balance in coronary bypass grafting with cardiopulmonary bypass, under hypothermia and normothermia. Rev Bras Anestesiol 2002;52:2:197-208.
- Duebener LF, Sakamoto T, Hatsuoka S, Stamm C, Zurakowski D, Vollmar B, et al. Effects of hematocrit on cerebral microcirculation and tissue oxygenation during deep hypothermic bypass. Circulation 2001;104:1260-4.
- Jonas RA, Wypij D, Roth SJ, Bellinger DC, Visconti KJ, du Plessis AJ, et al. The influence of hemodilution on outcome after hypothermic cardiopulmonary bypass: results of a randomized trial in infants. J Thorac Cardiovasc Surg 2003;126:1765-74.
- Shin'oka T, Shum-Tim D, Jonas RA, Lidov HGW, Laussen PC, Miura T, et al. Higher hematocrit improves cerebral outcome after deep hypothermic circulatory arrest. J Thorac Cardiovasc Surg 1996;112:1610-20.
- Kusunoki M, Kimura K, Nakamura M, Isaka Y, Yoneda S, Abe H. Effects of hematocrit variations on cerebral blood flow and oxygen transport in ischemic cerebrovascular disease. J Cereb Blood Flow Metab 1981;1:413-7.
- Hino A, Ueda S, Mizukawa N, Imahori Y, Tenjin H. Effect of hemodilution on cerebral hemodynamics and oxygen metabolism. Stroke 1992;23:423-6.