



Systemic Inflammatory Response Syndrome in Pediatric Patients Undergoing Cardiac Surgery

 Feride Karacaer,  Ebru Biricik

Department of Anesthesiology and Reanimation, Çukurova University Faculty of Medicine, Adana, Türkiye

ABSTRACT

Objectives: Cardiac surgery with cardiopulmonary bypass is a primary activator of the systemic inflammatory response syndrome (SIRS). To assess the association of SIRS with intraoperative variables and early postoperative outcomes, we compared SIRS incidence after cardiac surgery between cyanotic and acyanotic children.

Methods: Using binary logistic regression models, we evaluated the incidence of SIRS between cyanotic and acyanotic children and the effect of intraoperative variables on SIRS occurrence and the effects of SIRS on postoperative complications.

Results: A total of 175 children (69 cyanotic, 106 acyanotic) were included. Based on Mantel–Haenszel–Cochran analysis, considering the Risk Adjusted Classification for Congenital Heart Surgery score, the SIRS rate was higher at operation end in cyanotic children ($p < 0.001$; 95% confidence interval: 1.94–10.61). An association was detected between SIRS incidence and consumption of red blood cells intraoperatively and fresh frozen plasma postoperatively. Lactate levels were higher in cyanotic than in acyanotic children at the end of the operation and at the postoperative 6th and 24th hours ($p = 0.008$, 0.007 , and 0.016 , respectively). Lactate levels were higher in cyanotic children diagnosed with SIRS than in acyanotic children without SIRS at the end of the operation and the 6th postoperative hour ($p = 0.024$ and 0.011 , respectively). Vasoactive inotropic scores were higher in children with SIRS in the 6th and 24th postoperative hours ($p = 0.018$ and 0.029 , respectively).

Conclusion: The incidence of SIRS is higher in children with complex cyanotic heart disease. Perioperative consumption of blood products increases SIRS occurrence.

Keywords: Cardiopulmonary bypass, congenital heart disease, cyanosis, systemic inflammatory response syndrome

Please cite this article as: "Karacaer F, Biricik E. Systemic Inflammatory Response Syndrome in Pediatric Patients Undergoing Cardiac Surgery. GKDA Derg 2023;29(2):95-101".

Introduction

Cardiac surgery with cardiopulmonary bypass (CPB) is a primary activator of the systemic inflammatory response syndrome (SIRS) due to blood coming into contact with the air and the bypass circuit, ischemia–reperfusion injury (IRI), and surgical trauma. SIRS is considered a major contributor to postoperative complications, morbidity, and mortality.^[1]

Pediatric patients have different cardiac anomalies and hemodynamics, small circulating plasma volume, and immature organs. Hypothermia and transfusion are also two nonspecific factors that induce inflammation.^[2] Therefore, children are more vulnerable to inflammation than adults are. Furthermore, children with cyanotic

congenital heart disease (CCHD) have been assumed to be more susceptible to oxidative damage due to hypoxemia, circulation disorders, and a deficiency in their defense mechanisms.^[3]

Laboratory biomarkers have been generally used in studies investigating SIRS in cyanotic and acyanotic children undergoing cardiac surgery with CPB,^[4,5] while there is a lack of adequate clinical studies comparing these two patient groups.

In this study, we aimed to compare the incidence of postoperative SIRS after cardiac surgery between cyanotic and acyanotic children and to assess the association of postoperative SIRS with intraoperative variables and early postoperative clinical outcomes.

Address for correspondence: Feride Karacaer, MD. Çukurova Üniversitesi Tıp Fakültesi, Anesteziyoloji ve Reanimasyon Anabilim Dalı, Adana, Türkiye

Phone: +90 322 338 60 60-3289 **E-mail:** feridekaracaer@gmail.com

Submitted: January 31, 2023 **Revised:** April 10, 2023 **Accepted:** April 12, 2023 **Available Online:** May 30, 2023

The Cardiovascular Thoracic Anaesthesia and Intensive Care - Available online at www.gkdaybd.org

OPEN ACCESS This is an open access article under the CC BY-NC license (<http://creativecommons.org/licenses/by-nc/4.0/>).



Methods

Study Design

This prospective observational cohort study was conducted at the Çukurova University Faculty of Medicine Hospital from February 2020 to February 2021. Ethical committee approval (approval No. 93/01.11.2019) was obtained, and the study was registered with the Clinical Research Information Service (NCT04254744). We included children aged 2 months to 10 years undergoing cardiac surgery with CPB for cyanotic or acyanotic congenital heart disease (CHD) in this study. Patients with preoperative active infection, the use of anti-inflammatory and/or antioxidant drugs, renal failure, or hepatic disease were excluded.

Clinical Data

We recorded demographic and clinical data, including age, gender, body weight, diagnosis of CHD, presence of cyanosis, intensive care unit (ICU) length of stay (LOS), hospital LOS, duration of mechanical ventilation, vasoactive inotropic score (VIS),^[6] and mortality. The Risk Adjusted Classification for Congenital Heart Surgery (RACHS) was used to categorize the cardiac surgical procedures.^[7] We defined cardiac disease with right-to-left shunt as cyanotic cardiac disease. Intraoperative data included surgery, duration of CPB and aortic cross-clamp, duration of circulatory arrest if used, lowest body temperature reached during CPB, and amount of cardioplegia. We recorded the amount of crystalloid fluid therapy and volume of blood products administered intraoperatively and for 48 hours postoperatively.

Anesthetic, Surgical, and Postoperative Management

All patients received standardized anesthetic management. The children were premedicated with midazolam (0.5 mg/kg orally; Doren ampul, Pharmavision) preoperatively. In the operating room, after standard monitorization, anesthesia was induced with midazolam (0.1–0.2 mg/kg), fentanyl (5 µg/kg; Fentaver ampul, Haver), and rocuronium (0.6 mg/kg; Muscobloc, Polifarma) and maintained by inhaled sevoflurane (1%–2%), and fentanyl (5–10 µg/kg/h). Sevoflurane was administered through the oxygenator during CPB. Children were ventilated to maintain arterial pCO₂ in the range from 35 to 45 mm Hg. Before aortic cannulation, heparin (3–5 mg/kg) was used to achieve an activated clotting time of greater than 480 seconds.

We performed a standardized CPB protocol for all children. The CPB prime volume (1,000–1,500 mL, calculated from patient weight) contained lactate Ringer's solution, hetastarch, heparin, and red blood cell concentrate. A nonpulsatile flow (2.4–3.0 L/min/m²) was used, and a hematocrit of 28% to 30% was maintained in all patients during CPB.

Myocardial protection was provided with antegrade blood cardioplegia (20 mL/kg with KCl 30 mEq/L).

After CPB was terminated, protamine (for neutralization of heparin activity) and blood products were administered according to institutional clinical practice. The amount of blood product transfusion in each patient was managed according to the clinical situation. Packed red blood cells (RBCs) were transfused in the operating room after separation from CPB to maintain a hemoglobin level of >8 g/dL in acyanotic children and >9–10 g/dL in cyanotic children or in cases of persistent lactic acidosis or low superior cava saturation (SvO₂<70%). Platelet concentrates, cryoprecipitate, and fresh frozen plasma (FFP) were transfused after CPB in the presence of abnormal clinical bleeding, based on platelet count and standard coagulation tests.

All patients were transferred to the cardiac ICU postoperatively and administered standardized therapeutic regimens of inotropic support, fluid and transfusion management, and ventilator support. Patients with adequate spontaneous breathing and minimal oxygen support were extubated. Inotropic support was administered until the clinical and biochemical findings of low cardiac output syndrome disappeared. Patients weaned from ventilators and with stable hemodynamics without inotropic support were transferred to the ward.

Systemic Inflammatory Response Syndrome

We evaluated the occurrence of SIRS for each patient based on the pediatric sepsis consensus criteria,^[8] in which at least two of the following clinical parameters of SIRS are observed, one of which must be abnormal temperature or white blood cell count: (1) core body temperature >38.5°C or <36°C, (2) tachycardia or bradycardia for children <1 year of age, (3) mean respiratory rate above normal for age or mechanical ventilation unrelated to neuromuscular disease or general anesthesia, and (4) white blood cell count elevated or depressed for age. We disregarded an increased heart rate above the cutoff value due to a cardiac pacemaker and an abnormal respiratory rate caused by mechanical ventilation. The occurrence of SIRS was evaluated at the end of the operation and at the 6th, 24th, and 48th postoperative hours.

Statistical Analysis

Categorical variables were expressed as numbers and percentages, whereas continuous variables were summarized as mean and standard deviation. We used the chi-square test to compare categorical variables between groups and the Shapiro–Wilk test to verify the normality of distribution for continuous variables. To compare continuous variables between the two groups, we used an unpaired Student's t-test. To compare more than two groups, we used one-way analysis

Table 1. Demographic data included in the study according to the presence or absence of cyanotic congenital heart disease

	All patients	CCHD	ACHD	p
Age (month)	32.81±29.34	30.6±29.5	34.7±29.2	0.356 ^a
Body weight (kg)	11.57±53.27	10.9±5.2	11.2±5.4	0.647 ^a
Gender, n				
Male	101	49	52	0.49 ^b
Female	74	32	42	
RACHS1, n (%)				
1	8	0	8 (100)	0.000^b
2	45	12 (25.5)	33 (74.5)	
3	120	55 (46.4)	65 (53.6)	
4	2	2 (100)	0	
Preoperative Hb (mg/dl)	12.9±3.1	14.4±3.0	11.5±2.6	0.000^a
Postoperative Hb (mg/dl)	11.2±1.4	11.7±1.6	10.9±1.2	0.000^a
Preoperative Htc (%)	39.8±8	44.0±8.9	36.1±4.9	0.000^a
Postoperative Htc (%)	34.4±4.8	35.8±5.6	33.2±3.5	0.000^a
Preoperative platelet (10 ³ /μL)	311.1±93.9	281.7±100.4	336.4±80.1	0.000^a
Postoperative platelet (10 ³ /μL)	150.8±67.8	129.7±65.2	169.0±65.0	0.000^a
Duration of surgery (min)	194.8±50.4	204.5±55.9	186.1±43.4	0.018^a
CPB time (min)	75.1±37.7	83.9±40.1	67.5±33.9	0.002^a
ACC time (min)	45.0±31.4	48.7±35.0	44.5±30.1	0.219 ^a
Lowest temperature during CPB (°C)	30.9±3.5	30.8±4.0	31.0±2.8	0.698 ^a

^a: The unpaired Student's t test; ^b: Chi-square test. CCHD: Cyanotic congenital heart disease; ACHD: Acyanotic congenital heart disease; RACHS: Risk Adjusted Classification for Congenital Heart Surgery; Hb: Hemoglobin; Htc: Hematocrit; CPB: Cardiopulmonary bypass; ACC: Aortic cross clamp.

of variance. With regard to the homogeneity of variances, we used Tukey or Games & Howell tests for multiple comparisons of groups. Logistic regression analysis was performed to determine significant predictors of SIRS. In the univariate analysis (chi-square test or Student's t-test), variables significant at the $p < 0.25$ level (according to Hosmer and Lemeshow) were entered in the logistic regression analysis. All analyses were performed using the IBM SPSS Statistics version 20.0 statistical software package (IBM Corp., Armonk, NY, released 2011). The statistical significance for all tests was set at 0.05.

Results

Participant Demographics

We included 175 patients in this study. Sixty-nine patients were cyanotic, and 106 were acyanotic. Table 1 presents the demographic data, and Table 2 shows the frequencies of cardiac anomalies. Cyanotic children had a higher RACHS1 score ($p = 0.000$), longer duration of CPB ($p = 0.002$), longer duration of surgery ($p = 0.018$), and higher mortality rate ($p = 0.009$) as compared with acyanotic children. SIRS occurred in 98 (56%) of 175 children within 48 hours at least once after cardiac surgery. Forty-one (23.4%) patients at the end of the operation, 54 (30.9%) patients at the 6th hour postoperatively, 67 (38.7%) patients at the 24th hour

postoperatively, and 24 (14%) patients at the 48th hour postoperatively were diagnosed with SIRS.

According to the Cochran–Mantel–Haenszel (CMH) analysis, cyanotic children had 4.54 times the odds of SIRS at the end of the operation as compared with acyanotic children ($p < 0.001$; 95% confidence interval [CI]: 1.94–10.61). This odds ratio was adjusted by the RACHS score. In this study, SIRS was more common in older children than in younger children ($p = 0.006$; OR: 1.21, 95% CI: 1.05–1.38).

Fluid Therapy, Transfusion, and SIRS

Preoperative hemoglobin and hematocrit levels were higher and platelet counts were lower in cyanotic children (Table 1). Table 3 shows the number of blood products transfused and crystalloid fluid administered intraoperatively and in the postoperative 48-hour period. The amount of RBCs given intraoperatively as well as the amount of FFP and cryoprecipitate in the 48-hour postoperative period was higher in cyanotic children (Table 3). We observed a relationship between the amount of FFP in the 48-hour postoperative period and the incidence of SIRS at the 48th hour postoperatively in cyanotic children ($p = 0.018$). Intraoperative RBC consumption in cyanotic children diagnosed with SIRS (8.7 ± 7.1 mL/kg) was two times higher than in acyanotic children without SIRS (4.5 ± 5.5 mL/kg, $p = 0.005$).

Table 2. Frequency of congenital cardiac anomalies

RACHS1 (Risk category)	Cardiac anomalies	N
1	Atrial septal defect	8
2	Ventricular septal defect	12
	Subaortic stenosis resection	7
	Pulmonary valvotomy or valvuloplasty	2
	Total repair of tetralogy of Fallot	13
	Repair of total anomalous pulmonary veins at age >30 d	11
3	Repair of transitional or complete AV canal	18
	Repair of coarctation and ventricular septal defect closure	4
	Repair of tetralogy of Fallot with pulmonary atresia	15
	Fontan procedure	10
	Aortic valve replacement	4
	Mitral valvotomy or valvuloplasty	10
	Mitral valve replacement	4
	Tricuspid valvotomy or valvuloplasty	15
	Tricuspid valve repositioning for Ebstein anomaly at age >30 d	2
	Tricuspid valve replacement	3
	Annuloplasty	6
	Repair of double-outlet right ventricle with or without repair of right ventricular obstruction	17
	Right ventricular to pulmonary artery conduit	8
	Left ventricular outflow tract patch	5
4	Repair of transposition, VSD, and subpulmonary stenosis	2

RACHS: Risk Adjusted Classification for Congenital Heart Surgery; AV: Atrioventricular; d: Day; VSD: Ventricular septal defect

Hypothermia and SIRS

The lowest body temperature reached during CPB was comparable in cyanotic and acyanotic children ($p=0.698$, Table 4). We did not find a relationship between body temperature and incidence of SIRS in this study ($p=0.61$, Table 4).

Glucose, Lactate, Cyanosis, and SIRS

Table 4 shows the lactate and glucose levels at the control times of the study. Lactate levels were higher in cyanotic children than in acyanotic children at the end of the operation and at the postoperative 6th and 24th hours ($p=0.008$, $p=0.007$, and $p=0.016$, respectively). In addition, lactate levels were higher in cyanotic children diagnosed with SIRS than in acyanotic children without SIRS at the end of the operation and at the 6th postoperative hour ($p=0.024$ and $p=0.011$, respectively). Glucose levels were higher in cyanotic children diagnosed with SIRS than in acyanotic children without SIRS at the 48th postoperative hour ($p=0.05$).

Postoperative Variables, Mortality, and SIRS

Table 4 presents the postoperative variables. VISs were higher in cyanotic children than acyanotics at the control times of the study (Table 4). VISs were higher in children with SIRS in the 6th and 24th postoperative hours

Table 3. Fluid therapy and transfusion intraoperatively and in the postoperative 48-hour period

	Cyanotic patients	Acyanotic patients	p
IO crystalloid (ml/kg)	22.7±14.8	19.9±9.5	0.135
IO RBC (ml/kg)	8.0±6.5	3.8±5.3	0.000
IO FFP (ml/kg)	5.6±5.9	6.2±6.8	0.58
IO criopresipitat (ml/kg)	0.3±1.7	0	0.08
PO crystalloid (ml/kg)	133.9±38.1	132.3±35.0	0.772
PO RBC (ml/kg)	12.6±21.7	9.7±10.2	0.283
PO FFP (ml/kg)	3.8±9.4	5.9±17.9	0.011
PO crioprecipitate (ml/kg)	1.0±2.7	0.07±0.7	0.006

IO: Intraoperative; RBC: Red blood cell; FFP: Fresh frozen plasma; PO: Postoperative.

($p=0.018$ and $p=0.029$, respectively). In addition, VIS values were higher in cyanotic children with SIRS than in acyanotic children without SIRS ($p=0.025$ at the end of the operation, $p<0.001$ at the 6th postoperative hour, $p<0.001$ at the 24th postoperative hour, and $p=0.002$ at the 48th postoperative hour). The duration of mechanical ventilation was longer in cyanotic children than in acyanotic children ($p=0.003$). We found no significant association between the duration of mechanical ventilation, ICU LOS, hospital LOS, or SIRS incidence.

Table 4. Intraoperative and postoperative variables

	SIRS group	No SIRS group	p	Cyanotic patients	Acyanotic patients	p
Minimum temperature during CPB	30.8±3.0	31.1±4.1	0.61 ^a	30.8±4.0	31.0±2.8	0.698 ^a
Cardioplegia (ml/kg)	22.5±14.2	22.9±19.1	0.89 ^a	21.0±16.5	24.1±16.4	0.215 ^a
ACC time (minute)	48.1±31.6	40.9±30.8	0.13 ^a	48.7±35.0	44.5±30.1	0.219 ^a
CPB time (minute)	74.9±34.5	75.2±41.2	0.96 ^a	83.9±40.1	67.5±33.9	0.002^a
Duration of surgery (minute)	193.8±48.1	196.1±53.4	0.76 ^a	204.5±55.9	186.1±43.4	0.018^a
Lactate (EOP)	2.4±1.4	2.3±1.3	0.79 ^a	2.7±1.6	2.11±0.9	0.008^a
Lactate (PO 6 th hour)	3.3±2.1	2.8±1.8	0.12 ^a	3.6±2.4	2.7±1.4	0.007^a
Lactate (PO 24 th hour)	1.7±2.2	1.9±1.1	0.55 ^a	2.2±2.5	1.8±0.5	0.016^a
Lactate (PO 48 th hour)	1.8±2.2	1.4±0.9	0.134 ^a	1.9±2.4	1.5±0.9	0.09 ^a
Glucose (EOP)	197.1±57.8	188.2±47.5	0.27 ^a	200.4±54.7	186.9±51.9	0.96 ^a
Glucose (PO 6 th hour)	213.4±71.6	207.9±72.9	0.62 ^a	219.1±83.8	203.9±59.7	0.18 ^a
Glucose (PO 24 th hour)	144.3±41.7	150.2±40.2	0.35 ^a	153.4±47.1	141.0±39.2	0.038^a
Glucose (PO 48 th hour)	134.6±42.2	129.2±27.6	0.31 ^a	142.2±46.8	123.8±20.7	0.001^a
VIS (EOP)	12.2±10.1	11.3±8.7	0.66 ^a	11.5±5.5	11.0±6.6	<0.001
VIS (PO 6 th hour)	12.9±13.1	7.9±6.3	0.018^a	13.2±10.2	10.9±8.3	<0.001^a
VIS (PO 24 th hour)	8.9±13.3	5.5±7.0	0.029^a	9.6±13.8	5.6±7.8	<0.001^a
VIS (PO 48 th hour)	6.6±12.6	2.5±3.9	0.061 ^a	6.5±12.3	3.3±7.2	0.002^a
Duration of MV (hours)	45.0±115.3	42.1±114.2	0.28 ^a	58.6±147.3	31.1±74.9	0.003^a
ICU LOS (days)	6.4±5.4	6.5±4.6	0.57 ^a	6.7±5.4	5.8±4.5	0.372 ^a
Hospital LOS (days)	11.8±7.2	10.4±5.5	0.37 ^a	6.7±5.4	6.2±4.7	0.153 ^a
Mortality	10	7	0.81 ^b	13	4	0.009^b

^a: The unpaired Student's t test; ^b: Chi-square test. SIRS: Systemic inflammatory response syndrome; CPB: Cardiopulmonary bypass; ACC: Aortic cross clamp; EOP: End of the operation; PO: Postoperative; VIS: Vasoactive inotrop score; MV: Mechanical ventilation; ICU: Intensive care unit; LOS: Length of stay.

We observed postoperative complications in 36 patients (Table 5), but there was no significant difference between cyanotic and acyanotic children (p>0.05). In addition, we found no association between postoperative complications and SIRS incidence. Renal failure requiring dialysis occurred in two cyanotic children and two acyanotic children. Seventeen children died postoperatively. According to the CMH analysis, the mortality rate was higher in cyanotic children than in acyanotic children (p=0.016, OR: 4.98, CI: 1.35–18.39; OR adjusted by RACHS score). Examination of the relationship between cyanosis, SIRS, and mortality demonstrated an association between cyanosis and mortality (p=0.009). However, the incidence of SIRS in cyanotic and acyanotic children did not increase the mortality rate (p=0.81).

Discussion

Although SIRS is defined by clinical parameters rather than laboratory findings, multiple pediatric studies of the inflammatory response to CPB have investigated the relationship between inflammatory biomarkers and clinical outcome in a small number of patients.^[4,5] In this prospective study, we investigated the incidence of SIRS, its relationship with perioperative variables, and clinical effects following cardiac surgery with CPB in cyanotic and acyanotic children. We

Table 5. Postoperative complications

	Cyanotic patients	Acyanotic patients	p
Dialysis	2	2	0.75
Complete AV block	8	3	0.06
Reoperation	4	0	0.03
Reintubation	4	2	0.24
Postoperative ECMO	8	3	0.06
All complications	26	10	<0.001

AV: Atrioventricular; ECMO: Extracorporeal membrane oxygenation.

found a higher incidence of SIRS in children with complex CCHD than in acyanotic children, and we also identified a relationship between the amount of blood products, postoperative lactate levels, and postoperative VIS values and SIRS. Previous studies demonstrated a higher incidence of SIRS in patients with younger age and lower body weight.^[9] Younger and smaller children are more vulnerable to SIRS because of their greater metabolic demand, reactive pulmonary vasculature, immature organ systems, and CPB circuit size.^[10] However, in the current study, we found a lower incidence of SIRS in younger children, but there was no association between body weight and SIRS incidence. Similarly, Boehne et al.^[10]

showed that neonates undergoing cardiac surgery with CPB are more resistant to SIRS than older children are. In another study, inflammatory markers were not different between neonates and infants after CPB.^[11] The immune system is immature at birth and does not fully mature until around age 6.^[12] Therefore, the immune system of younger children may not be sufficient for a strong inflammatory reaction compared with that of older children. As a result, further studies investigating the incidence of SIRS after CPB are needed in certain pediatric age groups.

Children with CCHD have been assumed to be more susceptible to oxidative damage because of hypoxemia, circulation disorders, and a deficiency of their defense mechanism.^[13] Previous studies have demonstrated that, preoperatively, cyanotic patients have significantly higher levels of inflammatory cytokines and lower levels of myocardial antioxidant capacity than acyanotic patients do.^[3,14,15] Furthermore, children with CCHD have more complex anomalies requiring a longer duration of CPB. In this study, cyanotic children had higher RACHS1 scores and a longer duration of CPB and longer surgery time. According to the CMH analysis performed considering the RACHS1 score, the incidence of SIRS was significantly higher in cyanotic children.

Pediatric patients undergoing cardiac surgery are frequently administered blood products perioperatively because of their immature hemostatic system and hemodilution as well as hypothermia caused by CPB. The presence of cyanosis and/or intracardiac shunt, complex surgical procedure, and prolonged CPB time results in high hemorrhagic risk.^[16–18] Willems et al.^[17] demonstrated that CCHD is an independent predictive factor for FFP and platelet transfusion after cardiac surgery. In our study, children with CCHD had higher hemoglobin and hematocrit values and lower platelet counts during the study period. In addition, they were exposed to more intraoperative RBC transfusions and more FFP transfusions in the 48-hour postoperative period than acyanotic children were. Many studies have demonstrated that the side effects of the use of blood products are associated with systemic inflammation.^[19] In the current study, we observed that larger amounts of RBC and FFP administered perioperatively in cyanotic children significantly increased the incidence of SIRS.

Elevated intraoperative lactate levels are associated with higher morbidity and mortality in pediatric cardiac surgery. Inflammation induced by CPB and subsequent IRI result in mitochondrial dysfunction, reducing oxidative phosphorylation that directs pyruvate to lactate, thus contributing to type B hyperlactatemia.^[20] In addition, endogenous catecholamine release results in glycolysis and gluconeogenesis, increasing the production of glucose and lactate.^[20] In our study, cyanotic children with SIRS had significantly higher lactate and glucose levels than acyanotic children

without SIRS. According to our results, the incidence of SIRS leads to higher lactate and glucose levels.

Inflammatory mediators and IRI decrease systolic function, systemic arterial resistance, and systemic venous return.^[21] The inflammatory response to CPB may result in an increased need for inotropes and vasopressors.^[21] Furthermore, cyanotic children have a reduced ATP reserve and antioxidant enzymes because of pressure overload and chronic hypoxia, thus leaving the myocardium unprotected against oxidative injury.^[3,13] In our study, VIS values were higher in all children with SIRS and higher in cyanotic children with SIRS than in acyanotic children without SIRS postoperatively.

Systemic hypothermia is typically used for organ protection and has been associated with a reduction in SIRS during CPB in congenital cardiac surgery.^[22] However, with regard to the inflammatory response in children, Schmitt et al.^[23] found no difference between a moderately hypothermic perfusion temperature (32°C) and normothermic perfusion (36°C) during CPB. In this study, our patients had more complex cardiac anomalies and lower nasopharyngeal temperature levels during CPB than those in Schmitt et al.^[23] However, we could not find an association between hypothermia and the incidence of SIRS. It appears that body temperature plays only a minor role in multifactorial SIRS during CPB.

Limitations

This observational study has several limitations. The age range of our patients was wide, they had a wide variety of cardiac anomalies. We found a statistically significant difference between RACHS scores in the study groups because children with CCHDs have more complicated anomalies than acyanotic children do. To investigate the effects of intraoperative variables on SIRS, we observed our patients for 48 hours postoperatively. However, longer-term postoperative factors may affect the occurrence of SIRS and postoperative complications. In addition, the postoperative management provided in our institution might have affected the development of SIRS, so our results might not be generalizable.

Post-CPB inflammation occurs precisely, but severe consequences affect a few patients. Because we are still unable to predict which patients will be severely affected, intraoperative risk factors should be determined. This observational clinical study demonstrated that the incidence of SIRS is higher in children with complex CCHD. According to our results, the perioperative consumption of blood products increases the occurrence of SIRS, which leads to high lactate and glucose levels and VISs. Further randomized, controlled studies investigating the incidence of SIRS following congenital cardiac surgery are needed in categorized congenital diseases and certain pediatric age groups.

Disclosures

Ethics Committee Approval: The study was approved by The Çukurova University Faculty of Medicine Non-interventional Clinical Research Ethics Committee (Date: 01/11/2019, No: 93).

Informed Consent: Written informed consent was obtained from all patients.

Peer-review: Externally peer-reviewed.

Conflict of Interest: None declared.

Financial Disclosure: The authors declared that this study has received no financial support.

Authorship Contributions: Concept – F.K.; Design – F.K.; Supervision – F.K., E.B.; Data collection &/or processing – F.K.; Analysis and/or interpretation – F.K.; Literature search – E.B.; Writing – F.K.; Critical review – F.K., E.B.

References

1. Laffey JG, Boylan JF, Cheng DC. The systemic inflammatory response to cardiac surgery: Implications for the anesthesiologist. *Anesthesiology* 2002;97:215–52.
2. Durandy Y. Minimizing systemic inflammation during cardiopulmonary bypass in the pediatric population. *Artif Organs* 2014;38:11–8.
3. Fudulu D, Angelini G. Oxidative stress after surgery on the immature heart. *Oxid Med Cell Longev* 2016;2016:1971452.
4. Manso PH, Carmona F, Dal-Pizzol F, Petronilho F, Cardoso F, Castro M, et al. Oxidative stress markers are not associated with outcomes after pediatric heart surgery. *Paediatr Anaesth* 2013;23:188–94.
5. Chew MS, Brandslund I, Brix-Christensen V, Ravn HB, Hjortdal VE, Pedersen J, et al. Tissue injury and the inflammatory response to pediatric cardiac surgery with cardiopulmonary bypass: A descriptive study. *Anesthesiology* 2001;94:745–53.
6. Gaies MG, Gurney JG, Yen AH, Napoli ML, Gajarski RJ, Ohye RG, et al. Vasoactive-inotropic score as a predictor of morbidity and mortality in infants after cardiopulmonary bypass. *Pediatr Crit Care Med* 2010;11:234–8.
7. Jenkins KJ, Gauvreau K, Newburger JW, Spray TL, Moller JH, Iezzoni LI. Consensus-based method for risk adjustment for surgery for congenital heart disease. *J Thorac Cardiovasc Surg* 2002;123:110–8.
8. Goldstein B, Giroir B, Randolph A; International Consensus Conference on Pediatric Sepsis. International pediatric sepsis consensus conference: Definitions for sepsis and organ dysfunction in pediatrics. *Pediatr Crit Care Med* 2005;6:2–8.
9. Güvener M, Korun O, Demirtürk OS. Risk factors for systemic inflammatory response after congenital cardiac surgery. *J Card Surg* 2015;30:92–6.
10. Boehne M, Sasse M, Karch A, Dziuba F, Horke A, Kausen T, Mikolajczyk R, et al. Systemic inflammatory response syndrome after pediatric congenital heart surgery: Incidence, risk factors, and clinical outcome. *J Card Surg* 2017;32:116–25.
11. Allan CK, Newburger JW, McGrath E, Elder J, Psinos C, Laussen PC, et al. The relationship between inflammatory activation and clinical outcome after infant cardiopulmonary bypass. *Anesth Analg* 2010;111:1244–51.
12. de Fontnouvelle CA, Greenberg JH, Thiessen-Philbrook HR, Zapitelli M, Roth J, Kerr KF, et al. Interleukin-8 and tumor necrosis factor predict acute kidney injury after pediatric cardiac surgery. *Ann Thorac Surg* 2017;104:2072–9.
13. Calza G, Lerzo F, Perfumo F, Borini I, Panizzon G, Moretti R, et al. Clinical evaluation of oxidative stress and myocardial reperfusion injury in pediatric cardiac surgery. *J Cardiovasc Surg (Torino)* 2002;43:441–7.
14. Sharma R, Bolger AP, Li W, Davlouros PA, Volk HD, Poole-Wilson PA, et al. Elevated circulating levels of inflammatory cytokines and bacterial endotoxin in adults with congenital heart disease. *Am J Cardiol* 2003;92:188–93.
15. Nassef YE, Hamed MA, Aly HF. Inflammatory cytokines, apoptotic, tissue injury and remodeling biomarkers in children with congenital heart disease. *Indian J Clin Biochem* 2014;29:145–9.
16. Ranucci M, Baryshnikova E, Castelvechio S, Pelissero G; Surgical and Clinical Outcome Research (SCORE) Group. Major bleeding, transfusions, and anemia: The deadly triad of cardiac surgery. *Ann Thorac Surg* 2013;96:478–85.
17. Willems A, Patte P, De Groote F, Van der Linden P. Cyanotic heart disease is an independent predicting factor for fresh frozen plasma and platelet transfusion after cardiac surgery. *Transfus Apher Sci* 2019;58:304–9.
18. Zabala LM, Guzzetta NA. Cyanotic congenital heart disease (CCHD): Focus on hypoxemia, secondary erythrocytosis, and coagulation alterations. *Paediatr Anaesth* 2015;25:981–9.
19. Vlaar AP, Hofstra JJ, Determann RM, Veelo DP, Paulus F, Levi M, et al. Transfusion-related acute lung injury in cardiac surgery patients is characterized by pulmonary inflammation and coagulopathy: A prospective nested case-control study. *Crit Care Med* 2012;40:2813–20.
20. Stephens EH, Epting CL, Backer CL, Wald EL. Hyperlactatemia: An update on postoperative lactate. *World J Pediatr Congenit Heart Surg* 2020;11:316–24.
21. Giacinto O, Satriano U, Nenna A, Spadaccio C, Lusini M, Mastroianni C, et al. Inflammatory response and endothelial dysfunction following cardiopulmonary bypass: Pathophysiology and pharmacological targets. *Recent Pat Inflamm Allergy Drug Discov* 2019;13:158–73.
22. Anttila V, Hagino I, Zurakowski D, Lidov HG, Jonas RA. Higher bypass temperature correlates with increased white cell activation in the cerebral microcirculation. *J Thorac Cardiovasc Surg* 2004;127:1781–8.
23. Schmitt KR, Fedarava K, Justus G, Redlin M, Böttcher W, Delmo Walter EM, et al. Hypothermia during cardiopulmonary bypass increases need for inotropic support but does not impact inflammation in children undergoing surgical ventricular septal defect closure. *Artif Organs* 2016;40:470–9.