Renal Function and Inflammatory Response in Neonates Undergoing Cardiac Surgery With or Without Antegrade Cerebral Perfusion—A Post hoc Analysis

Timo Jahnukainen, Paula Rautiainen, Juuso Tainio, Tommi Pätilä, Jukka T Salminen, Juho Keski-Nisula
Departments of Pediatric Nephrology and Transplantation, 1Anesthesia and Intensive Care and 2Pediatric Surgery, New Children’s Hospital, University of Helsinki and Helsinki University Hospital, Helsinki, Finland

ABSTRACT

Background: Cardiopulmonary bypass (CPB) may lead to tissue hypoxia, inflammatory response, and risk for acute kidney injury (AKI). We evaluated the prevalence of AKI and inflammatory response in neonates undergoing heart surgery requiring CPB with or without antegrade cerebral perfusion (ACP).

Methods: Forty neonates were enrolled. The patients were divided into two groups depending on the use of ACP. AKI was classified based on the Kidney Disease: Improving Global Outcomes (KDIGO) criteria. Inflammatory response was measured using plasma concentrations of interleukins 6 (IL-6) and 10 (IL-10), white blood cell count (WBC), and C-reactive protein (CRP).

Results: Eight patients (20%) experienced AKI: five (29%) in the ACP group and three (13%) in the non-ACP group (P = 0.25). Postoperative peak plasma creatinine and urine neutrophil gelatinase-associated lipocalin were significantly higher in the ACP group than in the non-ACP group [46.0 (35.0–60.5) vs 37.5 (33.0–42.5), P = 0.044 and 118.0 (55.4–223.7) vs 29.8 (8.1–109.2), P = 0.02, respectively]. Four patients in the ACP group and one in the non-ACP group required peritoneal dialysis (P = 0.003). Postoperative plasma IL-6, IL-10, and CRP increased significantly in both groups. There were no significant differences between the ACP and non-ACP groups in any of the inflammatory parameters measured.

Conclusions: No significant difference in the AKI occurrence or inflammatory response related to CPB modality could be found. In our study population, inflammation was not the key factor leading to AKI. Due to the limited number of patients, these findings should be interpreted with caution.

Keywords: Antegrade cerebral perfusion, cardiopulmonary bypass, infant, kidney injury

INTRODUCTION

Despite recent advances in surgical techniques and treatment modalities, infant cardiac surgery requiring cardiopulmonary bypass (CPB) remains a high-risk procedure with relatively high morbidity and mortality rates. Acute kidney injury (AKI) is one of the complications of CPB with an occurrence rate of around 20–65% in pediatric population. AKI has been associated with increased postoperative mortality in children undergoing cardiac surgery, and fluid overload, hypotension and hypoxia, activation of the sympathetic nervous system and renin-aldosterone system, hemolysis, and CPB-associated systemic inflammation have been recognized as risk factors.
for AKI.\textsuperscript{[28–10]} The impact of CPB modality on AKI risk has been under discussion. There are only few reports available on CPB and AKI in neonates and the published patient series are understandably relatively small.\textsuperscript{[11–14]}

We have recently conducted a prospective, randomized, double-blinded, placebo-controlled study evaluating the effect of peri- and postoperative stress-dose corticosteroid (SDC) treatment on inflammatory reaction, postoperative ventricle function, and AKI risk in neonates undergoing open-heart surgery.\textsuperscript{[9,15]} We performed a post-hoc analysis of this data by dividing the study population into two groups based on whether antegrade cerebral perfusion (ACP) was used or not (non-ACP). There is a significant difference between these two forms of perfusion technique since during ACP, there is only blood flow to the brain and right upper limb. Therefore, during ACP, the visceral organs may be exposed to reperfusion inflammation and hypoxic damage.

We aimed to compare (1) the occurrence of AKI, (2) changes in key AKI biomarkers, such as plasma creatinine (P-Cr), cystatin c (P-Cys C), and neutrophil gelatinase-associated lipocalin (P-NGAL), urine NGAL (U-NGAL) and Kidney injury molecule-1 (U-KIM-1), and (3) post-CPB inflammatory response between the ACP and non-ACP groups by measuring plasma interleukin-6 (IL-6) and -10 (IL-10), C-reactive protein (P-CRP), and white blood cell count (B-WBC). Based on our previous findings, we hypothesized that reperfusion-induced inflammation is not the major cause of AKI in ACP-treated infants.

**METHODS**

The study was approved by the Ethics Committee of Helsinki University Hospital and by the Finnish Medicines Agency. This study was part of the clinical outcome trial registered in the European Union Drug Regulating Authorities Clinical Trials database (Eudra-CT 2011-005239-14). The study design and outcomes related to inflammation, adrenal insufficiency, hemodynamic outcome, and renal function have been published recently.\textsuperscript{[9,15]} Written informed consent was obtained from all parents of the patients before the study commenced.

A total of 51 neonates were eligible for the study; however, 11 patients were excluded due to parental refusal. Forty neonates (age ≤28 days) who were undergoing elective open-heart surgery with CPB due to congenital heart defects between April 2012 and October 2014 were finally enrolled. The decision about using antegrade cerebral perfusion (ACP) was made case by case depending on clinical factors. Antegrade cerebral perfusion (ACP) was used in patients who underwent isolated aortic arch reconstruction or arch reconstruction with another procedure [Table 1]. In the non-ACP group, standard aortic and bicaval cannulation techniques were used. Balanced anesthesia was attained with sufentanil, pancuronium, propofol or (S)-ketamine, and sevoflurane. CPB was established by using a pediatric hollow-fiber membrane oxygenator with a cardiotomy reservoir and a roller pump. Blood flow velocity and target body temperature were prescribed depending on the CPB modality and type of operation. In the ACP group, the blood flow was 15–30 mL/kg/min during ACP and target body temperature was 24°C–28°C while in the non-ACP group, the respective values were 150 mL/kg/min and 32°C–34°C. The pump prime solution consisted of packed red cells, fresh frozen plasma, and albumin. The hematocrit was adjusted to 30%. During rewarming, it increased to between 35 and 45% by hemofiltration and by adding packed red cells as necessary. The acid-base status was managed by using the modified alpha-stat protocol. Fresh gas flow in the CPB circuit was decreased in hypothermic patients in order to keep the arterial carbon dioxide tension (PaCO\(_2\)) values determined at a temperature of 37°C in the upper normal levels or higher. Near-infrared spectroscopy NIRO-100 (Hamamatsu Photonics, Hamamatsu, Japan) was also used to detect a possible decrease in brain oxygenation at low PaCO\(_2\) values.

In the ACP group, continuous low-flow cerebral perfusion was maintained by advancing an aortic cannula from the distal ascending aorta into the innominate artery or via a Gore-Tex graft sewn to the innominate artery. Bilateral cannulation was not performed due to a significant risk for thromboembolic events and
disturbances in brain circulation. Cerebral near infrared spectroscopy (NIRO-200NX, Hamamatsu Photonics K. K.) was recorded during the whole procedure to ensure adequate cerebral perfusion. Myocardial protection was accomplished by using a two-minute infusion of cold (24°C) blood cardioplegia, mixed at a ratio of 1:1 (blood:cardioplegia) during aortic cross clamp; after that, a one-minute infusion of cold blood cardioplegia was administered every 20 minutes. According to the original study protocol, half of the patients were randomized to receive an intravenous bolus of methylprednisolone (MP) 2 mg/kg, followed by hydrocortisone infusion 0.2 mg/kg/h six hours after the surgery with a tapering dose during a maximum of five days’ stay in the pediatric intensive care unit (PICU). The other half received a saline bolus at the induction of anesthesia and a placebo infusion in a similar fashion as the treatment group. All patients were operated by three experienced surgeons and a perfusion team. Milrinone or/and levosimendan were used as the first-line inotropes, and epinephrine or/and norepinephrine was added to support hemodynamics when needed.

Definition of AKI was based on the Kidney Disease: Improving Global Outcomes (KDIGO) classification as at least 50% or ≥26.5 µmol/L increase in P-Cr concentration from the lowest value, urine output less than 0.5 mL/kg/h lasting at least 6 h, or need for acute dialysis after the operation.[13] Dialysis was initiated due to decreased urine output, hypervolemia, and/or elevated plasma creatinine (P-Cr).

Sample acquisition
Blood samples were obtained at anesthesia induction before the study drug or saline bolus was administered (T1), five minutes after weaning from CPB (T2), six hours after weaning from CPB (T3), and thereafter at 6 a.m. on the following five postoperative days (T4-8). Urine samples were collected at time points T1 and T3-6. The collected blood and urine samples were processed and stored at -70°C for later analysis. P-Cr and P-Cys C concentrations were analyzed in the Helsinki University Hospital laboratory (HusLab, Helsinki, Finland) using standard procedures. P-NGAL and urine (U-NGAL) concentrations of NGAL and urine concentration of KIM-1 and creatinine (U-Cr) were analyzed using commercial ELISA kits (Quontikine, R&D Systems, Abington, UK). All samples were analyzed in duplicate. U-NGAL and -KIM-1 results were divided by the corresponding urinary creatinine concentration to standardize the changes in urine concentration. Urine NGAL and KIM-1 samples were lacking from six patients (ACP n = 3, non-ACP n = 3) due to inadequate sample collection. Physiological and clinical outcome parameters, such as urine output and need for vasoactive infusions, were also recorded. Information regarding peritoneal dialysis was collected from the intensive care database (Centricity Critical Care Clinisoft, GE Healthcare, Helsinki, Finland).

The inflammatory response was evaluated by measuring plasma concentrations of interleukins 6 (IL-6) and 10 (IL-10), plasma C-reactive protein (CRP), and white blood cell count (WBC). The plasma IL-6, and IL-10 concentrations were determined using commercial ELISA kits (QuantiKine, R&D Systems, Abington, UK) as described earlier.[9]

Statistics
This was a post-hoc analysis. Numerical data are presented as mean (SD; range) or median (interquartile range) as appropriate. Wilcoxon rank sum test or Chi-squared comparison or Fisher’s exact test was used for categorical data to compare groups with respect to background characteristics. Repeated measurements were compared using the Friedman Test to answer the research question of whether there were changes in the parameters across time points within the two study groups. Mann-Whitney test was performed between different groups at different time points. P values less than 0.05 were considered to be statistically significant.

Statistical analyses were performed using the Statistical Package for the Social Sciences (SPSS/Windows version 19.0, SPSS Inc., Chicago, IL, USA).

RESULTS

Subjects and demographics
There were no significant differences in the baseline demographics between the ACP (n = 17) and the non-ACP (n = 23) group as shown in Table 2. Preoperative P-Cr and P-Cys C tended to be higher among the ACP patients; however, the difference did not reach statistical significance [Table 2]. None of the patients required dialysis prior to surgery. The underlying diagnosis differed between the groups. Norwood procedure dominated in the ACP (41.2%) group while in the non-ACP group, the majority of the operations were corrections of transposition of great arteries (69.6%). Due to the unequal distribution of diagnoses between the groups, the RACH score was significantly higher for patients in the ACP group than in the non-ACP group [Table 2].

Postoperative outcome
The 30-day mortality rate was 5.0% [Table 3]. One patient died after truncus arteriosus repair, followed by ECMO treatment, while another tetralogy of Fallot patient with
severely hypoplastic pulmonary arteries died of multiple organ failure. The median length of stay in PICU was 7.5 (5–10) days, being longer in the ACP group than in the non-ACP group [Table 3]. On arrival to PICU, the ACP group had a significantly higher inotropic score than the non-ACP group; however, after POD 1, no significant difference could be found [Table 3]. Arterial postoperative lactate was also higher until POD 3 in the ACP group than in the non-ACP group [Figure 1].

Renal function
A total of eight patients (20%) experienced AKI; five (29%) in the ACP group and three (13%) in the non-ACP group. Peritoneal dialysis was started in four patients in the ACP group and in one patient in the non-ACP group (P = 0.003) [Table 3]. In both groups, all measured renal parameters increased significantly after the operation, except for P-Cr concentration and U-NGAL/Cr ratio in the non-ACP group [Figure 1]. Postoperative P-Cr was

---

**Table 2: Patient demographics and perioperative data in the neonates undergoing cardiac surgery with or without antegrade cerebral perfusion**

| Variable                          | ACP n=17 | Non-ACP n=23 | P   |
|-----------------------------------|----------|--------------|-----|
| Age, days                         | 7.0±2.4  | 8.0±±4.2     | 0.140|
| Weight, kg                        | 3.4±0.5  | 3.5±0.5      | 0.602|
| Male gender, n (%)                | 9 (53.0) | 18 (78.0)    | 0.177|
| Gestational age, weeks            | 39.2±1.5 | 39.8±1.2     | 0.722|
| Ventilation support before operation, n (%) | 15 (88.0) | 16 (70.0)    | 0.256|
| Nasal CPAP                        | 1 (6.0)  | 4 (17.0)     | 0.632|
| Mechanical ventilation            | 1 (6.0)  | 3 (13.0)     | 0.624|
| RACHS score                       | 4 (4-6)  | 3 (3-3)      | <0.001|
| Baseline P-TnT, ng/L              | 50.0 (33.5-72.8) | 43.0 (30.0-75.0) | 0.558|
| Baseline P-Cr, µmol/L             | 42.0±10.54 | 36.5±4.50   | 0.188|
| Baseline P-Cys C, mg/L            | 1.58±0.28 | 1.3.6±0.34   | 0.056|
| SDC, n (%)                        | 9 (53.0) | 11 (49.0)    | 1.000|
| CPB support time, min             | 179.0±46.0 | 165.0±60.0  | 0.452|
| ACC time, min                     | 89.6±35.4 | 100.4±41.3   | 0.402|
| ACP time, min                     | 50±13.4  |              |     |

**Table 3: Patient demographics and perioperative data in the neonates undergoing cardiac surgery with or without antegrade cerebral perfusion**

| Variable                          | ACP n=17 | Non-ACP n=23 | P   |
|-----------------------------------|----------|--------------|-----|
| pH on arrival to PICU             | 7.40±0.0891 | 7.42±0.0895 | 0.370|
| P-Lactate on arrival to PICU, mmol/L | 4.894±2.183 | 3.761±1.534 | 0.061|
| ScvO2 on arrival to PICU, %       | 55.8±13.2 | 62.1±14.8    | 0.094|
| PICU days                         | 10.0 (6.5–12.0) | 7.0 (5.0–9.0) | 0.046|
| Intubation days                   | 6.9 (4.0–10.0) | 4.1 (3.2–5.9) | 0.087|
| First isotope score at PICU       | 27.4±8.6  | 22.4±6.8     | 0.048|
| Inotrope score 24 h               | 18.1 (14.0–28.5) | 13.9 (10.6–24.3) | 0.133|
| Inotrope score 48 h               | 12.5 (9.8–25.8) | 12.1 (7.5–21.6) | 0.600|
| Hospital mortality, n (%)         | 0 (0)     | 2 (8.7)      | 0.499|
| AKI, n (%)                        | 5 (29.4)  | 3 (13.0)     | 0.250|
| Dialysis, n (%)                   | 4 (2.35)  | 1 (4.3)      | 0.003|
| Diuresis POD 1, mL/kg             | 73.1±24.6 | 76.0±22.6    | 0.253|
| Balance POD 1, mL                 | 21.0 (10.5–82.5) | 13.0 (11.0–40.0) | 0.366|
| P-ProBNP at T2, ng/L              | 17 440±844 | 19 165±9610 | 0.602|
| Peak P-Cr, µmol/L                 | 46.0 (35.0–60.5) | 37.5 (33.0–42.5) | 0.044|
| Peak P-Cys C, mg/L                | 1.50±0.30 | 1.48±0.19    | 0.812|
| Peak P-NGAL, ng/ml                | 29.5 (22.4–35.8) | 33.9 (22.2–43.6) | 0.836|
| Peak U-NGAL/Cr, mg/l              | 118 (55.4–223.7) | 29.8 (8.1–109.2) | 0.020|
| Peak U-KIM-1/Cr, mg/l             | 25.3 (10.3–36.3) | 21.0 (6.6–35.1) | 0.637|
| Peak B-WBC, E9/L                  | 10.4 (9.1–13.1) | 9.6 (8.0–10.5) | 0.089|
| Peak P-CRP, mg/l                  | 75.8±40.2 | 109.5±63.7   | 0.079|
| Peak P-IL-10, pg/ml               | 206.7 (65.5–329.3) | 192 (44.6–426.1) | 0.978|
| Peak P-IL-6, pg/ml                | 201.0 (150.7–771.8) | 371.1 (173.4–981.9) | 0.678|

ACP, Antegrade cerebral perfusion; P, Plasma; PICU, Paediatric intensive care unit; ScvO2, Central venous saturation; AKI, Acute kidney injury; POD, Postoperative day; ProBNP, N-terminal pro b-type natriuretic peptide; T2, six hours after cardiopulmonary bypass; P-Cr, plasma creatinine, P-Cys C, plasma cystatin C; NGAL, Neutrophil gelatinase-associated lipocalin; U, Urine; KIM-1, Kidney Injury Molecule-1; B, Blood; WBC, White blood cell count; CRP, C-reactive protein; IL, Interleukin Values are presented as mean±standard deviation (SD) or number of patients (%)
significantly higher on POD3 in the ACP group than in the non-ACP group [Table 3 and Figure 1] and U-NGAL/Cr ratio was higher six hours after CPB, respectively [Figure 1]. There were no statistically significant differences between the groups in P-Cyc C, P-NGAL, or U-KIM-1/Cr ratio [Figure 1 and Table 3].

**Inflammatory response in ACP and non-ACP groups**

IL-6, IL-10, and CRP increased significantly after the operation in both groups [Figure 2] while WBC remained relatively unchanged. There were no significant differences between the ACP and non-ACP group in any of the inflammatory parameters measured [Table 3 and Figure 2]. Perioperative MP was given to equal proportions of patients in both groups [Table 2].

**DISCUSSION**

The overall prognosis of infants undergoing open cardiac surgery requiring cardiopulmonary bypass (CPB) has improved significantly in recent decades. However, despite this progress, open-heart surgery remains a high-risk procedure with relatively high morbidity and mortality rates. In many cases, the general condition of an infant with a congenital heart defect is unstable, which further increases these risks. AKI is one of the complications of CPB and it has been shown to increase mortality in neonates. One possible explanation for CPB-induced AKI is inflammatory response, induced by foreign surfaces in the perfusion set, surgical trauma, anesthesia, and insufficient organ perfusion due to CPB. In the present study, we compared the prevalence of AKI in infants with or without ACP and the inflammatory response in these groups. In our study population, the occurrence of AKI was relatively low, being only 20%. We did not find any significant difference in either AKI prevalence or level of inflammation between the two groups. However, patients treated with ACP had significantly higher postoperative peak P-Cr and they required more often peritoneal dialysis, suggesting that AKIs were more severe in the ACP group than in the non-ACP group.

The slightly higher P-Cr and U-NGAL/cr ratio found in ACP-treated patients was not associated with inflammatory response. We could not find significant differences in the levels of IL-6, IL-10, CRP or WBC between the two groups. Cardiac surgery and CPB induce systemic inflammatory response leading to increased concentrations of circulating cytokines. This inflammatory response has been linked to an increased risk for organ damage and multiorgan failure. Our previous data in this same patient material suggested that perioperative MP does not influence AKI occurrence, suggesting that CPB-related inflammatory response is not the major cause of AKI.
Regional perfusion modality has been developed to prevent neurological morbidity in children undergoing cardiac surgery.\[19,20\] However, there has been increasing concern about the effect of ACP on other organ systems, such as the liver, kidneys and intestine.\[13,14\] Therefore, alternative perfusion methods have been developed.\[13,21\]

Recently, double perfusion methods have been introduced in order to avoid both cerebral and visceral hypoperfusion and the risk for end-organ damage.\[13,22\] The study by Fernández-Doblas et al. compared double-perfusion technique and ACP in neonates undergoing aortic arch repair.\[13\] In this non-controlled study, patients with double-perfusion had significantly higher urine output intraoperatively, but no significant difference in plasma creatinine or estimated GFR. However, the authors were able to show better liver function in patients treated with double-arterial cannulation. This finding is supported by the retrospective study of Kreuzer et al. describing outcome in 407 children. ACP may pose a significant risk for visceral hypoperfusion leading to kidney and liver failure.\[23\]

The present study has several shortcomings. First, the number of patients was small and due to various reasons, urine samples were not available from all patients. However, all samples were collected prospectively and the patients were meticulously documented and followed up. Second, as in most previous studies, there were differences in the severity of the underlying heart defect between the ACP and non-ACP groups, which may have influence on postoperative AKI risk. Third, this was a post-hoc analysis of our double-blinded, placebo-controlled study designed to compare anti-inflammatory response, adrenocortical function, and hemodynamic outcome of stress-dose corticosteroid and placebo groups, and the present study was therefore not powered to show differences in kidney injury biomarkers or the incidence of AKI in ACP versus non-ACP groups. Fourthly, the creatinine-based AKI criterion is relatively insensitive among neonates, which may have led to underdiagnosis of AKI in this study.

In conclusion, the AKI occurrence was 29.4% in the ACP group and 13.0% in the non-ACP group. The difference did not reach statistical significance. However, patients in the ACP group appeared to have more severe AKI, since dialysis was required significantly more often in the ACP-treated patients. Our observations about inflammatory biomarkers suggest that CPB-related inflammatory response is probably not the major factor leading to AKI in these patients. Because the present study was not powered to show differences in kidney injury biomarkers or the incidence of AKI, but rather in the inflammatory response, these findings should be interpreted with caution, and future studies with larger study populations are needed.

Clinical trial registry number Eudra-CT 2011-005239-14.

Declaration of patient consent
The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.
Acknowledgements
The study has been supported by the Foundation for Pediatric Research and the Päivikki and Sakari Sohlberg Foundation. Dr. Pertti Suominen (deceased January 9, 2018) had significant contribution to this study.

Financial support and sponsorship
Nil.

Conflicts of interest
There are no conflicts of interest.

REFERENCES
1. Misfeld M, Leontyev S, Borger MA, Gindensperger O, Lehmann S, Legare JF. What is the best strategy for brain protection in patients undergoing aortic arch surgery? A single center experience of 636 patients. Ann Thorac Surg 2012;93:1502-8.
2. Bennett M, Dent CI, Ma Q, Dastrala S, Grenier F, Workman R, et al. Urine NGAL predicts severity of acute kidney injury after cardiac surgery: Prospective study. Clin J Am Soc Nephrol 2008;3:665-73.
3. Morgan CJ, Zappitelli M, Robertson CMT, Alton GY, Sauve RS, Joffe AR, et al. Risk factors for and outcomes of acute kidney injury in neonates undergoing complex cardiac surgery. J Pediatr 2013;162:120-7.
4. Parikh CR, Devarajan P, Zappitelli M, Sint K, Thiessen-Philbrook H, Li S, et al. Postoperative biomarkers predict acute kidney injury and poor outcomes after pediatric cardiac surgery. J Am Soc Nephrol 2011;22:1737-47.
5. Aydin SI, Seiden HS, Blaufox AD, Parnell VA, Chounhury T, Punnoose A, et al. Acute kidney injury after surgery for congenital heart disease. Ann Thor Surg 2012;94:1589-95.
6. Checcia PA, Bronicki RA, Costello JM, Nelson DP. Steroid use before pediatric cardiac operations using cardiopulmonary bypass: An international survey of 36 centers. Pediatr Crit Care Med 2005;6:441-4.
7. Bronchi RA, Bucker CL, Baden HP, Mavroidis C, Crawford SE, Green TP. Dexamethasone reduces the inflammatory response to cardiopulmonary bypass in children. Ann Thorac Surg 2000;69:1490-5.
8. Keski-Nisula J, Pesonen E, Olkkola KT, Peltola K, Neuvonen PJ, Tuominen N, et al. Methylprednisolone in neonatal cardiac surgery: Reduced inflammation without improved clinical outcome. Ann Thorac Surg 2013;95:2126-32.
9. Suominen P, Keski-Nisula J, Ojala T, Rautiainen P, Jahnukainen T, Hästbacka J, et al. Stress-dose corticosteroids versus placebo in neonatal cardiac surgery: A randomized controlled trial. Ann Thorac Surg 2017;104:1378-85.
10. McBride WT, Allen S, Gormley SMC, Young IS, McClean E, MacGowan SW, et al. Methylprednisolone favorable alters plasma and urinary cytokine homeostasis and subclinical renal injury at cardiac surgery. Cytokine 2004;27:81-9.
11. Algra S, Kornmann VNN, van der Tweel I, Schouten ANJ, Jansen NJG, Haas F. Increasing duration of circulatory arrest, but not antegrade cerebral perfusion, prolongs postoperative recovery after neonatal cardiac surgery. J Thorac Cardiovasc Surg 2012;143:375-82.
12. Algra SO, Schouten ANJ, van Oeveren W, van der Tweel I, Schoof PH, Jansen NJG, et al. Low-flow antegrade cerebral perfusion attenuates early renal and intestinal injury during neonatal aortic arch reconstruction. J Thorac Cardiovasc Surg 2012;144:1323-8.
13. Fernández-Doblas J, Ortega-Loubon C, Pérez-Andreu J, Linés M, Fernández-Molina M, Abella RE. Selective visceral perfusion improves renal flow and hepatic function in neonatal aortic arch repair. Interact Cardiovasc Thorac Surg 2018;27:395-401.
14. Kornilov IA, Sinelnikov YS, Soinov IA, Ponomarev DN, Kshanovskaya MS, Krivoschapina AA, et al. Outcomes after aortic arch reconstruction for infants: Deep hypothermic circulatory arrest versus moderate hypothermia with selective antegrade cerebral perfusion. Eur J Cardiothorac Surg 2015;48:e45-50.
15. Jahnukainen T, Keski-Nisula J, Taimio J, Valkonen H, Pätilä T, Jalko H, et al. Efficacy of corticosteroids in prevention of acute kidney injury in neonates undergoing cardiac surgery – A randomized controlled trial. Acta Anaesthesiol Scand 2018. doi: 10.1111/aas.13134.
16. Selewski DT, Charlton JR, Jetton JG, Guillot R, Mhanna MJ, Askenazi DJ, et al. Neonatal acute kidney injury. Pediatrics 2015;136:e463.
17. Hassinger AB, Backer CI, Lane JC, Raymond S, Wang D, Wald EL. Predictive power of serum cystatin C to detect acute kidney injury and pediatric-midified RIFLE class in children undergoing cardiac surgery. Pediatr Crit Care Med 2012;13:435-40.
18. Bjarnadóttir M, Grubb A, Olafsson I. Promoter-mediated, dexamethasone-induced increase in cystatin C production by HeLa cells. Scand J Clin Lab Invest 1995;55:617-23.
19. Pigula FA, Nemoto EM, Griffith BP, Sievers RD. Regional low-flow perfusion provides cerebral circulatory support during neonatal aortic arch reconstruction. J Thorac Cardiovasc Surg 2000;119:331-9.
20. Asou T, Kado H, Imoto Y, Shiokawa Y, Tominaga R, Kawachi Y, et al. Selective cerebral perfusion technique during aortic arch repair in neonates. Ann Thorac Surg 1996;61:1546-8.
21. Tehervenkov CI, Chu VF, Shum-Tim D, Laliberte E, Reyes TU. Norwood operation without circulatory arrest: A new surgical technique. Ann Thorac Surg 2000;70:1730-3.
22. Hammel JM, Deptula JJ, Karamlou T, Wedemayer E, Abdullah I, Duncan KF. Newborn aortic arch reconstruction with descending aortic perfusion: Prospective study. Clin J Am Soc Nephrol 2008;3:665-73.
23. Haas F. Increasing duration of circulatory arrest, but not antegrade cerebral perfusion, prolongs postoperative recovery after neonatal cardiac surgery. Ann Thorac Surg 2013;96:1721-6.
24. Kreuzer M, Sames-Dolzer E, Schausberger L, Tulzer A, Ratschiller T, Kreuzer M, et al. Outcomes after aortic arch reconstruction. Ann Thorac Surg 2018;27:742-8.