

THE RISK OF RENAL AND NEUROLOGICAL COMPLICATIONS AFTER RECONSTRUCTIVE SURGERY OF THE AORTIC ARCH IN NEWBORNS

Yuriy SINELNIKOV

ID : <https://orcid.org/0000-0002-8294-662X>

Novosibirsk Research Institute of Blood Circulation Pathology of the Ministry of Health of the Russian Federation, named after Meshalkin E; Russian Federation

Elnur HASANOV

ID : <https://orcid.org/0000-0001-6695-5772>

National Centre of Surgery of the Azerbaijani Ministry of Health, named after Topchibashev, Baku, Azerbaijan

Faig MIRZAZADE

ID : <https://orcid.org/0000-0001-5076-017X>

National Centre of Surgery of the Azerbaijani Ministry of Health, named after Topchibashev, Baku, Azerbaijan

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ABSTRACT

When reconstructing the aortic arch (AA), it is necessary to select a method that provides optimal protection of the internal organs and the brain. It was previously believed that the hypothermic circulatory method was optimal. However, recently, the application of antegrade cerebral perfusion with moderate hypothermia has proved preferable when performing reconstructive operations on the aorta on adult patients and some children. In these instances, continuous cerebral perfusion reduces the incidence of neurological complications. However, the degree of damage to the organ systems distal to the AA remains unclear. The objective of this study was to assess the effectiveness and safety of various methods for protecting the brain and internal organs during reconstructive operations on the AA in small children. A retrospective analysis of 60 patients who had received reconstructive operations on the AA was undertaken. The neurological status and the degree of damage to internal organs in the short- and long-term, combined with the application of various methods for protecting the brain, were assessed. Surgical correction of the congenital pathology of the AA under deep hypothermic circulatory arrest conditions was performed in 26 patients (Group I) and antegrade unilateral selective perfusion of the brain was used for 34 patients (Group II). Nervous system complications were detected in 28.5% of patients in Group I, whereas it affected 7.9% of patients in Group II. Thus, the odds ratio for development of the neurological case was significantly lower for Group II: 0.17 (0.06–0.69), $p = 0.02$. However, in this Group, patients with renal dysfunction equated to 58.7%, whereas this figure was 23.7% for Group I, $p = 0.02$.

Key words: AA reconstruction, newborn, profound hypothermia, antegrade cerebral perfusion, renal dysfunction



INTRODUCTION

Currently, AA reconstructive operations rank amongst the most challenging for surgical treatment (4,5). This is primarily attributable to the need for a bloodless field and, secondly, due to the necessity for adequate brain protection, the latter being crucial when performing surgical treatment of congenital AA pathology (1,3,15). For many years, the optimal protection method was deep hypothermic circulatory arrest (DHCA). Its main pathogenetic mechanism is to reduce the intensity of metabolic processes and, consequently, oxygen consumption by the cells which significantly increases the resistance of the body to hypoxia (2). The application of deep hypothermia leads to a decrease in brain metabolism and slowing of biochemical reactions in the brain tissue, thereby increasing the time during which circulatory arrest is safe for the organism (2,12), but use of the hypothermia method causes adverse side effects at a systemic level. These include the development of coagulopathies, the formation of respiratory and renal insufficiency and the activation of cascades in the systemic inflammatory reaction (4,13,18).

Towards the end of the 20th century, T.Asou (1996) proposed a new method of protection against antegrade perfusion of the brain (APB) when undertaking AA surgery in newborn infants (1,2,8). When utilising the brain perfusion method, residual cerebral metabolism is provided, and thus the use of APB with moderate hypothermia for adults and some children suffering with AA pathology has become the preferred method in some clinics (9–12,15). There are currently several cerebral perfusion methods that facilitate a significant reduction in the development of neurological complications (2,8,17), but questions regarding the extent

of damage to organs and systems due to the lack of blood flow more distal from the AA (19) remain open and inconclusive (7). It is acknowledged that ischemia-reperfusion (6), whereby there is the activation of the systemic inflammation cascade mechanism reaction, through the formation of ‘vicious circles’, can lead to the dysfunction of internal organs, including the kidneys, liver and intestines. This can result in serious problems in managing the patient in the postoperative period because, with the development of internal organ dysfunction, there is a greater likelihood of a lethal outcome (12,16). Consequently, there is an increased requirement for additional scientific research into the various methods of protecting the internal organs during the surgical treatment of the congenital pathology of the AA.

PURPOSE

The objective of this study was to assess the effectiveness and safety of various methods for protecting the brain and internal organs during reconstructive operations on the AA in small children.

MATERIAL AND METHODS

This retrospective study assessed 60 patients (42 boys and 18 girls) aged from 1–98 days, with an average age of 53.1 ± 11.21 days. All patients underwent surgery at the Centre for Paediatric Cardiac Surgery and the Surgery of Newborns named after Meshalkin E. NRIBCP FSBI at the Russia Ministry of Health from 2010–19. Surgical correction of AA congenital pathology under either conditions of artificial circulation (AC) and deep hypothermic circulatory arrest (DHCA) (Group I, 26 patients), or by using the antegrade unilateral selective perfusion

of the brain (uSACP) method, (Group II, 34 patients) were undertaken.

In the preoperative period, the patients underwent a standard examination and, in all cases, multispiral computed tomography was performed to determine the size of different segments of the AA and plan the extent of surgical intervention. The neurological status was assessed during the postoperative period, and a computed tomography (CT) scan was performed if gross neurologic disorders in the patient were suspected. Using the risk, injury, failure, loss of kidney function, and end-stage kidney disease (RIFLE) designation, the degree of renal dysfunction was established (2). Inotropic support index calculation was undertaken during the first two days following the reconstructive operation (5). All patients were reassessed within three years after hospital discharge.

SURGICAL TACTICS

Surgical treatment was performed on all patients under general combined anaesthesia, induced using sevoran 6–7 ob/%, fentanyl at a dosage of 5–6 mkg/kg and arduan 0.06 mg/kg. To maintain adequate anaesthesia, a combination of drugs was used of sevoran (1–1.5 ob/%), fentanyl at 5–7 mkg/kg per hour and arduan at 0.03 mkg/kg per hour. Control of arterial pressure on the right radial and femoral arteries was undertaken during surgical treatment. Saturation in the cerebral vessels was monitored using the INVOS 5100 regional oxygen saturation device (Somanetics, USA) throughout surgical treatment. Artificial blood circulation was performed using the D901 Dideco Lilliput I newborn hollow fibre oxygenator (Sorin, Italy). The extracorporeal circuit was filled with a primary volume of 200–220 ml. The primary volume comprised donor erythrocyte mass in order to maintain hematocrit at a minimum level of 30%; fresh-frozen plasma, equating to 10 ml/kg; 20% albumin, equating

to 5 ml/kg, and 4% hydrogen carbonate, mannitol and heparin. Median sternotomy was used to access the heart and main vessels.

The following aortic cannulation methods were used to perform systemic perfusion. The most popular was cannulation using a heparinised polytetrafluoroethylene prosthesis made from GoreTex 3.0–3.5 mm, anastomosed with the proximal part of the brachiocephalic trunk (45.4% of cases). In 36.1% of cases, double cannulation was carried out, whereby one cannula was placed in the ascending aorta or heparinised prosthesis, with the second cannula being conducted through the arterial duct into the descending aorta for perfusion of the lower half of the body. Altogether, 18.5% of patients underwent direct cannulation to the ascending aorta. In all cases, there was separate cannulation of the hollow veins. If necessary, drainage of the left ventricle (LV) via the right upper lobar pulmonary vein was undertaken. The volume perfusion speed of the artificial circulation was 150 ml/kg, with patient cooling for at least 20 minutes before reaching the core temperature (rectal temperature) in the range of 18–27°C, with the temperature gradient between the perfusate and the body temperature of the patient being a maximum of 5°C. Deep hypothermic circulatory arrest was achieved when the rectal temperature had reached 20°C. The blood gas composition was monitored every 20 minutes throughout surgical treatment, being maintained in the α -stat mode.

Following occlusion of the aorta to protect the myocardium, a 40ml/kg Custodiol (crystalloid cardioplegic solution of Bretschneider) dose was administered antegradely in the root of the aorta. The method of antegrade selective perfusion of the brain was performed through the GoreTex prosthesis, anastomosed with a brachiocephalic artery (BCA) with a blood flow velocity of 30 ml/kg min. This was the first stage of AA surgical correction.

In this study, two methods of reconstruction were utilised, either comprising an extension of the narrowed portion of the AA using a xenopericardium patch or the formation of end-to-side anastomosis between the descending and ascending aorta, solely using the tissues of the patient. This surgical technique was proposed by S. Fraser and R. Mee, being improved by H. Rajasinghe *et al.* (10,14,15). Without fail, prior to the start of antegrade unilateral cerebral perfusion, the left common carotid artery, the left subclavian artery and the descending aorta were pinched. After reconstruction of the AA and restoration of artificial circulation, the intracardiac defects were eliminated. Following the conclusion of the main stage of surgical treatment, the patient was warmed up with a mandatory gradient of a maximum of 5°C between the perfusate and the actual body temperature of the patient. After disconnecting the patient from the cardiopulmonary bypass apparatus, modified ultrafiltration was undertaken using a BC20 Hemoconcentrator (Maquet, Sweden), following which a statistical analysis of the results was performed. Continuous variables are represented in the form of a median (25th, 75th percentile) and categorical variables were represented as percentages of numbers. Methods of nonparametric statistical analysis for biological systems were applied to evaluate intergroup comparisons, namely the Mann-Whitney method, the CI-square or Fisher criteria.

In order to identify the probability of neurological or renal complications, the binary logistic regression method has been used, whereas ordinal logistic regression was utilised to assess the relationship between the severity of renal dysfunction (RIFLE scale) and the perfusion type performed. To develop the final regression model, a step-by-step procedure for multifactorial logistic regression analysis with a 0.2 p-value cut-off was used.

RESULTS

None of the patients had a significant difference in age and weight. The age of those in Group I was 21.2 (+6.9, 32.7) days, whereas this was 21.0 (11.7, 29.4) days for Group II. Those in both groups had comparable values for the left ventricular ejection fraction (LVEF) and the left ventricular end diastolic volume (LV EDV). The main characteristics of the patient groups are given in Table 1.

Table 1: The main characteristics of patients in this study (median 25th, 75th percentile or numeric percentage is presented)

Index	Group I (n = 26)	Group II (n = 34)	p value
Age (days)	21.2 (+6.9; 32.7)	21.0 (11.7; 29.4)	0.51
Weight (kg)	3.3 (2.4; 4.1)	3.4 (2.9; 4.0)	0.31
LVEF (%)	74 (65; 80)	76 (64; 82)	0.81
LV EDV (ml)	11.9 (9.0; 17.1)	12.9 (8.0; 23.0)	0.41

Surgical treatment was successful in all cases and there were no lethal outcomes during the operation. In total, the study recorded nine deaths, all of which occurred in the immediate postoperative period. The assessment of the lethality by group is presented as follows.

In Group I, the mortality rate was 19.2% of patients, of which 7.7% of deaths were attributable due to the development of multi-organ failure, with 7.7% of patients dying from sepsis in combination with multiple organ failure and sepsis, and one case (3.8%) being due to the development of a cerebral edema and its wedging. During the follow-up period of three years, there were no lethal outcomes in this group. In Group II, 11.7% of patients died, the most frequent cause being the development of multiple organ failure in

combination with sepsis (5.9%), followed by 2.9% of deaths being due to the development of multiple organ failure and another 2.9% of deaths being caused by brain edema. During the following observation period of three years, a further two patients died. In this instance, the cause of death was the development of cardiovascular insufficiency

in combination with pneumonia. Intra- and postoperative characteristics of patients are presented in Table 2.

Table 2: Intra- and postoperative characteristics of patients, where values are represented by the median (25th, 75th percentile) or numerical values as a percentage

Index	Group I (n = 26)	Group II (n = 34)	p value
Time of AC (mins)	152 (129; 193)	129 (101; 154)	0.001
Occlusion of the aorta (mins)	69 (44; 92)	54 (39; 73)	0.29
Rectal temperature (°C)	20 (18; 21)	25 (24; 27)	0.001
Time of circulatory arrest (mins)	24 (20; 27)	22 (19; 33)	0.69
Fluid balance (ml/kg)	-5 (-22.9; 15.1)	25.4 (2.8; 57.1)	<0.001
Intraoperative haemorrhage (ml/kg)	13.5 (6.9; 18.1)	16.1 (11; 21.1)	0.19
Postoperative haemorrhage (ml/kg)	17.9 (10.9; 35)	22.1 (13.1; 37.3)	0.51
Blood transfusion (ml/kg)	23 (13.1; 56.2)	37.1 (25.1; 62)	0.03
Ventilation of lungs (hrs)	121 (64; 210)	151 (81; 331)	0.07
LV EF (%)	72 (70; 81)	75 (71; 83)	0.72
LV EDV (ml)	13 (9; 19)	8.9 (6; 17)	0.002
Inotropic index (hrs)	7 (4; 9)	10.5 (4 14)	0.05
24	6 (4; 9)	10 (5; 11)	0.5
48			
Neurological complications (%)	9 (37.5)	3 (8.8)	0.002
Acute renal damage (RIFLE) (n)	6 (25)	22 (64.7)	0.03
(%)			
Risk	3 (11.5)	3 (8.8)	
Injury	1 (3.8)	5 (14.7)	
Failure	2 (7.6)	14 (41.1)	0.001
Loss	0	0	
ESRD	0	0	
Mortality (n) (%)	5 (19.2)	4 (11.7)	0.41

Table 2 indicates that a reliably significant difference in results can be obtained when comparing groups during the period of artificial circulation. In the Group I patients, the mean time of administration is significantly higher than that of the Group II patients. Furthermore, the aorta occlusion is not significantly different between the groups studied. Group I patients indicated a negative fluid balance, in contrast with Group II. The evaluation of perioperative blood loss did not reveal any significant differences between groups, but the patients of Group II received more blood transfusions: 37.1 (25.1, 62) vs. 23 (13.1, 56.2) ml/kg in Group I, where $p = 0.03$. When assessing the course of the early postoperative period, there was a greater percentage of neurological complications amongst Group I patients, whereas the neurological status of Group II patients only changed in 8.8% of patients. Only two Group II patients experienced temporary motor dysfunctions, which regressed within a month. Altogether, 7.7% of Group I patients developed serious neurological complications associated with the development of cerebral edema, and one patient in this group died of multiple organ failure in combination with sepsis. Thus, the odds ratio (OR) for neurological complications was significantly lower in Group II: OR (95% DI) 0.19 (0.04-0.72), $p = 0.02$.

During multifactorial logistic regression analysis, the isolated groups were the only factor that had a significant effect on the entire treatment results. There was a greater incidence of acute renal damage in Group II patients. In this instance, the multifactorial logistic regression analysis demonstrated that, in relation to the development of acute renal damage, the OR = 0.17 (0.03-0.70), $p = 0.02$. When the maximum inotropic

index increases at 10 unit increments, there is a threefold increase in OR for acute renal damage where, on the first day, OR (95% DI) 2.98 (1.94-4.01), $p = 0.03$. Such multifactorial models do not include such factors as the intraoperative fluid balance and temperature that independently influence the outcome. This is attributable to the multicollinearity problem and the rather limited sample size. In order to assess the effects of group isolation in relation to the severity of acute damage to the renal tissue, ordinal logistic regression was used. In this case, the RIFLE scale has been applied as an outcome variable.

The analysis indicated that the severity of kidney damage under the RIFLE scale is significantly higher in Group II patients. Thus, the risk of developing severe renal dysfunction is significantly higher when utilising the APB method. These data are statistically confirmed by the higher frequency of application of peritoneal dialysis in this group during the postoperative period, when the procedure was undertaken in 58.3% of cases. Multivariate analysis is indicative that the maximum inotropic index during the first 24 hours is an independent predictor of the development of dysfunction in kidney tissue. Furthermore, there is a strong positive correlation (95% CI) between the level of rectal temperature and the incidence of intraoperative disorders of the acid-base state (blood lactate level). The data concurs with scientific data from the experimental papers (1,11,12). This fact may indicate more severe hypoxic changes in the lower half of the trunk, including vital organs in the abdominal cavity, when the circulation of the lower body stops at a higher temperature.

CONCLUSIONS

The study findings indicate that patients with congenital aortic pathology constitute a high-risk group regarding the incidence of perioperative complications and death. This is attributable to the initial severity of this congenital pathology and the complexity of surgical treatment. Reconstructive operations on the AA using selective antegrade perfusion as a brain protection method are accompanied by a decreased incidence of neurological complications, when compared with the deep hypothermic circulatory arrest method, but have a greater impact on the development of renal complications.

CONFLICT OF INTERESTS

The authors declare that there are no conflict of interests.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available from the corresponding author upon reasonable request.

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None.

STUDY ASSOCIATION

This study is not associated with any thesis or dissertation work.

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XÜLASƏ

Yeni doğulmuş körpələrdə aorta qövsünün rekonstruktiv cərrahi əməliyyatından sonra böyrək və nevroloji fəsadların yaranma riski

Yuriy SINELNIKOV

Rusiya Federasiyası Səhiyyə Nazirliyinin Akademik E. Meşalkin adına Novosibirsk Elmi-Tədqiqat Qan Dövranı Patologiyası İnstitutu, Rusiya Federasiyası

Elnur HƏSƏNOV

Azərbaycan Respublikası Səhiyyə Nazirliyinin M.Topçubaşov adına Milli Cərrahiyyə Mərkəzi, Bakı, Azərbaycan

Faiq MİRZƏZADƏ

Azərbaycan Respublikası Səhiyyə Nazirliyinin M.Topçubaşov adına Milli Cərrahiyyə Mərkəzi, Bakı, Azərbaycan

Aorta qövsünün (AQ) bərpası zamanı daxili orqanların və beynin optimal müdafiəsini təmin edəcək üsulun seçilməsi çox önəmlidir. Əvvəllər hipotermik qan dövranı üsulunun ən optimal üsul olduğu düşünülürdü. Lakin, son zamanlar yetkin xəstələrdə və bəzi uşaqlarda aortada rekonstruktiv əməliyyatlar apararkən orta dərəcədə hipotermiya ilə anteqrad serebral perfuziyanın tətbiqi daha üstün olmuşdur. Belə hallarda, davamlı serebral perfuziya nevroloji fəsadların tezliyini azaldır. Lakin, AQ-dən ən uzaq məsafədə yerləşən orqan sistemlərinə dəyən zərərin dərəcəsi qeyri-aydın olaraq qalır.

Bu tədqiqatın məqsədi kiçik yaşlı uşaqlarda AQ-də rekonstruktiv əməliyyat zamanı beynin və daxili orqanların mühafizəsinin müxtəlif üsullarının effektivliyinin və təhlükəsizliyinin qiymətləndirilməsindən ibarətdir.

AQ-də rekonstruktiv əməliyyat keçirmiş 60 pasiyentin retrospektiv təhlili aparılmışdır. Beynin mühafizəsi üçün müxtəlif üsullar tətbiq etməklə, nevroloji vəziyyət və daxili orqanlara dəyən zərərin dərəcəsi qısa və uzunmüddətli perspektivdə qiymətləndirilmişdir. Dərin hipotermik qan dövrasının dayandırılması şəraitində AQ-nün anadangəlmə patologiyasının cərrahi korreksiyası 26 xəstədə (I Qrup) aparılmış və 34 xəstədə beynin anteqrad birtərəfli selektiv perfuziyası istifadə edilmişdir (II Qrup). Sinir sistemində fəsadlar I Qrup pasiyentlərin 28.5% -də, II Qrup pasiyentlərin isə 7.9% -də aşkar edilmişdir. Beləliklə, nevroloji halın inkişafı ilə bağlı risk nisbəti II Qrup pasiyentlərdə əhəmiyyətli dərəcədə aşağı olmuşdur: 0.17 (0.06–0.69), $p = 0.02$. Yalnız, bu Qrupun pasiyentlərində böyrək disfunksiyası 58.7%, I Qrupun pasiyentlərində isə bu göstərici 23.7% təşkil etmidir ki, burada $p = 0.02$.

Açar sözlər: AQ-nün rekonstruksiyası, yeni doğulmuş körpə, dərin hipotermiya, anteqrad serebral perfuziya, böyrək disfunksiyası

РЕЗЮМЕ

Риск почечных и неврологических осложнений после реконструктивных операций дуги аорты у новорожденных

Юрий А.СИНЕЛЬНИКОВ

Новосибирский Научно-Исследовательский Институт Патологии Кровообращения им. Академика Е. Мешалкина Минздрава России, Российская Федерация

Эльнур ГАСАНОВ

Национальный Центр Хирургии им. М. Топчубашова Министерства Здравоохранения Азербайджанской Республики, Баку, Азербайджан

Фаиг МИРЗААДЕ

Национальный Центр Хирургии им. М. Топчубашова Министерства Здравоохранения Азербайджанской Республики, Баку, Азербайджан

Очень важно выбрать метод, который обеспечит оптимальную защиту внутренних органов и головного мозга при реконструкции дуги аорты (ДА).

Ранее наиболее оптимальным методом считался гипотермический метод кровообращения. Однако в последнее время предпочтение отдается использованию антеградной церебральной перфузии с умеренной гипотермией при реконструктивной хирургии аорты у взрослых пациентов и некоторых детей. В таких случаях постоянная церебральная перфузия снижает частоту неврологических осложнений. Однако степень повреждения систем органов на самом удалении от ДА остается неясной. Целью данного исследования было оценить эффективность и безопасность различных методов защиты мозга и внутренних органов во время реконструктивных операций у детей раннего возраста. Проведен ретроспективный анализ 60 пациентов, перенесших реконструктивную операцию ДА. Используя различные методы защиты мозга, оценивали неврологическое состояние и степень повреждения внутренних органов в краткосрочной и долгосрочной перспективе. Хирургическая коррекция врожденной патологии ДА на фоне глубокой гипотермической остановки кровообращения проведена 26 пациентам (I группа), а 34 пациентам (II группа) применена антеградная односторонняя селективная перфузия головного мозга. Осложнения со стороны нервной системы выявлены у 28,5% пациентов I группы и 7,9% пациентов II группы. Таким образом, коэффициент риска развития неврологических состояний у пациентов II группы был значительно ниже: 0,17 (0,06–0,69), $p = 0,02$.

Только у пациентов этой группы нарушение функции почек составило 58,7%, а у пациентов I группы этот показатель составил 23,7%, где $p = 0,02$.

Ключевые слова: Реконструкция ДА, новорожденный, глубокая гипотермия, антеградная церебральная перфузия, нарушение функции почек