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Original Article / Özgün Makale

Aortic arch and intracardiac repair without circulatory arrest in neonates and infants

Yenidoğan ve infantlarda dolaşım aresti uygulamadan aortik arkus ve intrakardiyak tamiri

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Background: In this article, we aimed to report our surgical experiences with selective antegrade cerebral perfusion combined with the aortic arch and intracardiac surgery in neonates and infants.

Methods: Medical data of 27 consecutive patients (18 boys, 9 girls; mean age 9.9+1.7 days; range 1 to 26 days) who undergoing aortic arch and intracardiac repair between March 2007 and April 2012 were retrospectively analyzed. The link between perioperative risk factors and 30-day mortality following surgery were investigated.

Results: The mean body weight of patients were 3.2±0.9 kg. Major associated cardiac defects were present in 12 and included truncus arteriosus (Vaan Pragh type 4) (n=2), transposition of the great arteries (n=5), double outlet right ventricle with Taussing Bing anomaly (n=2), and aortopulmonary window defect (n=3). Renal insufficiency and dialysis were statistically significantly associated with mortality [Chi square 27 (p=0.000) and 20.66 (p=0.000), respectively].

Conclusion: Aortic arch repair with simultaneous intracardiac surgical repair can be done with selective antegrade cerebral perfusion at a single stage in neonates and infants.

Keywords: Antegrade cerebral perfusion; aortic arch intracardiac surgery; neonatal infant.

Amaç: Bu yazıda yenidoğan ve infantlarda aortik arkus ve intrakardiyak tamir ile birlikte, selektif antegrad serebral perfüzyon ile yapılan cerrahi deneyimimiz bildirildi.

Çalışma planı: Mart 2007 - Nisan 2012 tarihleri arasında arkus aort ve intrakardiyak tamiri uygulanan 27 ardışık hastanın (18 erkek, 9 kız; ort. yaş 9.9+1.7 gün, dağılım 1-26 gün) tıbbi verileri retrospektif olarak incelendi. Ameliyat sırası risk faktörleri ve ameliyat sonrası 30 günlük mortalite arasındaki ilişki incelendi.

Bulgular: Hastaların ortalama vücut ağırlığı 3.2±0.9 kg idi. On iki hastada majör kardiyak defekt vardı ve bunlar trunkus arteriozus (Vaan Pragh tip 4) (n=2), büyük arterlerin transpozisyonu (n=5), çift çıkışlı sağ ventrikülde Taussing Bing anomalisi (n=2) ve aortopulmoner pencere defekti (n=3) idi. Böbrek yetmezliği ve diyaliz ile mortalite arasında istatistiksel olarak anlamlı bir ilişki bulundu [Ki kare, sırasıyla 27 (p=0.000) ve 20.66 (p=0.000)].

Sonuç: Yenidoğanlarda ve infantlarda, intrakardiyak cerrahi tamir ile eş zamanlı arkus aort tamiri, tek aşamalı selektif antegrad serebral perfüzyon ile yapılabilir.

Anahtar sözcükler: Antegrad serebral perfüzyon; arkus aort intrakardiyak cerrahi; yenidoğan bebek.

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Intracardiac defects associated with aortic arch obstruction are rare congenital anomalies and have a high surgical risk. The use of correct surgical techniques for the protection of the brain, spinal cord, and myocardium is crucial in concomitant surgery featuring aortic arch and intracardiac surgical repairs. Single-stage repair through a median sternotomy either with or without circulatory arrest has been adopted and has recently gained popularity among surgeons with good results.[1,2] In these surgical strategies, cerebral protection is provided by the use of hypothermic circulatory arrest (HCA) or selective antegrade cerebral perfusion (SACP) in infants. Hypothermia has been proven to decrease cellular metabolism by lowering oxygen consumption, thus reducing the adverse impact of ischemia.[3] However, deep HCA and SACP, which are used as perfusion strategies for aortic arch repair in neonates and infants, may induce cerebral dysfunction and myocardial ischemia. In the last decade, several technical advances in neonatal and infant aortic arch repair surgery have diminished the incidence of cerebral dysfunction and myocardial ischemia. However, we believe that the use of SACP for brain protection in conjunction with improvements in anesthesia and cardiac intensive care provide better outcomes for these critical patients. Hence, the aim of this study was to identify the perioperative factors that influence patient outcomes after aortic arch and intracardiac surgical repairs.

PATIENTS AND METHODS

Twenty-seven consecutive patients (18 boys and 9 girls; mean age 9.9±1.7 days; range 1 to 26 days) who underwent surgery for the single-stage repair of a hypoplastic or interrupted aortic arch and aortic coarctation (AoCo) associated with intracardiac anomalies were evaluated in a retrospective study over an almost five-year period from March 2007 to April 2012. The mean weight of the patients was 3.2±0.9 kg (range 2.600 to 4.350 kg), and the basal surface area (BSA) was 0.38 m^2 (Table 1).

The clinical characteristics included a simple ventricular septal defect (VSD), either with or without an atrial septal defect (ASD), in 15 patients. In addition, major associated cardiac defects were present in 12 patients, with two having truncus arteriosus (Vaan Pragh type 4), five having transposition of the great arteries (TGA), two having double outlet right ventricle (DORV) with the Taussig Bing anomaly, and three having an aortopulmonary window. Furthermore, 16 patients had AoCo, eight had AoCo with a hypoplastic arch, and three had an interrupted aortic arch. The surgery was performed mainly by four surgeons and their associates, and the study was approved by the hospital institutional ethics committee.

The following prognostic risk factors were used to determine postoperative 30-day morbidity and mortality: *(i)* preoperative parameters such as age, height, weight, gender, BSA, renal failure, and congestive heart failure), *(ii)* intraoperative parameters such as cardiopulmonary bypass (CPB) time, aortic cross-clamp (ACC) time, and SACP time, and *(iii)* postoperative parameters such as cardiac and renal failure, the use of peritoneal dialysis, postoperative permanent and temporary neurological dysfunction, treatment in the intensive care unit (ICU), and length of in-hospital stay.

All of the infants who underwent elective surgery underwent a preoperative evaluation made up of electrocardiography, chest radiography, echocardiography, and routine blood tests for major surgical procedures. Other than for emergency procedures, each patient had their preoperative evaluation one day prior to the surgery, and in the operating room, the patients had intravenous access placement prior to the standard anesthesia for induction. The equipment used during routine

Table 1. Demographic and diagnostic properties of the patients

	Alive (n=28)				Dead (n=4)				
	Mean±SD	Min.-Max.	Median	IR	Mean±SD	Min.-Max.	Median	IR	*p*
Gestational age (weeks)	26.5±1.8	23-29	26.5	3	24.2±0.5	24-25	24	1	0.023*
Birth weight (grams)	852±127	540-990	855	185	630±111	490-730	650	210	0.01*
Age at time of operation (days)	29.1±2.2	25-34	29	4	27.5±1.2	26-29	27.5	3	0.15‡
Weight of the patients at time of operation (grams)	848±120	490-980	890	145	640±134	510-800	625	255	0.01*
Length of operation (min)	17.7±3.2	13-25	17.5	5	23.2±5.6	15-28	25	10	0.06*

IR: Interquartile ranges; * Mann-Whitney U test was used; ‡ Student t-test was used.

monitoring included three-lead electrocardiography, a central venous catheter, invasive right radial artery monitoring, pulse oximetry, blood gas values, and esophageal temperatures. Furthermore, all of the patients were premedicated with intramuscular ketamine 5 mg/kg, midazolam 0.1 mg/kg, and atropine 0.02 mg/kg. Induction of anesthesia was performed via midazolam 0.1-0.2 mg/kg, fentanyl 8-10 mcg/kg, and ropivacaine 0.6 mg/kg, and after the tracheal intubation, it was maintained with midazolam 0.04 mg/kg/h, fentanyl 5-8 mcg/kg/h, and ropivacaine 0.2 mg/kg every half an hour. An additional volatile anesthetic (sevoflurane 1-2%) was provided during the surgical procedure, and dopamine, dobutamine, milrinone, and epinephrine were ordered for the patients based on dose micrograms per kilogram per minute (mcg/kg/min). Conventional ultrafiltration was also performed before weaning from CPB.

A median sternotomy was used in all surgical procedures, and the thymus was totally excised. The aortic arch with its branches and ducts was then dissected and visualized, and the descending thoracic aorta was totally mobilized without sacrificing the intercostal arteries. Next, the neck vessels were mobilized and looped, and elastic snares were passed around them. Alpha-stat acid-base management was employed for all of the patients as well. During cooling, the descending thoracic aorta was completely mobilized to achieve a tension-free anastomosis, with great care being taken not to damage the recurrent laryngeal nerve. When the esophageal temperature reached 28 °C, the neck vessels were snared down to initiate SACP. After completion of the aortic anastomosis, a needle was inserted into the proximal part of the aortic arch for de-airing, and once the flow in the aorta was established, the neck vessel snares were released.

When AoCo occurred, the arterial cannula was inserted into the lateral side of the distal ascending aorta with a 6F or 8F a DLP® pediatric one piece arterial cannula (Medtronic, Inc, Minneapolis, MN, USA) The patent ductus arteriosus (PDA) had been ligated and divided routinely at the initial phase of CPB. The coarcted aortic segment was then proximally and distally clamped and excised, and an end-to-end anastomosis was completed with a 7/0 polypropylene continuous suture.

For repair of AoCo with a hypoplastic arch, the arterial cannula was inserted into the lateral side of the distal ascending aorta (close to the innominate artery). In cases where the distal ascending aorta was not sufficient for cannulation, direct innominate artery cannulation was done with a 6F DLP® pediatric one piece arterial cannula (Medtronic, Inc., Minneapolis, MN, USA). Next, SACP was established by inserting and snaring the aortic cannula into the innominate artery through the ascending aorta, and the left subclavian and left common carotid arteries were also looped and snared. Afterwards, a longitudinal incision was made along the undersurface of the arch, and the arch reconstruction was completed with a 7/0 polypropylene continuous suture after the coarcted segment and ductal tissue were excised (Figure 1).

Just as an interrupted aortic arch where the lower body perfusion depends on the ductus, when we encountered ductal-dependent circulation, both the right and left pulmonary arteries were looped and snared before CPB was performed. The two primary arterial cannulation sites were the brachiocephalic and main pulmonary artery. The cannulas were then Y-connected, CPB was started, and cooling was initiated. A clamp was then placed on the distal arch, and SACP was established in the same manner that was previously described. After the pulmonary artery cannula was removed, the PDA was divided and resected, and the aortic anastomosis was performed.

For the duration of SACP, the pump flows were reduced between 50 and 100 mL kg^{-1} min^{-1} to maintain the right radial artery pressure at 40-60 mmHg and avoid cerebral hyperperfusion syndrome. Following

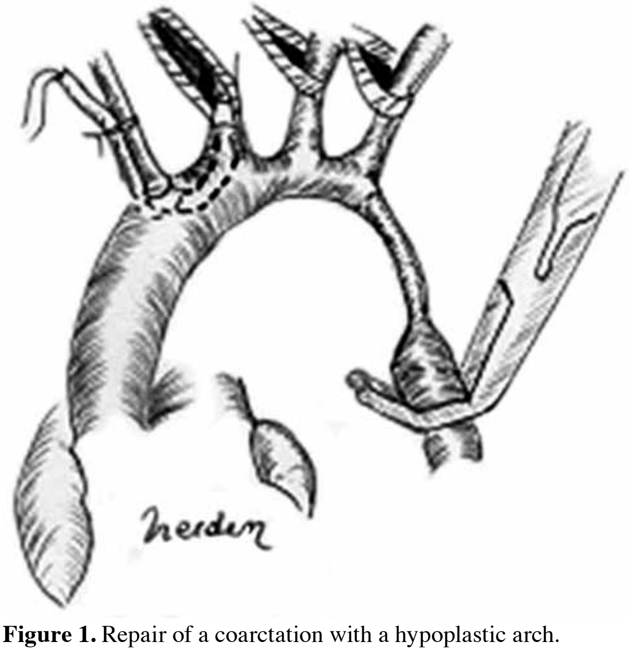

Figure 1. Repair of a coarctation with a hypoplastic arch.

Table 2. Peroperative continuous variables of the patients

	Alive	Dead	
	Mean±SD	Mean±SD	*p*
Age (days)	10.8±8.8	6.2±10.5	0.138
Weight (gr)	3374±466	2890±96	0.005**
Length (cm)	51.0±2.1	48.8±1.3	0.038*
Body surface area (m^2)	3.900±0.0	3.880±0.0	0.005**
Operation age (days)	19.1±7.6	11.2±10.6	0.060
Aortic cross clamp time (minutes)	108.0±32.3	162.2±21.5	0.004**
Cardiopulmonary bypass time (minutes)	158.0±21.1	188.2±27.1	0.024*
Anteograde cerebral perfusion time (minutes)	38.2±5.9	51.6±8.7	0.002**
Intensive care unit (days)	6.7±3.5	23.0±11.9	0.001**
In hospital stay time (days)	18.8±3.2	27.4±12.4	0.220

SD: Standard deviation; * p<0.05; ** p<0.01.

the completion of the aortic arch reconstruction, adequate de-airing was completed, the neck vessel snares were released, the aortic cannula was reposed into the aortic arch, and the flows were increased to normal levels (150-200 mL kg^{-1} min^{-1}). For the duration of the aortic arch reconstruction and intracardiac repair, antegrade blood cardioplesia was given at 20-minute intervals, and the left ventricle was vented through the interatrial incision. Under cardioplegic arrest, the required intracardiac repairs were then performed.

Statistical analysis

The SPSS version 16.0 for Windows statistical program (SPSS Inc., Chicago, IL, U.S.A.) was used for all analyses, and the categorical variables between the groups were analyzed by using a chi-square test. For each continuous variable, normality was checked via the Kolmogorov-Smirnov test, and comparisons between groups were carried out using a one-way independent samples t-test for normally distributed data. In addition, discriminate analysis was used to evaluate any associations between mortality and prognostic risk factors, with mortality being accepted as the dependent variable. A *p* value of 0.000 suggested that the observed counts are significantly different than what we expected, with a p value of <0.05 being statistically significant.

RESULTS

After the operation, five patients (two girls and three boys) died (18.5%). All of them were analyzed for their continuous variables, and we determined that there was a mean CPB time of 163±2 minutes, an mean ACT time of 118±4 minutes, and a mean SACP time of 40±8 minutes. The average age at the time of the operation was 17±8 days. Additionally, there was an average ICU stay of 9.7±8.5 days, and an average in-hospital stay of 20±6.6 days (Table 2). An analysis of variance (ANOVA) along with a t-test was performed to identify the variables that differed significantly between the two groups, and for those variables, a stepwise discriminant analysis (a multivariate method that allows for the classification of individuals into one of a number of known groups (e.g., dead and alive) according to the values of the perioperative factors) was conducted to isolate predictive factors. Furthermore, the rate of correct prediction was also calculated for the same factors. Moreover, all of these continuous variables were normally distributed at a 0.05 significance level, and each of these variables was tested for mean

Table 3. Perioperative characteristics of the deceased patients

Age/sex	Weight (kg)	BSA (m^2)	Aortic coarctation	VSD	DORV	Truncus arteriosus	TGA	Operatin age (days)	ACC (min)	CPB (min)	SACP (min)	ICU stay days	Renal insufficiency	Periteneol dialysis	Length of in-hospital stay
25/M	2.9	0.38	+	+	-	-	-	30	126.0	140	46	40	+	-	45
2/F	2.85	0.38	+		-	-	+	5	170.0	200	50	15	+	+	18
2/M	3	0.39	+		-	-	+	8	160.0	196	48	30	+	+	36
1/M	2.75	0.38	+	+	-	+	-	6	175.0	200	47	11	+	+	18
1/F	2.95	0.38	+	+	+	-	+	7	180.0	205	67	19	+	+	20

BSA: Body surface area; VSD: Ventricular septal defect: DORV: Double outlet right ventricle; TGA: Transposition of great arteries; ACC: Aortic cross-clamp time; CPB: Cardiopulmonary bypass; SACP: Selective antegrade cerebral perfusion; ICU: Intensive care unit.

values in both the deceased and living patients with an independent samples t-test.

For predicting the perioperative mortality with these parameters, mortality was a dependent variable while the other variables (ACC, SACP, CBP, ICU, BSA, weight, operation age, length of in-hospital stay) were independent. Discriminate analysis was used to determine the effect that these variables had on mortality, and this showed a 0.78 probability of mortality when in the patients were in the ICU. Furthermore, the probability of mortality was 0.569 during CBP, 0.481 during ACC, 0.372 during SACP, and 0.405 during the in-hospital stay. Hence, the perioperative factors that affected mortality in order of importance were length of ICU stay, CPB time, ACC time, length of in-hospital stay, and SACP time, whereas those with the lowest probability of mortality were BSA (0.336), weight (0.308), and age at time of surgery (0.264). Thus, we can speculate that younger age, lower body weight, and lower BSA had a negative effect on survival.

All of the five patients who had renal insufficiency died after surgery, so the non-continuous parameters of renal insufficiency and dialysis were not included in our discriminant function. However, these two factors were tested using a chi-square test for statistical significance regarding mortality, and the values were 27 (p=0.000) and 20.66 (p=0.000), respectively.

In our study group, we only had two patients whose mortality could not be predicted by discriminant function analysis. One of them was a newborn who was brought to the hospital on the first day of his life who was diagnosed with truncus arteriosus (type II), AoCo, and VSD. He underwent an operation on the sixth day and had elapsed times of 200 minutes, 175 minutes, and 47 minutes for the CPB, ACC, and SACP, respectively. After the surgery, the patient had low cardiac output followed by renal insufficiency. Peritoneal dialysis was initiated, but he died on the postoperative 11th day. This patient was predicted to live according to our discriminant function. The second patient was supposed to die according to our analysis. He was also a one-day-old baby who weighed 2,850 g and had been diagnosed with DORV, TGA, AoCo, and VSD. He underwent surgery on the seventh day and had an elapsed CBP time of 190 minutes along with an ACC time of 168 minutes and SACP time of 48 minutes. He stayed in the ICU for 17 days and was discharged from the hospital on the postoperative 28th day.

Five patients died after their operation in the ICU, two of whom had been diagnosed with AoCo and TGA. Both had long CPB, ACC, and SACP times and died due to low cardiac output within the first 24 hours. The third patient was diagnosed with AoCo and VSD and suffered from a fever after spending three days in the ICU. He died due to sepsis. The fourth patient had a preoperative diagnosis of DORV and AoCo as well as preoperative congestive heart failure. This baby weighed 2,750 g at surgery and had necrotizing enterocolitis after the initiation of feeding via a nasogastric tube, postoperatively. The fifth patient had been diagnosed with DORV, TGA, AoCo, and VSD. This baby also had a coronary anomaly, discovered during surgery, in which all of the coronary arteries were originating from a single orifice. Although the baby was not injured during the operation, he had low cardiac output and died three weeks later. All five of these patients had renal insufficiency, and four underwent peritoneal dialysis in the ICU.

DISCUSSION

In infants and neonates, repair of the hypoplastic aortic arch and associated cardiac anomalies presents a surgical challenge.[4] The surgical treatment of the hypoplastic aortic arch and associated cardiac anomalies depends on the pathological involvement of the ascending, transverse, and proximal part of the descending thoracic aorta. In our study, we determined that the independent predictors of mortality were the length of ICU and in-hospital stays along with the SACP, ACC, and CPB times. We also noted that the non-continuous variables, such as postoperative renal failure and use of peritoneal dialysis, were statistically significant.

The SACP technique for single-stage total arch repair has been successfully used in neonates and infants in our clinic, and we have seen no postoperative permanent or temporary neurological dysfunction. Therefore, we can speculate that the perfusion strategy for an aortic arch anomaly using the continuous cerebral perfusion technique has minimized the neurological complications. The mortality rate of our study was higher than other previously published series,[1,2] but this might have been due to the complex conditions associated with our patients and the steep learning curve.

Hypothermic circulatory arrest may induce neurological complications, and deep hypothermia is suspected of being responsible for the generalized inflammatory reaction tissue damage on the brain, the lung capillary leak syndrome, and coagulopathy. Hence, deep hypothermia should be combined with a higher degree of hemodilution to counteract the increased fluid viscosity and cell membrane rigidity, which subsequently reduces the blood's oxygen carrying capacity.[5] Recent studies have shown the superiority of brain protection associated with higher hematocrit levels.[6] During hypoplasic aortic arch surgery, the main concern is protecting cerebral and myocardial functions. We believe that when SACP is carried out, there is no longer a need for deep hypothermia. Thus, a moderate grade of hypothermia with a mild degree of hemodilution might prove to be effective in protecting other organs from ischemic damage and would also optimize the cerebral oxygen supply. Even though deep HCA provides significant protection from brain damage, it may be associated with transient cerebral dysfunction and delayed psychomotor development. Since the adverse effects of HCA during arch repair have previously been described,[2,3] the current trend is to avoid it whenever possible.

In addition to the neurological adverse effects of HCA, low cardiac output states can persist after coarctation and hypoplastic aortic arch repair as a result of CPB time and preoperative left ventricular dysfunction. For this reason, some centers prefer to perform the isolated myocardial perfusion technique to minimize myocardial ischemia during total circulatory arrest.[7] Nearly one decade ago, a technique was described in which extended aortic arch anastomosis was used in conjunction with selective cerebral perfusion and a working beating heart.[8] Afterwards, Lim et al.,[9] described a combined perfusion technique that used two cannulas, with one being placed into the innominate artery and the other into the aortic root. By this method, an extended end-to-side anastomosis was performed with continuous cerebral perfusion and a nonworking beating heart.

In this study, we used an innominate artery perfusion technique for cerebral protection in the patients who underwent extended aortic arch reconstruction, and brain perfusion was done through the right innominate artery to avoid the neurological complications associated with the circulatory arrest method.[10] We believe that the use of this method reduced the risk of cerebral edema due to the higher arterial blood flow during SACP because it involves careful monitoring of the right radial artery pressure and near-infrared spectroscopy.[11] The appropriate perfusion rate for the brain in neonates during selective cerebral perfusion remains controversial. An ideal flow rate of between 50 and 100 ml kg^{-1} min^{-1} has been advocated on the basis of theoretical calculations, but many different protocols have been proposed.[12,13] This uncertainty regarding the optimum cerebral flow and management of SACP has prompted surgeons to utilize control systems such as transcranial Doppler ultrasonography (USG) and near-infrared spectroscopy to evaluate the effectiveness of cerebral perfusion.[14] In our experience, the use radial arterial pressure has proven to be a simple and reliable method for adjusting the flow rate during SACP. In our study populations, there was no evidence of cerebral hyperperfusion syndrome, and a flow rate of between 50 and 100 mL kg^{-1} min^{-1} was used to maintain a perfusion pressure of between 40 and 60 mmHg on the radial artery. Therefore, we hypothesize that the pressure in the radial artery is related to cerebral blood flow and not the flow rate.[15]

In conclusion, for infants who are scheduled to undergo aortic arch repair with concomitant intracardiac surgical repair, surgery can be safely performed via selective cerebral perfusion at a single stage.

Declaration of conflicting interests

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