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Original Article / Özgün Makale

Late primary arterial switch operation in patients with transposition of great arteries and intact ventricular septum

Büyük arterlerin transpozisyonu ve intakt ventriküler septumlu hastalarda geç primer arteriyel switch ameliyatı

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ABSTRACT

Background: This study aims to report the results of late arterial switch operation performed in patients with transposition of the great arteries and intact ventricular septum after the third week of life.

Methods: Between January 2010 and November 2015, a total of 14 patients (8 boys, 6 girls; mean age 42 days; range 22 to 125 days) with the diagnosis of transposition of the great arteries and intact ventricular septum in whom arterial switch operation was performed after the postnatal third week were retrospectively analyzed using the hospital database.

Results: Eight patients had severe cyanosis (SO_2 ≤70%), 11 patients were receiving prostaglandin E_1 infusion, and four patients were on mechanical ventilation support at baseline. Balloon atrial septostomy was on three patients previously. Preoperative cardiac catheterization was performed on four patients. Twelve patients were transferred to the intensive care unit with opened chest postoperatively. The median duration of mechanical ventilation, intensive care unit and hospital stay were seven days, 12 days and 17 days, respectively. Peritoneal dialysis was performed on three patients. Three patients developed rhythm problems and three patients developed sepsis during the intensive care unit stay. One patient needed extracorporeal life support. No mortality was seen in any patient.

Conclusion: Late arterial switch operation can be performed safely in patients with transposition of the great arteries and intact ventricular septum after a detailed evaluation and with an efficient, advanced, and suitable postoperative intensive care unit monitorization.

Keywords: Arterial switch operation; newborn; transposition of the great arteries.

ÖZ

Amaç: Bu çalışmada büyük damarların transpozisyonu ve intakt ventriküler septumlu hastalarda yaşamın üçüncü haftasından sonra yapılan geç dönem arteriyel switch ameliyatı sonuçları sunuldu.

Çalışma planı: Ocak 2010 - Kasım 2015 tarihleri arasında, hastanenin veri tabanı kullanılarak doğum sonrası üçüncü haftada büyük damarların transpozisyonu ve intakt ventriküler septum tanısı ile arteriyel switch ameliyatı yapılan toplam 14 hasta (8 erkek, 6 kız; ort. yaş 42 gün; dağılım 22-125 gün) geriye dönük olarak incelendi.

Bulgular: Başlangıçta sekiz hastada şiddetli siyanoz (SO_2 ≤%70) vardı, 11 hasta prostaglandin E_1 infüzyonu kullanıyordu ve dört hastaya mekanik ventilasyon desteği verilmekteydi. Üç hastaya daha önce balon atriyal septostomi yapılmıştı. Dört hastaya ameliyat öncesi kardiyak kateterizasyon uygulandı. Ameliyat sonrası 12 hasta sternum açık şekilde yoğun bakım ünitesine nakledildi. Medyan mekanik ventilasyon, yoğun bakım ünitesi ve hastanede kalış süreleri sırası ile yedi gün, 12 gün ve 17 gün idi. Üç hastaya periton diyalizi yapıldı. Yoğun bakım ünitesinde kalınan süre içerisinde üç hastada ritim sorunu ve üç hastada sepsis gelişti. Bir hastada ekstra korporeal yaşam desteği gereksinimi doğdu. Hiçbir hastada mortalite gözlenmedi.

Sonuç: Ayrıntılı ameliyat öncesi değerlendirme sonrasında ve etkili, gelişmiş ve uygun ameliyat sonrası yoğun bakım ünitesinde monitörizasyon ile büyük damarların transpozisyonu ve intakt ventriküler septumlu hastalarda geç dönemde arteriyel switch ameliyatı güvenle uygulanabilir.

Anahtar sözcükler: Arteriyel switch ameliyatı; yenidoğan; büyük arterlerin transpozisyonu.

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Transposition of the great arteries (TGA) is the most common cyanotic congenital heart disease in the neonatal period.[1] The arterial switch operation (ASO) became the first choice for correction of TGA.[2,3] However, the feasibility of this operation after postnatal three weeks of age is still controversial. There are articles advocating atrial switch or two-stage ASO in children presenting late with TGA.[4] Recently, primary-ASO was reported in patients with TGA and intact ventricular septum (IVS) presenting after the first three weeks of life.[4-8] In this study, we report the results of late ASO performed in patients with TGA and IVS after the third week of life.

PATIENTS AND METHODS

A total of 14 patients (8 boys, 6 girls; mean age 42 days; range 22 to 125 days) with TGA in whom late ASO was performed after three weeks of age in our clinic between January 2010 and November 2015 were retrospectively analyzed using the hospital database. A written informed consent was obtained from each parent. The study protocol was approved by the local ethics committee. The study was conducted in accordance with the principles of the Declaration of Helsinki.

Patients with complex transposition (with ventricular septal defect and/or pulmonary stenosis) and those with single ventricle physiology were excluded. The presenting symptoms on admission and demographic characteristics of the patients including age, body weight, and gender were recorded in combination with their echocardiographic and catheterization findings. The type and duration of the operation, the cross-clamp time, length of intensive care unit (ICU) stay, and mechanical ventilation support were also recorded. In addition, problems during the ICU stay were noted.

On hospital admission, two-dimensional echocardiography (ECHO) was performed and the left ventricular geometry (dimension, shape and wall thickness) with the interventricular septal motion were evaluated. The parasternal and subcostal views were used to assess the configuration of the IVS. The patients were classified into three groups according to the interventricular septum-left ventricular geometry on preoperative ECHO: type 1: IVS bulging into the right ventricle (n=7), type 2: straightened IVS (n=4), and type 3: IVS bulging into the left ventricle (banana-shaped) (n=3). The left ventricular geometry was classified as conditioned (type 1 and type 2), or de-conditioned (type 3) left ventricle with ECHO. In addition, the presence of atrial septal defect (ASD), patent ductus arteriosus (PDA), aortic arch anatomy, or left ventricular outflow obstruction which can modify the left ventricular inflow and afterload were also analyzed. The left main coronary artery from sinus-1 and right coronary artery from sinus-2 were designated as normal patterns. Other coronary exit patterns were accepted as coronary abnormalities.

Restrictive interatrial communication was noted, if the peak gradient between the two atria was ≥8 mmHg by pulse wave (PW) Doppler ECHO.[1] In patients with a de-conditioned left ventricular catheter angiography was carried out. If the left ventricle/right ventricle pressure was >0.6, ASO was performed.

The continuation of patency of ductus by prostaglandin E_1 (PGE_1) infusion was targetted in all patients with a patent ductus. In patients with restrictive interatrial septum or metabolic acidosis, ductus tried to be kept opened with PGE_1 infusion even in patients without a visible patent ductus. Mechanical ventilation was initiated in patients who were unresponsive to medical treatment with ongoing hypoxia. These patients were operated without balloon atrial septostomy (BAS), even in case of hypoxia which was unresponsive to mechanical ventilation or PGE_1 treatment. Prostaglandin E_1 treatment was not initiated only in two patients of 60 and 125 days old. Balloon atrial septostomy was performed on two patients before their admission to our clinic. The only BAS procedure was performed on a patient with hypoxia due to ASD restriction in our clinic in whom the operation was postponed due to the presence of an infection.

All patients received enteral feeding until surgery. All operations were performed by a single surgeon.

Surgical technique

The operation was conducted with cardiopulmonary bypass (CPB) through standard aortic and bicaval cannulae under mild hypothermia. Cold blood cardioplegia was utilized approximately every 20 minute during cross-clamping. Cardioplegia was given into the aortic root before opening the aorta. A retrograde approach via the coronary sinus was used for the maintenance. More recently, cardioplegia strategy was replaced with the single dose Custadiol® HTK solution (Köhler Chemie GmbH, Germany) application. Following preparation of coronaries as small buttons, Lecompte maneuver was performed and the ascending aorta was reconstructed by an end-to-end anastomosis. Then, the aortic cross-clamp was released to allow the neoaortic root to be distended. The ideal locations for coronaries on the neoaorta were marked with a sterile pen. A stab wound was made at that mark taking care not to injure the previously marked anterior neoaortic commissure marked with a prolene suture. The aortic cross-clamp was re-applied. Through this tiny hole, the location of the neoaortic commissure was confirmed and the opening was enlarged to accommodate the coronary buttons. In all patients, pulmonary artery reconstruction was performed after the removal of cross-clamp. The pulmonary trunk was reconstructed with a single, three minute gluteraldehide-treated autologous pericardial patch. Ultrafiltration during bypass and modified ultrafiltration after bypass were used. A left atrial pressure monitoring line was inserted through the right superior pulmonary vein before weaning from CPB. The chest was left open at the end of surgery in all patients, except two due to safer early ICU follow-up in terms of hemodynamic stability and pulmonary dynamics. The chest was closed at the end of surgery at the discretion of the surgeon similar to the early ASO patients.

Electrocardiography (ECG), oxygen saturation, end-tidal carbondioxide (etCO), central venous pressure (CVP), invasive arterial pressure, left atrial pressure (with left atrial catheter), and cranial near-infrared spectroscopy (NIRS) were monitorized in all of the patients during the ICU stay.

Inotropic support was typically administered as milrinone (0.5 μg/kg/min) and a low dose of epinephrine (0.05 μg/kg/min) for the first few postoperative hours. Noradrenaline treatment was added, if coronary perfusion pressure (aortic diastolic pressure-central venous pressure) was found to be less than 20 mmHg. Selected patients were followed with borderline systemic pressures with cerebral and renal NIRS observations without increasing the inotropic support. Fentanyl and midazolam were used for sedation and analgesia. Total parenteral nutrition (TPN) support and minimal enteral feeding via nasogastric feeding tubes were initiated at the first postoperative day in all patients. An excessive volume load was avoided. In cases of low cardiac output not responding to inotropic vasodilator therapy, core cooling, paralysis, and peritoneal dialysis were performed. Mechanical support with extracorporeal membrane oxygenation (ECMO) was initiated in case of failure of conventional measures. Daily ECHO evaluation was performed during the ICU stay. Postoperative care included inotropic dosing, and extubation was achieved based on the quality of the left ventricular function at ECHO.

RESULTS

The median weight of the patients was 4 kg (range 2.3 to 5.4 kg). Two patients were two months or older during operation, of whom one was older than four months.

Eight patients were severely cyanotic (SO_2 ≤70%) and 11 patients were receiving PGE_1 infusion. Ten patients were followed with milrinone support, while four patients needed mechanical ventilation support preoperatively. Six patients had patent foramen ovale or small ASD and four patients had a large PDA.

Balloon atrial septostomy was performed on two patients before their admission to our clinic. It was done only in a patient with hypoxia and acidosis due to ASD restriction in our clinic in whom the operation was postponed due to the presence of an infection. Acidosis and hypoxia were improved; however, the type 1 configuration of the interventricular septum changed into type 2 after the BAS. The patient was operated at the seventh day of admission, when the infection resolved and discharged without any problem. The rest of the patients did not undergo BAS.

Eleven patients had well-conditioned left ventricular geometry (IVS type 1 and 2) and three patients had de-conditioned left ventricle (IVS type 3). The spatial relation of the great arteries was D-malposition in nine patients and side by side in five patients. The coronary artery patterns were 1LCX-2R pattern in 12 patients and 1L-2RCX pattern in two patients.

Preoperative cardiac catheterization was performed on four patients. Three patients had regressed (type 3-banana-shaped) left ventricle, which was suggestive of low left ventricular systolic pressure. Catheterization was performed to a patient, although the IVS was type 2, as he was 125 days old at the time of the initial diagnosis. The left ventricle/right ventricle pressure ratio was >0.6 in all patients.

The demographic and clinical data for the late switch patients are summarized in Table 1. The mean CPB time was 197±38.3 min, while the mean aortic cross-clamp time was 97±25.1 min. Twelve patients required delayed sternal closure. The median duration of sternal closure was three days (range 0 to 10 days). Postoperatively, the patients required a median of seven days of ventilation support (range 2 to 33 days), 12 days of ICU stay (range 3 to 48 days), and 17 days of hospitalization before discharge (range 7 to 57 days). The intraoperative and postoperative data for the late switch patients are shown in Table 2.

As there was low cardiac output in five patients, inotropic support with milrinone, adrenaline, and noradrenaline was initiated. Transient peritoneal

Table 1. The demographic and clinical data

Patient	Age (day)/ Gender	Weight (kg)	BSA (m^2)	BAS	ASD	Preoperative angiography	Significant PDA	Ventricular septal type	SO_2 %
1	25/M	4.2	0.26	Yes	Nonrestrictive	Yes	0	Type 3	>70
2	25/M	4.0	0.22	No	Restrictive	No	0	Type 2	>70
3	45/F	3.1	0.2	Yes	Nonrestrictive	No	0	Type 1	>70
4	43/F	4.0	0.23	No	Nonrestrictive	Yes	0	Type 3	<70
5	125/M	5.4	0.29	No	Restrictive	Yes	0	Type 2	<70
6	43/M	3.2	0.21	No	Restrictive	No	Large	Type 1	>70
7	24/F	3.3	0.2	No	Restrictive	No	0	Type 1	<70
8	23/M	3.2	0.2	No	Nonrestrictive	No	Large	Type 2	>70
9	60/F	4.6	0.24	No	Nonrestrictive	Yes	0	Type 3	<70
10	40/M	4.5	0.25	No	Nonrestrictive	No	0	Type 1	>70
11	22/M	2.3	0.16	No	Nonrestrictive	No	Large	Type 1	>70
12	43/F	3.4	0.2	No	Restrictive	No	Large	Type 1	<70
13	26/F	3.6	0.22	No	Restrictive	No	0	Type 1	<70
14	55/M	4.4	0.23	Yes	Restrictive	No	0	Type 2	<70

BSA: Body surface area; BAS: Balloon atrial septostomy; ASD: Atrial septal defect; PDA: Patent ductus arteriosus.

dialysis was performed on three of these patients, due to persistent metabolic acidosis and oliguria, despite the inotropic support.

Hemodynamically significant cardiac arrhythmia was observed in three patients during the ICU stay. Two of the patients were diagnosed with supraventricular tachyarrhythmia (SVT) and one of the patients had junctional ectopic tachycardia (JET). Tachyarrhytmias were resolved with intravenous adenosine administration in two patients with SVT. Core cooling and amiodarone infusion were initiated to the patient with JET. Sinus rhythm was recovered at the postoperative 48th hour.

Klebsiella pneumonia in hemocultures of two patients and *Pseudomonas aeruginosa* in the endotracheal aspirate culture of one patient were demonstrated and treated with antibiotics.

Only one patient (aged 23 days, with type 2 IVS) required six days of ECMO support for the left ventricular failure. The ECMO support was initiated at the postoperative sixth day, due to sudden hypotension and bradycardia. The ECMO support was discontinued six days later without any problems. He was discharged at the postoperative 57th day.

The oldest patient was 125 days old. He was diagnosed at three months of age and he had a further delay before the referral to our institution. Systemic arterial oxygen saturation was 50% to 60% on admission. Echocardiography confirmed the diagnosis of TGA-IVS and revealed a restrictive

Table 2. The intraoperative and postoperative data

Patient	CPB hypothermia (°C)	ECLS used	XC time (min)	CPB time (min)	Delayed sternal closure	Sternal closure duration (d)	MV support (h)	ICU stay (d)	Hospital stay (d)
1	20	N	104	238	Yes	5	240	14	18
2	20	N	118	253	Yes	4	240	13	20
3	22	N	170	228	Yes	3	144	8	18
4	22	N	102	225	Yes	3	292	11	13
5	23	N	95	169	Yes	2	192	9	15
6	24	N	79	177	Yes	3	216	15	21
7	25	N	91	184	Yes	4	96	20	27
8	34	Y	106	208	Yes	10	792	48	57
9	34	N	89	163	No	0	192	13	16
10	34	N	92	190	No	0	36	7	10
11	34	N	94	226	Yes	2	96	14	20
12	34	N	64	160	Yes	4	144	10	14
13	34	N	104	221	Yes	1	36	3	7
14	34	N	60	116	Yes	3	96	5	8

CPB: Cardiopulmonary bypass; ECLS: Extracorporeal life support; XC time: Aortic cross-clamp time; MV: Mechanical ventilation; ICU: Intensive care unit; h: Hour; d: Day.

ASD with a small PDA. Although he had a type 2 IVS, cathetherization was performed due to his age. Cardiac catheterization documented a left ventricular systolic pressure of 80 mmHg and a right ventricular systolic pressure of 115 mmHg. Septostomy was not performed. Surgery was uneventful and the sternum was left open for 48 hours. He was extubated at the postoperative eighth day and discharged at the postoperative 15th day without any complication.

There was no early mortality in any patient. All three patients with type 3 IVS demonstrated normal IVS configuration and all of the operated patients had normal left ventricular systolic function on ECHO performed at the time of the discharge. The mean duration of follow-up was 24 months (range 1 to 50 months). None of the patients needed re-do surgery during follow-up. Mild neo-aortic valve regurgitation in three patients and mild neo-pulmonic valve stenosis in two patients were detected during follow-up.

DISCUSSION

Although the age limit is not clear, ASO has been suggested before three weeks of life.[7,8] However, around 3 to 24% of the children with TGA-IVS are diagnosed after this period. The ratio is higher in developing countries, in particular.[9,10] Currently, there was no consensus on the surgical procedure in these late referrals.

The early experiences on late ASO after three weeks of life showed a high mortality and morbidity rates.[5] In 1988, Norwood et al.[11] reported the mortality of late TGA as 33% in their series. Due to this high mortality, atrial switch or two-stage ASO for conditioning the left ventricle were primarily preferred in these patients.[12-14] Atrial switch operation has some disadvantages such as sinus node dysfunction, systemic right ventricle, and systemic tricuspid valve.[6,14] Besides, poor results of ASO in terms of physical functioning, mental health, self-respect, and general health perception can be also reduced by ASO.[15] Progressive deterioration, particularly after the second decade of life, is diverting the families and the institutions from this option.[16] Another procedure for treating simple TGA with involution of left ventricle is two-stage ASO.[13] The main morbidities associated with two-stage ASO include left ventricular dysfunction, trauma and distortion of the pulmonary artery and branches after the first stage, surgical challenges due to the adhesions during the second stage, and neoaortic valve regurgitation.[14] The need for an extrapulmonary blood supply due to postoperative cyanosis or late diastolic dysfunction are other disadvantages.[17]

In recent years, the age limit for primary ASO has been extending. In contrast to earlier data, recent reports suggest that ASO can be performed without any problem up to three to four months of age. In a multi-center study conducted in 19 European centers, Sarris et al.[10] reported that 52 patients with TGA/IVS who were older than four weeks of age (36 were older than eight weeks) underwent primary ASO with a mortality comparable to the younger patients (2% vs. 3%, respectively). Currently, the main reason to perform primary ASO is to protect the left ventricular functions with the advancement of the ICU support and increased use of ECMO and assist devices. Hence, the age limit for ASO has been increased up to nine months thanks to these supports.[18]

In the present study, 14 patients in whom late ASO performed with the diagnosis of TGA/IVS were evaluated and no mortality and morbidity was seen. Of note, one of the patients was older than four months during the operation.

Echocardiography is the key diagnostic method to define the suitable surgical procedure for late cases.[9,10] The straightness or convexity of the IVS towards the left ventricle, age-appropriate thickness of the left ventricular posterior wall, and >35 g/m^2 left ventricular myocardial mass indicate the adequacy of left ventricle, in other words, the suitability for primary ASO. However, clinical applications mainly depend on the visual appearance of the left ventricle and IVS motion on the transthoracic cross-sectional echocardiography.[12]

The gradual decrease in the pulmonary vascular resistance (PVR) postnatally leads to reduced left ventricular afterload in TGA/IVS patients. In general, as a result of this unequal afterload, IVS shifts towards the left ventricle.[12] This adaptation starts initially by the change in the shape of the left ventricle, of IVS motion, and subsequently its muscle mass.[6,8,12] Therefore, the cross-sectional shape of the left ventricle changes from spherical to a D-shape and to a banana-shape, eventually.[19] The presence of systolic bulging of the ventricular septum towards the left ventricular cavity (type 3 or banana-shaped septum) indicates a low left ventricular pressure, reflecting the significant pressure gradient between the two ventricles. Drop in pulmonary arteriolar resistance, the presence of blood flow in the ductus arteriosus, and the size of the ASD clearly influence the left ventricular preload and afterload; however, other factors, possibly genetically predetermined, may also play a role in documenting the left ventricular performance. In addition, BAS is life-saving in case of a postponed operation or in patients with restrictive ASD and hypoxia unresponsive to prostaglandin perfusion.[8] On the other hand, BAS may lead to the decompression of the left ventricle and shift of the IVS to the left in patients with late TGA. It can also impair the left ventricular functions in patients with a scheduled primary ASO. In our study, the left ventricular adequacy was confirmed echocardiographically in 11 out of 14 patients.

In a postmortem study of 61 non-operated infants with dTGA/IVS, the left ventricular wall thickness was shown to be about normal up to two months of age[20] and ECHO data were suggested to be non-significant.[6] Besides, primary anatomic correction was suggested directly in several clinics independent from the position of the LV.[7] The most striking result of these studies was that the preoperative ECHO (left ventricular geometry, mass index, wall thickness, volume index, and mass/volume ratio) alone was not adequate to evaluate the suitability of the patient for operation before two months of age.[7] Although that is an important factor in assessing the ventricular performance, it should not be used in isolation, as several children within the neonatal period may have a very compressed left ventricle and may undergo uneventful primary correction.[8]

In the present study, the left ventricular geometry was found to be echocardiographically unsuitable for ASO in three patients and cardiac catheterization was performed on these patients. The left ventricle/right ventricle pressure ratio was found to be >0.60 and ASO was performed uneventfully.

For the success of the primary ASO, the left ventricle should adapt quickly to the increased afterload postoperatively.[2,12] In general, the unfavorable left ventricular geometry is accepted as a contraindication for the primary ASO; however, it is reported to be transient and can be treated by pharmacological means and ECMO support.[12] This change in the left ventricular shape is due to low afterload, but not an intrinsic change in the left ventricular myocardial properties, and it is reversible.[12] In the present study, only one patient needed ECMO support. Other patients were supported by medical treatment. The NIRS was also helpful in the postoperative follow-up. The left ventricular geometry was improved in all patients postoperatively.

Nonetheless, our study has some limitations. Small sample size and retrospective design of the study were the main limitations. In addition, the study was carried out based on a single-center. Therefore, further large-scale, multi-center, prospective studies are required to confirm these findings.

In conclusion, the echocardiographic evaluation of the left ventricle is the most critical stage in determining the type of the surgical procedure. In case of inappropriate echocardiographic data for primary arterial switch operation, the patients should be evaluated with cardiac catheterization and angiography. Large patent ductus arteriosus or restrictive atrial septal defect are vital to protect the left ventricular preload, but have no use in the postoperative period. We suggest primary arterial switch operation without an initiating BAS in hypoxic patients, despite medical stabilization and prostaglandin E_1 treatment, unless contraindicated. The need for extracorporeal membrane oxygenation is not more than expected, but extracorporeal membrane oxygenation support should be available. Based on our study findings, we conclude that late arterial switch operation can be performed safely in patients with transposition of the great arteries and intact ventricular septum after a detailed evaluation and with an efficient, advanced, and suitable postoperative intensive care unit monitorization.

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