Cardiology in the Young

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Long-term outcomes after the arterial switch operation

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Original Article

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Abstract

Objectives: The aims of this study were to evaluate the 16-year experience with arterial switch operation at Beijing Children's Hospital and to determine early and late mortality and late morbidity, to explore risk factors for late complications and reintervention, and finally to evaluate whether the neoaortic sinotubular junction reconstruction technique reduces late complications of arterial switch operation. *Methods:* The clinical data of 185 patients with transposition of the great arteries who underwent arterial switch operation in Beijing Children's Hospital from January 2006 to January 2022 and 30 patients who underwent modified arterial switch operation with neoaortic sinotubular junction reconstruction technique in Fuwai Hospital during the same period were retrospectively analysed. Propensity score matching was also used to match the neoaortic sinotubular junction reconstruction patients in Fuwai Hospital with 30 non-neoaortic sinotubular junction reconstruction patients in Beijing Children's Hospital. *Results:* There were 13 early deaths (7.03%) and five late deaths (3.01%). Nineteen patients (11.45%) developed new aortic valve regurgitation and 28 patients (16.87%) developed aortic root dilation. Late right ventricular outflow tract obstruction occurred in 33 patients (19.88%). Late reintervention occurred in 18 cases (10.84%). Multivariate analysis showed that aorto-pulmonary diameter mismatch, previous pulmonary artery banding, and mild moderate or above new aortic valve regurgitation at discharge were independent risk factors for late new aortic valve regurgitation and aortic root dilation. Low surgical weight was an independent risk factor specific to new aortic valve regurgitation, and bicuspid native pulmonary valve was an independent risk factor specific to aortic root dilation. Older surgical age and aortic root dilation were independent risk factors for late right ventricular outflow tract obstruction. Older surgical age, operation before 2014, late right ventricular outflow tract obstruction, and late aortic root dilation were independent risk factors for late intervention. Propensity score matching showed that new aortic valve regurgitation and aortic root dilation were not followed up in the neoaortic sinotubular junction reconstruction group, while seven cases of aortic root dilation and five cases of new aortic valve regurgitation occurred in the non-neo-aortic sinotubular junction reconstruction group, respectively, and the differences were statistically significant ($P = 0.003$; $P = 0.015$). *Conclusions:* The increased incidence of new aortic valve regurgitation, aortic root dilation, and right ventricular outflow tract obstruction as children age is a major concern outcome in the future and may mean more late reintervention. neoaortic sinotubular junction reconstruction technique may reduce the incidence of new aortic valve regurgitation and aortic root dilation, and improve the late prognosis of arterial switch operation. Careful follow-up of neo-aortic valve and root function is imperative, especially in patients with aorto-pulmonary diameter mismatch, previous pulmonary artery banding, mild new aortic valve regurgitation at discharge, low surgical weight, and bicuspid native pulmonary valve structures.

About 150,000 to 200,000 children with CHD are born every year in our country,[1] and transposition of the great arteries accounts for 5 to 7%, which is the most common subtype of complex CHD.[2] The anatomical relationship of its aorta is reversed. Unlike its normal location, the aorta originates from the right ventricle and lies anterior to the pulmonary artery, which originates behind the aorta and originates from the left ventricle. Common cardiac anomalies associated with transposition of the great arteries include patent patent ductus arteriosus, atrial septal defect, ventricular septal defect, pulmonary stenosis, coarctation of the aorta, and aortic interruption. From the initial balloon atrial septotomy and pulmonary artery ligation for palliative treatment, to Mustard and Senning intra-atrial barrier surgery for physiological correction, and then to arterial switch operation, it has become the first choice for major children's heart centres. According to The Society of Thoracic Surgeons Congenital Heart Surgery Database, from 2013 to 2016, the cumulative operative mortality rates for infant arterial switch operation and arterial switch operation with ventricular septal defect repair in developed regions were as low as 2.2 and 5.1%, respectively. The 20-year survival rate after arterial switch

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operation was reported in most developed regions is higher than 90%. Surgical results with low perioperative mortality over the last decades have now led to focus on the long-term outcomes. Theoretical long-term complications after the arterial switch include suprapulmonary stenosis, aortic root dilation, new aortic valve regurgitation, coronary artery malformation, and arrhythmias. Since 2011, neoaortic sinotubular junction reconstruction technique has been routinely performed in children with aortopulmonary artery diameter less than 1:2. By folding the new aortic wall at the level of the sinus tubular junction, the diameter ratio of the sinus tubular junction to the aortic annulus of the new aorta was 0.8, which was closer to the normal aortic root anatomy. Although the management of transposition of the great arteries has been optimised in developed countries over the past 60 years, arterial switch operation operation has achieved good results. However, arterial switch operation has been carried out in developing countries for only 20 years, and there are few summaries of the long-term outcomes after arterial switch operation. The aim of this study was to evaluate the 16-year arterial switch operation experience at Beijing Children's Hospital and to determine early and late mortality and late morbidity, as well as the need for reoperation and catheter intervention, and second, to investigate risk factors for late complications and reintervention. Finally, propensity matching was used to determine the role of the neoaortic sinotubular junction reconstruction technique in arterial switch operation. Patients treated with neoaortic sinotubular junction reconstruction n Fuwai Hospital were matched with patients treated with non-neoaortic sinotubular junction reconstruction Beijing Children's Hospital using the closest propensity score matching to evaluate whether neoaortic sinotubular junction reconstruction reduces long-term complications of arterial switch operation.

Materials and methods

Study design

Institutional Committee on Clinical Investigation of Beijing Children's Hospital affiliated with Capital Medical University and Fuwai Hospital approved this protocol with a waiver of informed consent. Patients who received arterial switch operation biventricular correction in Beijing Children's Hospital from January 2006 to January 2022 and patients who (not) combined with other intracardiac corrections were included as research subjects. Included diagnoses included Transposition of the great arteries-Intact ventricular septum, Transposition of the great arteries-Ventricular septal defect, and Transposition of the great arteries-Taussig-Bing anomaly. A total of 185 patients were enrolled. Thirty patients who underwent modified arterial switch operation with neoaortic sinotubular junction reconstruction technique after 2011 in Fuwai Hospital were also included. Perioperative clinical data and postoperative follow-up data of all children were collected from the ward medical record system, outpatient medical record system, and telephone follow-up in our hospital. Patients underwent outpatient review at 1, 3, 6, and 12 months in the first postoperative year and annually thereafter. Echocardiography chest X-ray and electrocardiogram were routinely performed during follow-up.

Definition

Emergency surgery was defined as life-saving surgery requiring surgery within 24 hours of admission. Early mortality was defined as death that occurred during hospitalisation. Late mortality was defined as death that occurred after discharge from the hospital. Mild, moderate, and severe aortic valve regurgitation was defined as the proportion of the valve regurgitation area in the left ventricular outflow tract <25, 25 to 65%, and ≥65%. Right ventricular outflow tract obstruction was considered mild with an echocardiographic peak gradient between 20 and 40 mmHg, moderate between 40 and 80 mmHg, and severe ≥80 mmHg. To account for the range in body size for neo-aortic measurements during childhood (0–18 years), Z-scores were calculated for each patient by using paediatric reference values and body surface area (DuBois method).[4] Aortic root dilation was defined as Z-score ≥3. Late reintervention includes late reoperation and catheter intervention. Aorto-pulmonary diameter mismatch was defined when the ratio of pulmonary artery root diameter to aortic root diameter was found to be >1.5 during the operation.

Surgery

The authors previously reported the surgical technique of arterial switch operation performed by the cardiac surgery team of Beijing Children's Hospital.[5] All patients underwent moderate hypothermic cardiopulmonary bypass under general anaesthesia with endotracheal intubation. The median incision was used to establish cardiopulmonary bypass through the aorta and superior and inferior vena cava, histidine-tryptophan-ketoglutarate cardioplegia was perfused for myocardial protection, and the ascending aorta was clamped. Coronary artery was removed free from the anatomic aortic sinus in a "U" shape or button and replanted in the corresponding anatomic pulmonary sinus. The surgical procedure of Fuwai Hospital is basically the same as that of Beijing Children's Hospital, but the technique has been improved since 2011. neoaortic sinotubular junction reconstruction technique was routinely performed in patients with aortopulmonary artery diameter less than 1:2. The reconstruction more closely approximated normal aortic root anatomy by folding the new aortic wall at the level of the sinotubular junction, resulting in a sinotubular junction to annulus diameter ratio of 0.8 in the new aorta (Supplementary Figure 1).

Statistical analyses

Mean ± SD or median (min, max) was used to describe continuous variables, and the Student's *t*-test or the Wilcoxon–Mann–Whitney *U*-test was used to compare differences between groups. Descriptive statistics for categorical variables were reported as frequency/percentage and were compared using the Pearson's χ^2 or Fisher's exact test. Freedom from time-dependent endpoints was studied using Kaplan-Meier and Log-rank calculations. Multivariate logistic regression was used to identify predictors of new aortic valve regurgitation, aortic root dilation, right ventricular outflow tract obstruction, and reintervention. Freedom from time-dependent endpoints was studied using Kaplan-Meier and Log-rank calculations. Propensity score matching was performed on the neoaortic sinotubular junction reconstruction group and the non-neoaortic sinotubular junction reconstruction group. Demographic characteristics and preoperative basic clinical data were used as synergistic variables, and the calliper value was set at 0.01. Propensity score matching was performed using the logistic regression formula with a matching ratio of 1:1, and the propensity score value and weight were calculated. The clinical data of the two groups after matching were analysed, and the late complications and morbidity of the two groups after matching were compared. All

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Table 1. Clinical baseline data of 185 patients

Patient characteristics	Number(%)/Median (Min, Max)/Mean ± SD
Gender (Male)	131(70.81)
Surgical weight (kg)	3.54(2.20,7.30)
Surgical age (day)	24(1,240)
Prematurity	25(13.51)
Prenatal diagnosis	36(19.46)
Emergency operation	19(10.27)
Surgery period	
2006–2014	109(58.92)
2014–2022	76(41.08)
Anatomical type	
TGA-IVS	100(54.05)
TGA-VSD	64(34.59)
TGA-TBA	21(11.35)
Associated cardiac lesion	
PDA	171(92.43)
ASD/PFO	168(90.81)
COA	11(5.95)
LVOTO	21(11.35)
Preoperative mechanical ventilation	30(16.22)
Coronary artery malformation	20(10.81)
APDMM	67(36.22)
BPV	35(18.92)
Previous PAB	15(8.11)
Great aorta relationship	
Anterior	71(38.38)
Anterior right	73(39.46)
Side-by-side	24(12.97)
Anterior left	17(9.19)
Preoperative moderate or severe TR	28(18.67)
Preoperative moderate or severe PR	14(7.57)
Preoperative cardiac dysfunction	28(15.14)
CPB time (min)	182.66 ± 42.20
Cross-clamp time (min)	100.16 ± 23.44
Concomitant arch repair	11(5.95)
Concomitant LVOTO Resection	21(11.35)
ICU stay time (days)	7(1,30)
Duration of ventilation (h)	160(2,661)
Delayed chest closure	97(52.43)
Extracorporeal membrane oxygenation support	6(3.24)
Hospital stay (day)	21(3,50)
Early mortality	13(7.03)
Follow-up completion rate	166(96.51)
AR at discharge	35(20.35)
Late mortality	5(3.01)
Late reintervention due to any cause	18(10.84)
Late reoperations	8(4.82)
Catheter based late reinterventions	10(6.02)
ARD	28(16.87)
NAR	19(11.45)
RVOTO	33(19.88)
New York Heart Function Class I-II	156(96.89)

AR = aortic valve regurgitation; ARD = aortic root dilation; ASD = atrial septal defect; BPV = bicuspid native pulmonary valve; CICU = cardiac intensive care unit; COA = coarctation of the aorta; ECMO = extracorporeal membrane oxygenation; IVS = intact ventricular septum; LVOTO = left ventricular outflow tract obstruction; NAR = new aortic valve regurgitation; PAB = pulmonary artery banding; PDA = patent ductus arteriosus; PFO = patent foramen ovale; PR = pulmonary regurgitation; RVOTO = right ventricular outflow tract obstruction; TBA = Taussig–Bing anomaly; TGA = transposition of the great arteries; TR = tricuspid regurgitation; VSD = ventricular septal defect.

statistical analyses were performed by SPSS 22.0 software, and $P \leq 0.05$ was considered statistically significant.

Results

Patient characteristics

From January 2006 to January 2022, a total of 185 patients underwent arterial switch operation in Beijing Children's Hospital, including 100 (54.05%) Transposition of the great arteries-Intact ventricular septum patients, 64 (34.59%) Transposition of the great arteries-Ventricular septal defect patients, and 21 (11.35%) Transposition of the great arteries-Taussig-Bing anomaly patients. Among the patients, there were 131 males (70.81%) and 54 females (29.19%). The proportion of prenatal diagnosis was 19.46%, and the proportion of premature infants was 13.51%. There were 109 (58.92%) cases and 76 (41.08%) cases in the two periods before and after January 2014. The median age at surgery was 24 (1,240) days, and the median surgical weight was 3.54 (2.2, 7.3) kg. Before arterial switch operation, 15 (8.11%) patients received pulmonary artery banding. Eleven (5.95%) with coarctation of the aorta, 20 (10.81%) with coronary malformation, 67 (36.22%) with aorto-pulmonary diameter mismatch, 35 (18.92%) with bicuspid native pulmonary valve. Nineteen (10.27%) of the patients underwent emergency surgery. The average CPB time and cross-clamp time in arterial switch operation patients were 182.66 min and 100.16 min, respectively. After the operation, the median duration of mechanical ventilation was 160 hours, and 6 (3.24%) patients underwent extracorporeal membrane oxygenation. To ensure the stability of pulmonary artery pressure and the normal work of the right ventricle, 97 (52.43%) patients delayed chest closure. The median ICU stay and hospital stay were 7 days and 21 days, respectively. The general information about the patients is shown in Table 1.

Early mortality

The early postoperative mortality was 7.03%. Among the 13 patients who died, nine patients died of circulatory failure caused

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by left heart failure, two patients died of being unable to withdraw from cardiopulmonary bypass after the operation and parents gave up ECOM assistance, and one patient died of pulmonary arterial hypertensive crisis on the first day after the operation. The remaining one patient died of cardiac arrest caused by malignant arrhythmia. Univariate analysis showed that prematurity (P = 0.000), preoperative emergency operation (P = 0.000), preoperative mechanical ventilation (P = 0.003), Transposition of the great arteries-Intact ventricular septum and Transposition of the great arteries-Taussig-Bing anomaly (P = 0.000), concomitant arch repair (P = 0.032) and left ventricular outflow tract obstruction resection (P = 0.000), previous pulmonary artery banding (P = 0.010), coronary artery malformation (P = 0.000), preoperative moderate or severe TR (P = 0.000), preoperative moderate or severe PR (P = 0.001), preoperative cardiac dysfunction (P = 0.000), prolonged CPB time (P = 0.005), and prolonged cross-clamp time (P = 0.003) were risk factors for early postoperative mortality in arterial switch operation patients, while delayed chest closure (P = 0.028) was a protective factor (Table 2). We found that most of the early deaths occurred within 3 days after arterial switch operation. Multivariate analysis found no independent risk factors.

Late mortality

Of the 185 patients, 13 died early, six were lost to follow-up, and 166 completed long-term follow-up. The median follow-up time was 88.5 (2,190) months. There were five deaths (3,01%) during follow-up. One Transposition of the great arteries-Intact ventricular septum patient died of massive myocardial infarction caused by left coronary embolism 8 months after arterial switch operation. One Transposition of the great arteries-Taussig-Bing anomaly patient died of internal tunnel obstruction complicated with infective endocarditis 18 months after the operation. A Transposition of the great arteries-Ventricular septal defect patient underwent aortic valve replacement due to severe aortic regurgitation 13 months after arterial switch operation and died suddenly 5 months after the operation. The cause of death was unknown. One TGA-TAB patient with arterial switch operation underwent coarctation resection and anastomosis at the same time. The re-examination found that anastomotic stenosis underwent coarctation balloon dilatation 6 months after the operation, and died of chronic heart failure 6 months after the operation. The last Transposition of the great arteries-Ventricular septal defect patient developed aortic root dilation and new aortic valve regurgitation 18 months after arterial switch operation, underwent aortic valvuloplasty, and died of malignant arrhythmia 6 months after the operation. Among them, four (4.55%) died patients who underwent arterial switch operation before 2014, and one (1.28%) underwent arterial switch operation after 2014, however, the comparison between groups was not statistically significant (P = 0.360) (Fig. 1A). The overall survival rate of the arterial switch operation hospital survivors was 98.7% at 1 year, 97.4% at 2 years and 96.7% at 5 and 15 years(Fig. 1B); the survival curve was significantly different between transposition of the great arteries subgroups (P = 0.005) (Fig. 1C).

New aortic valve regurgitation

Of the 166 follow-up patients, 19 developed late new aortic valve regurgitation. Univariate analysis found that Aorto-pulmonary diameter mismatch (P = 0.000), Bicuspid native pulmonary valve (P = 0.031), concomitant left ventricular outflow tract obstruction resection (P = 0.045), and new aortic valve regurgitation at discharge (P = 0.003) were risk factors for late new aortic valve regurgitation (Table 3). Multivariate analysis suggested that low surgical weight (OR = 0.336, P = 0.036), Aorto-pulmonary diameter mismatch (OR = 11.364, P = 0.000), preoperative Pulmonary artery banding (OR = 7.895, P = 0.042), and new aortic valve regurgitation at discharge (OR = 3.639, P = 0.036) were independent risk factors for late new aortic valve regurgitation (Table 4).

Aortic root dilation

Twenty-eight cases developed aortic root dilation during late follow-up, including 13, 10, and 5 cases of Transposition of the great arteries-Intact ventricular septum, Transposition of the great arteries-Ventricular septal defect, and Transposition of the great arteries-Taussig-Bing anomaly, respectively. Univariate analysis showed that low birth weight infant (P = 0.006), aorto-pulmonary diameter mismatch (P = 0.001), bicuspid native pulmonary valve (P = 0.000), prolonged duration of ventilation (P = 0.040) and new aortic valve regurgitation at discharge (P = 0.016) were risk factors for late aortic root dilation. Compared with non-aortic root dilation, patients with late aortic root dilation had a trend of more Transposition of the great arteries-Ventricular septal defect and Transposition of the great arteries-Taussig-Bing anomaly proportions in anatomical types, but the difference was not statistically significant (P = 0.067) (Table 5). Multivariate analysis found that aorto-pulmonary diameter mismatch (OR = 4.762, P = 0.002), bicuspid native pulmonary valve (OR = 6.906, P = 0.000), preoperative pulmonary artery banding (OR = 7.092, P = 0.019), and new aortic valve regurgitation at discharge (OR = 2.933, P = 0.040) were independent risk factors for late aortic root dilation (Table 6). Late aortic root dilation occurred in 28 hospital survivors, with a median time delay of 54 (7,133) months. Cumulative incidence rate of late aortic root dilation at 1, 5, and 10 years was 3.1, 10.8, and 24% respectively (Fig. 2A). Patients with Transposition of the great arteries-Taussig-Bing anomaly had a higher trend of occurring aortic root dilation than patients with Transposition of the great arteries-Intact ventricular septum and patients with Transposition of the great arteries-Ventricular septal defect (P = 0.080), although the statistical difference was not particularly significant (Fig. 2B). The cumulative incidence rate of late aortic root dilation was significantly different between concomitant arh repair group and non-arh repair group (P = 0.000) (Fig. 2C). The cumulative incidence rate of late aortic root dilation was significantly different between APDM group and aorto-pulmonary diameter mismatch group (P = 0.005) (Fig. 2D).

Right ventricular outflow tract obstruction

Late right ventricular outflow tract obstruction occurred in 33 patients during follow-up. Among them, 15 were Transposition of the great arteries-Intact ventricular septum, 13 were Transposition of the great arteries-Ventricular septal defect, and five were Transposition of the great arteries-Taussig-Bing anomaly. Univariate analysis showed that older surgical age (P = 0.027), low birth weight infant (P = 0.020), aorto-pulmonary diameter mismatch (P = 0.002), and late aortic root dilation (P = 0.000) were risk factors for late right ventricular outflow tract obstruction. Patients with Transposition of the great arteries-Ventricular septal defect and Transposition of the great arteries-Taussig-Bing anomaly had a higher tendency to develop right ventricular outflow tract obstruction compared with patients with

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Table 2. Univariable analysis of early mortality [Number (%)/Median (Min, Max)/Mean ± SD]

Variable	Total (n = 185)	Early mortality (n = 13)	Early survival (n = 172)	P-value
Gender (Male)	131(70.81)	9(69.23)	122(70.93)	1.000
Surgical weight (kg)	3.54(2.20,7.30)	4.00(2.50,5.00)	3.60(3.09,6.00)	0.757
Surgical age (day)	24(1,240)	12(2,127)	24(1,197)	0.160
Prematurity	25(13.51)	11(84.62)	14(8.14)	0.000
Prenatal diagnosis	36(19.46)	2(15.38)	34(19.77)	0.983
Emergency operation	19(10.27)	10(76.92)	9(5.23)	0.000
Surgery period				0.433
2006–2014	109(58.92)	9(69.23)	100(58.14)	
2014–2022	76(41.08)	4(30.77)	72(41.86)	
Anatomical type				0.000
TGA-IVS	100(54.05)	0(0.00)	100(58.14)	
TGA-VSD	64(34.59)	6(46.15)	58(33.72)	
TGA-TBA	21(11.35)	7(53.85)	14(8.14)	
Associated cardiac lesion				
ASD/PFO	168(90.81)	12(92.31)	156(90.70)	1.000
COA	11(5.95)	3(23.08)	8(4.65)	0.032
LVOTO	21(11.35)	8(61.54)	13(7.56)	0.000
Preoperative mechanical ventilation	30(16.22)	9(69.23)	21(12.21)	0.003
Coronary artery malformation	20(10.81)	7(53.85)	13(7.56)	0.000
APDMM	67(36.22)	6(46.15)	61(35.47)	0.636
BPV	35(18.92)	2(15.38)	33(19.19)	1.000
Previous PAB	15(8.11)	4(30.77)	11(6.40)	0.010
Great aorta relationship				0.478
Anterior	71(38.38)	7(53.85)	64(37.21)	
Anterior right	73(39.46)	4(30.77)	69(40.12)	
Side-by-side	24(12.97)	2(15.38)	22(12.79)	
Anterior left	17(9.19)	0(0.00)	17(9.88)	
Preoperative moderate or severe TR	28(18.67)	8(61.54)	20(11.63)	0.000
Preoperative moderate or severe PR	14(7.57)	5(38.46)	9(5.23)	0.001
Preoperative cardiac dysfunction	28(15.14)	10(76.92)	18(10.47)	0.000
CPB time (min)	182.66 ± 42.20	278.15 ± 107.90	175.44 ± 18.80	0.005
Cross-clamp time (min)	100.16 ± 23.44	139.77 ± 40.68	97.17 ± 18.63	0.003
Concomitant arch repair	11(5.95)	3(23.08)	8(4.65)	0.032
Concomitant LVOTO Resection	21(11.35)	8(61.54)	13(7.56)	0.000
ICU stay time (days)	7(1,30)	1(1,7)	9(5,18)	0.000
Duration of ventilation (h)	160(2,661)	19(2,164)	121(98,324)	0.000
Delayed chest closure	97(52.43)	3(23.08)	94(54.65)	0.028
Extracorporeal membrane oxygenation support	6(3.24)	1(7.69)	5(2.91)	0.358

APDMM = aorto-pulmonary diameter mismatch; ASD = atrial septal defect; BPV = bicuspid native pulmonary valve; CICU = cardiac intensive care unit; COA = coarctation of the aorta; ECMO = extracorporeal membrane oxygenation; IVS = intact ventricular septum; LVOTO = left ventricular outflow tract obstruction; PAB = pulmonary artery banding; PFO = patent foramen ovale; PR = pulmonary regurgitation; TBA = Taussig-Bing anomaly; TGA = transposition of the great arteries; TR = tricuspid regurgitation; VSD = ventricular septal defect.

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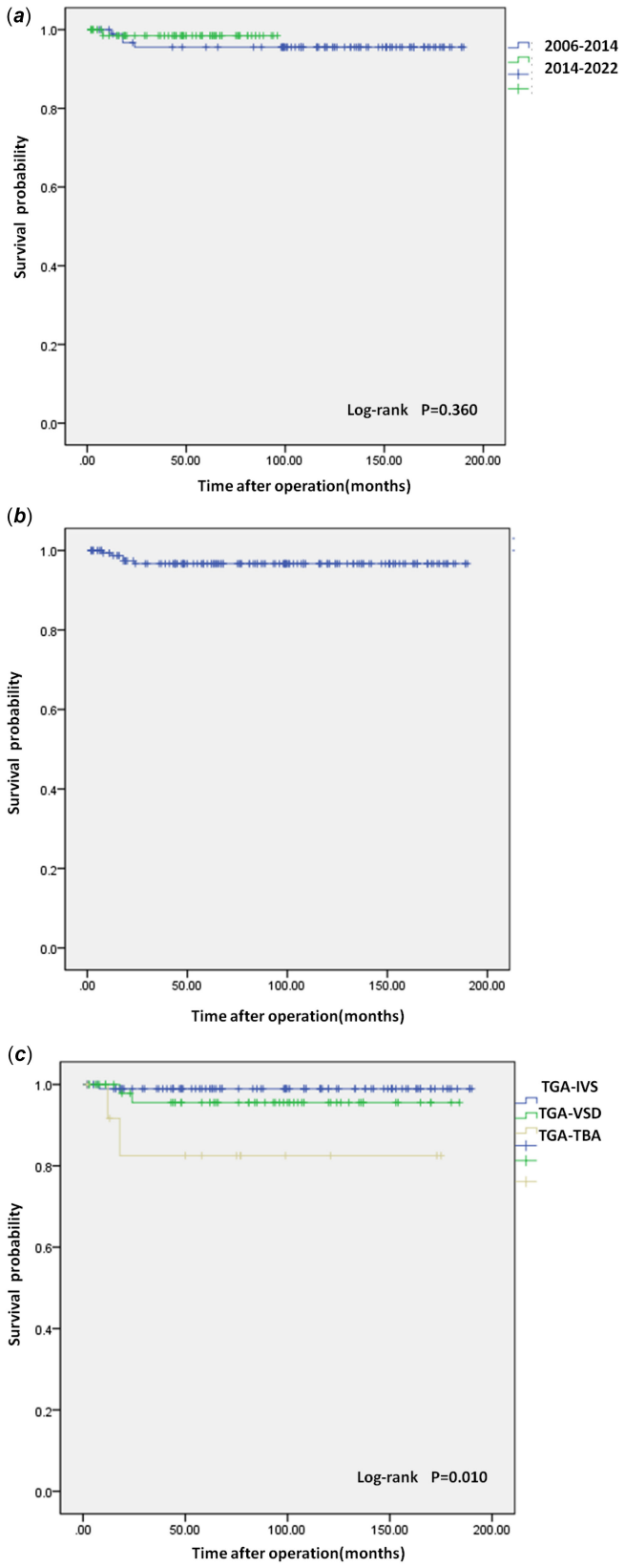


Figure 1. (***a***) Survival curve. Kaplan-Meier curves show the relationship between surgery period and mortality. (***b***) Overall Survival curve. (***c***) Survival curve. Kaplan-Meier curves show the relationship between the anatomical type and mortality. TGA-IVS = Transposition of the great arteries-Intact ventricular septum; TGA-TBA = Transposition of the great arteries-Taussig-Bing anomaly; TGA-VSD = Transposition of the great arteries-Ventricular septal defect.

Transposition of the great arteries-Intact ventricular septum, although the difference was not statistically significant (P = 0.091). The intraoperative concomitant arch repair group appeared to have a higher proportion of patients with late right ventricular outflow tract obstruction than the non-arh repair group, although this was not statistically significant (P = 0.083). Multivariate analysis showed that older surgical age (OR = 1.012, P = 0.002) and late aortic root dilation (OR = 12.596, P = 0.000) were independent risk factors for late right ventricular outflow tract obstruction.

Late intervention

A total of 18 patients (10.84%) needed a first reoperation or catheter intervention. Eight (44.44%) of these were open reoperations, ten were catheter interventions. The actuarial freedom from late reintervention was 96.3, 90.7, 88.8, 76.6% at 1, 5, 10, and 15 years, respectively (Fig. 3E). Late follow-up found that Transposition of the great arteries-Intact ventricular septum patients were more likely to be free from reintervention at a later stage than those of the other two groups (P = 0.003) (Fig. 3A). The Neonate group was more likely to be free from late reintervention than the Infant group (P = 0.000) (Fig. 3B). The non-aortic root dilation group was more likely to be free from reintervention at a later stage than the aortic root dilation group (P = 0.000) (Fig. 3C). The right ventricular outflow tract obstruction group had a higher probability of later reintervention than the Non-right ventricular outflow tract obstruction group (P = 0.000) (Fig. 3D). Cardiac reinterventions included percutaneous pulmonary artery (including its branches) stenosis stenting/percutaneous pulmonary artery stenosis balloon dilation/percutaneous pulmonary angioplasty (n = 5), aortic coarctation balloon dilation (n = 5), cardiac Pacemaker implantation (n = 3), aortic valvuloplasty (n = 2), aortic valve replacement (n = 1), pulmonary valve replacement (n = 1), and aortic root replacement (n = 1). Most reinterventions in this cohort occurred in the left and right ventricular systems, and coronary reinterventions were not found. Three patients died in the late stage of the reintervention, and they died 5 months, 6 months, and 6 months after the reintervention, respectively. Univariate analysis suggested that older surgical age (P = 0.002), Low birth weight infant (P = 0.026), complex anatomical type (P = 0.003), preoperative mechanical ventilation (P = 0.041), aorto-pulmonary diameter mismatch (P = 0.011), concomitant arch repair (P = 0.000), aortic root dilation (P = 0.000), 2006–2014 surgical period (P = 0.015) and right ventricular outflow tract obstruction (P = 0.000) were risk factors for late reintervention. Multivariate analysis found that older surgical age (OR = 1.015, P = 0.002), aortic root dilation (OR = 5.451, P = 0.017), right ventricular outflow tract obstruction (OR = 7.008, P = 0.003), and 2006–2014 surgical period (OR = 0.221, P = 0.041) were independent risk factors for late intervention.

Neoaortic sinotubular junction reconstruction technique improves aortic valve function and durability

In order to improve the surgical effect and reduce the incidence of new aortic valve regurgitation, 30 consecutive transposition of the great arteries patients with aorto-pulmonary diameter mismatch underwent arterial switch operation and neoaortic sinotubular junction reconstruction in 2011 in Fuwai Hospital, and they were classified as neoaortic sinotubular junction reconstruction group. Propensity score matching was used to select 30 patients who did

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Table 3. Univariable analysis of NAR [Number (%)/Median (Min, Max)/Mean ± SD]

Variable	Total (n = 166)	NAR (n = 19)	Non-NAR (n = 147)	P-value
Gender (Male)	118(71.08)	13(68.42)	105(71.43)	0.786
Surgical weight (kg)	3.50 (2.20,7.30)	3.50 (2.20,4.70)	3.72 (3.09,7.00)	0.078
Surgical age (day)	24(1,240)	32(2,61)	24(1,240)	0.218
Prematurity	13(7.83)	2(1.05)	11(7.48)	0.991
Emergency operation	9(7.63)	2(1.05)	7(5.44)	0.613
Anatomical type				0.618
TGA-IVS	99(67.35)	10(52.63)	89(60.54)	
TGA-VSD	54(32.53)	8(42.11)	46(31.29)	
TGA-TBA	13(7.83)	1(5.26)	12(8.16)	
Preoperative mechanical ventilation	21(12.65)	4(21.05)	17(11.56)	0.421
APDMM	57(34.34)	14(73.68)	43(29.25)	0.000
BPV	31(18.67)	7(36.84)	24(16.33)	0.031
Previous PAB	11(6.63)	2(10.53)	9(6.12)	0.813
CPB time (min)	177.5(137,217)	176(141,200)	182 (150,204)	0.262
Cross-clamp time (min)	97.23 ± 18.61	90.47 ± 11.52	98.11 ± 19.19	0.093
Concomitant arch repair	8(4.82)	1(5.26)	7(4.76)	1.000
Concomitant LVOTO Resection	12(7.23)	4(21.05)	8(5.44)	0.045
ICU stay time (days)	7(1,30)	10(3,30)	7(5,25)	0.161
Duration of ventilation (h)	162(12,661)	236(46,661)	144(45,330)	0.070
AR at discharge	32(19.28)	9(47.37)	23(15.65)	0.003

APDMM = aorto-pulmonary diameter mismatch; AR = aortic valve regurgitation; BPV = bicuspid native pulmonary valve; CICU = cardiac intensive care unit; IVS = intact ventricular septum; LVOTO = left ventricular outflow tract obstruction; NAR = new aortic valve regurgitation; PAB = pulmonary artery banding; TBA = Taussig-Bing anomaly; TGA = transposition of the great arteries; VSD = ventricular septal defect.

Table 4. Risk factors for NAR by multivariable analysis

Variable	B value	SE value	Wald value	P-value	OR value	95% confidence interval
Surgical weight (kg)	−1.090	0.519	4.406	0.036	0.336	0.122–0.930
APDMM	2.430	0.697	12.156	0.000	11.364	2.899–44.557
Previous PAB	2.066	1.015	4.148	0.042	7.895	1.081–57.672
AR at discharge	1.292	0.616	4.404	0.036	3.639	1.089–12.163
Constant	0.085	1.904	0.002	0.964	1.089	–

APDMM = Aorto-pulmonary diameter mismatch; AR = aortic valve regurgitation; NAR = new aortic valve regurgitation; PAB = pulmonary artery banding.

not undergo neoaortic sinotubular junction reconstruction in Beijing Children's Hospital during the same period as the non-neoaortic sinotubular junction reconstruction group. As shown in Table 7, the preoperative baseline characteristics of the two groups were similar and there were no significant differences. In the neoaortic sinotubular junction reconstruction group, the ratio of new sinus tube junction to aortic annulus diameter was 0.7 immediately after surgery. None of the 30 patients in neo-aortic sinotubular junction reconstruction group developed new aortic valve regurgitation or aortic root dilation during follow-up. Aortic cross-clamp time and CPB time were longer in the neoaortic sinotubular junction reconstruction group than in the non-neoaortic sinotubular junction reconstruction group, but the difference was not statistically significant (P = 0.093; P = 0.262). In the non-neoaortic sinotubular junction reconstruction group, aortic root dilation and new aortic valve regurgitation occurred in seven and five cases, respectively, which was statistically significant compared with the neoaortic sinotubular junction reconstruction group (P = 0.003; P = 0.015).

Discussion

Surgical treatment of transposition of the great arteries has historically been established and used many surgical methods until

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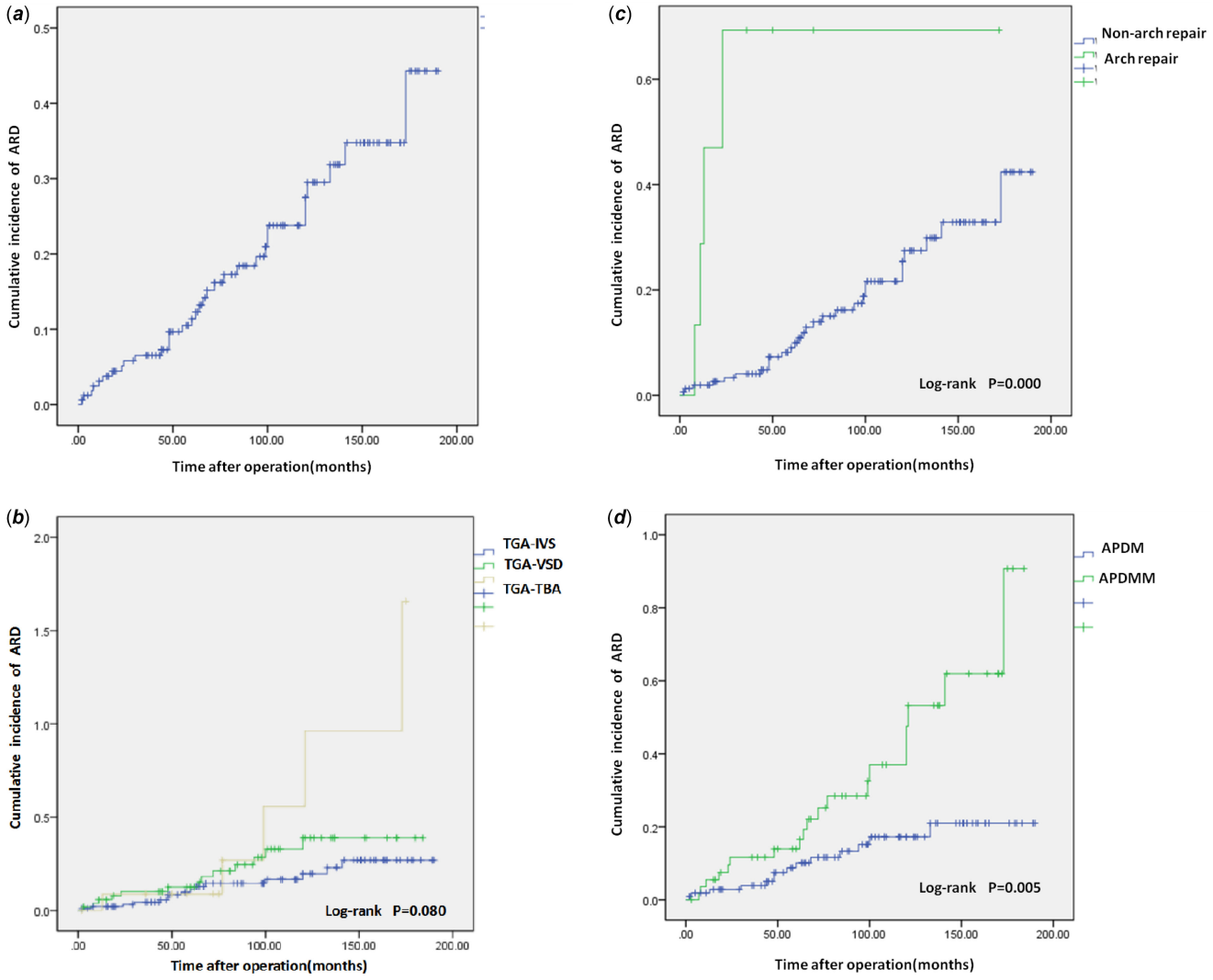


Figure 2. (***a***) Overall cumulative incidences curve about aortic root dilation. (***b***) Cumulative incidences curve. The curves show the relationship between the anatomical type and aortic root dilation. (***c***) Cumulative incidences curve. The curves show the relationship between the arch repair and aortic root dilation. (***d***) Cumulative incidences curve. The curves show the relationship between the aorto-pulmonary diameter mismatch and aortic root dilation. TGA-IVS = Transposition of the great arteries-Intact ventricular septum; TGA-TBA = Transposition of the great arteries-Taussig-Bing anomaly; TGA-VSD = Transposition of the great arteries-Ventricular septal defect.

the advent of new treatments that limited their use. Physiological correction based on early atrial dam surgery is aimed at redirecting systemic and pulmonary venous return into the ventricle connected to the correct aorta. Atrial barrier surgery has excellent early clinical outcomes, but presents long-term problems of superior vena cava obstruction, barrier leakage, atrial and ventricular arrhythmias, tricuspid regurgitation, and right heart failure.[6,7] arterial switch operation has largely replaced atrial barrier surgery with excellent early and long-term outcomes. At present, arterial switch operation has become the consensus of domestic and foreign experts as the preferred surgical procedure for children with transposition of the great arteries. In four decades of arterial switch operation, a significant decrease in perioperative mortality to rates below 5% in high-volume heart centres has been achieved.[8] In this study, the early mortality rate of arterial switch operation patients was 7.03%, and the late mortality rate was 3.0%. The early mortality rate was slightly higher than that of high-volume heart centres in some developed countries. Considering the basic medical conditions of our country, many patients are over-aged. The average age of operation is high, the optimal operation period is missed, and the perioperative management is more difficult.

New aortic valve regurgitation and Aortic root dilation

Neo-aortic regurgitation and root dilatation are common findings in patients with transposition after arterial switch operation. Histological studies have found that even in patients with transposition of the great arteries, the pulmonary artery differs significantly from the aorta in terms of the elastic layer of the arterial wall and smooth muscle actin. Although there are no obvious morphological and histological differences between the aortic and pulmonary arteries in neonates, the elastic fibrous tissue of the pulmonary valve shrinks with age in the low-pressure pulmonary circulation. Since the original pulmonary valve is used as the aortic valve after arterial switch operation, such patients are at risk of developing new aortic valve regurgitation in the long term.[9] In this study, 19 (11.45%) patients developed new aortic valve regurgitation, and 28 (16.87%) patients developed aortic root dilation. The team at Leuven University Hospitals reported the

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Table 5. Univariable analysis of ARD [Number (%)/Median (Min, Max)/Mean ± SD]

Variable	Total (n = 166)	ARD (n = 28)	Non-ARD (n = 138)	P-value
Gender (Male)	118(71.08)	21(75.00)	97(70.29)	0.616
Surgical weight (kg)	3.50(2.20,7.30)	3.54(2.20,4.70)	3.55(3.00,7.30)	0.250
Surgical age (day)	24(1,240)	32(2,151)	19.5(1,240)	0.676
Prematurity	13(7.83)	3(10.71)	10(7.25)	0.813
Low birth weight infant (<2.5 kg)	9(5.42)	5(17.86)	4(2.90)	0.006
Emergency operation	9(5.42)	2(7.14)	5(3.62)	0.742
Anatomical type				0.067
TGA-IVS	99(59.64)	13(46.43)	86(62.32)	
TGA-VSD	54(32.53)	10(35.71)	44(31.88)	
TGA-TBA	13(7.83)	5(17.86)	8(5.80)	
Preoperative mechanical ventilation	21(12.65)	5(17.86)	16(11.59)	0.550
APDMM	57(34.34)	17(60.71)	40(28.99)	0.001
BPV	31(18.67)	13(46.43)	18(13.04)	0.000
Previous PAB	11(6.63)	3(10.71)	8(5.80)	0.591
CPB time (min)	175.26 ± 18.92	171.57 ± 19.17	176.01 ± 18.85	0.259
Cross-clamp time (min)	97.23 ± 18.61	92.11 ± 14.49	98.28 ± 19.22	0.110
Concomitant arch repair	8(4.82)	2(7.14)	6(4.35)	0.884
Concomitant LVOTO Resection	12(7.23)	4(14.29)	8(5.80)	0.237
ICU stay time (days)	7(1,30)	8(1,30)	7(3,25)	0.266
Duration of ventilation (h)	162(12,661)	234.5(20,661)	152(12,552)	0.040
AR at discharge	32(19.28)	10(35.71)	22(15.94)	0.016

APDMM = aorto-pulmonary diameter mismatch; AR = aortic valve regurgitation; ARD = aortic root dilation; BPV = bicuspid native pulmonary valve; CICU = cardiac intensive care unit; IVS = intact ventricular septum; LVOTO = left ventricular outflow tract obstruction; PAB = pulmonary artery banding; TBA = Taussig-Bing anomaly; TGA = transposition of the great arteries; VSD = ventricular septal defect.

Table 6. Risk factors for ARD by multivariable analysis

Variable	B value	SE value	Wald value	P-value	OR value	95% confidence interval
APDMM	1.561	0.511	9.311	0.002	4.762	1.748–12.974
BPV	1.932	0.512	14.258	0.000	6.906	2.533–18.831
Previous PAB	1.959	0.836	5.489	0.019	7.092	1.377–36.514
AR at discharge	1.076	0.523	4.228	0.040	2.933	1.052–8.182
Constant	−3.271	0.488	44.967	0.000	0.038	–

APDMM = aorto-pulmonary diameter mismatch; AR = aortic valve regurgitation; ARD = aortic root dilation; BPV = bicuspid native pulmonary valve; PAB = pulmonary artery banding.

results of a 35-year follow-up of 318 patients at their institution who experienced arterial switch operation from October 1981 to July 2018. They found that 12 percent (35) of survivors had moderate to severe new aortic valve regurgitation at the most recent follow-up.[10] Roel L.F. van der Palen et al.[11] retrospectively analysed the clinical data of 490 children treated with arterial switch operation at the Leiden University Medical Center, Leiden, between January 1977 and January 2020. They completed a 43-year long-term follow-up. After right ventricular outflow tract obstruction (50/83, 60.2%), aortic root dilation was the second most common indication for reoperation (15/83, 18.1%). In this study, the incidence of reoperation for new aortic valve regurgitation with root dilation was 22% (4/18), which was slightly higher than that of the former, considering that our centre is more active in the intervention of late complications. Yaqiong Xiao et al.[12] reported the mid-term follow-up results of 119 patients who received arterial switch operation in Union Hospital, Huazhong University of Science and Technology from 2007.1 to 2013.12. Ninety-three (85.3%) patients completed follow-up, and it was found that four patients (4.3%) developed moderate to severe new aortic valve regurgitation, which is better than this study. Because of their shorter follow-up time, we believe that with longer follow-up, more patients will develop new aortic valve regurgitation. Shinichiro Oda et al.[13] reported that 145 patients underwent angiographic

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Table 7. Baseline characteristics and clinical outcomes of patients in the neoaortic sinotubular junction reconstruction nd non-neoaortic sinotubular junction reconstruction roups after propensity score matching [Number (%)/Median (Min, Max)/Mean ± SD]

Variable	NNSJR roup (n = 30)	non-NNSJR roup (n = 30)	P-value
Gender (Male)	18(60.00)	17(56.67)	0.793
Surgical weight (kg)	4.80(2.70,7.20)	5(3.10,7.10)	0.852
Surgical age (day)	29(1,71)	30(4,69)	0.781
Prematurity	15(50.00)	16(53.33)	0.796
Prenatal diagnosis	8(26.67)	7(23.33)	0.766
Emergency operation	5(16.67)	6(20.00)	0.739
Surgery period			0.739
2006–2014	6(20.00)	5(16.67)	
2014–2022	24(80.00)	25(83.33)	
Anatomical type			0.254
TGA-IVS	18(60.00)	18(60.00)	
TGA-VSD	10(33.33)	9(30.00)	
TGA-TBA	2(6.67)	3(10.00)	
Associated cardiac lesion	11(36.67)	10(33.33)	0.787
Preoperative mechanical ventilation	5(16.67)	6(20.00)	0.739
Coronary artery malformation	1(3.33)	1(3.33)	1.000
APDMM	28(93.33)	30(100.00)	0.150
BPV	1(3.33)	0(0.00)	0.313
Previous PAB	1(3.33)	0(0.00)	0.313
Preoperative moderate or severe PR	0(0.00)	1(3.33)	0.313
Preoperative cardiac dysfunction	3(10.00)	2(6.67)	0.640
CPB time (min)	171.63 ± 30.43	181.21 ± 41.20	0.412
Cross-clamp time (min)	90.21 ± 20.33	100.01 ± 22.41	0.563
ICU stay time (days)	7(1,25)	7(2,28)	0.657
Early mortality	2(6.70)	0(0.00)	0.492
AR at discharge	3(10.00)	0(0.00)	0.237
Late mortality	1(3.57)	0(0.00)	0.296
Late intervention	3(10.71)	0(0.00)	0.066
ARD	7(25.00)	0(0.00)	0.003
NAR	5(17.86)	0(0.00)	0.015
RVOTO	3(10.71)	1(3.33)	0.268

APDMM = aorto-pulmonary diameter mismatch; AR = aortic valve regurgitation; ARD = aortic root dilation; BPV = bicuspid native pulmonary valve; IVS = intact ventricular septum NAR new aortic valve regurgitation; NNSJR = neoaortic sinotubular junction reconstruction; PAB = pulmonary artery banding; RVOTO = right ventricular outflow tract obstruction; TBA = Taussig-Bing anomaly; TGA = transposition of the great arteries.

follow-up for at least 10 years, of which 21 (14.5%) patients developed neo-aortic valve insufficiency, which was similar to the results of this study. Tyson A. Fricke et al.[14] retrospectively analysed the clinical data of 844 patients undergoing arterial switch operation at the Royal Melbourne Hospital from 1983 to 2015. Many patients with arterial switch operation have good long-term survival but develop significant new aortic valve regurgitation or require new aortic valve replacement after 25 years. 15% of patients had moderate neo-aortic valve regurgitation or required neo-aortic valve replacement after 25 years. Slightly higher than the results of this study, considering its longer follow-up time span.

Risk factors for new aortic valve regurgitation and aortic root dilation have been reported in recent years, but the results reported by different institutions are not the same. In this study, we found that aorto-pulmonary diameter mismatch, previous pulmonary artery banding, and minimal new aortic valve regurgitation at discharge were common independent risk factors for late new aortic valve regurgitation and aortic root dilation. However, low surgical weight was an independent risk factor specific to new aortic valve regurgitation, and bicuspid native pulmonary valve was an independent risk factor specific to aortic root dilation. Roel L F van der Palen et al.[15] reported findings from their centre in

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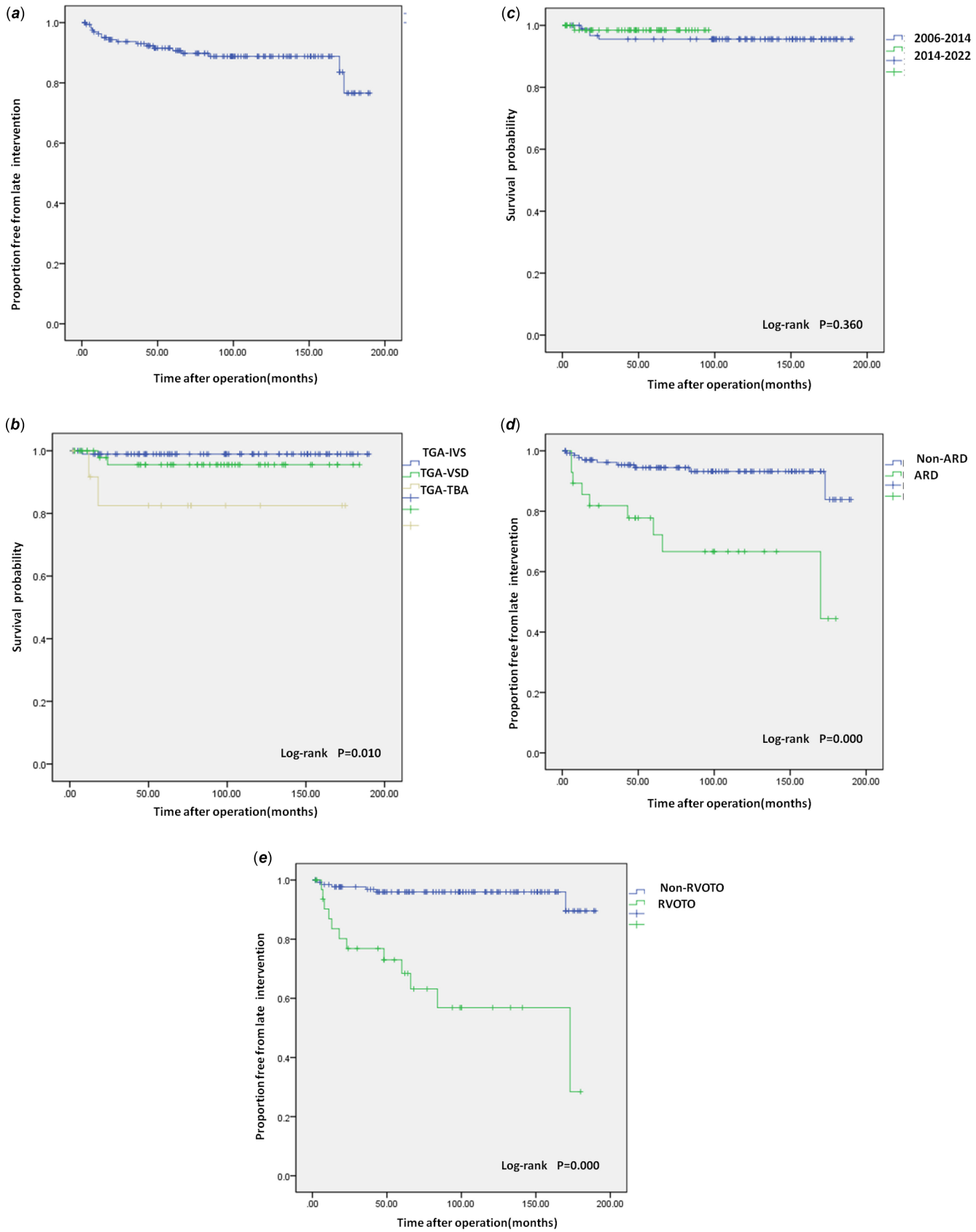


Figure 3. (***a***) Overall late intervention survival curve. (***b***) Late intervention survival curve. Kaplan-Meier curves show the relationship between the anatomical type and late intervention. (***c***) Late intervention survival curve. Kaplan-Meier curves show the relationship between the age group and late intervention. (***d***) Late intervention survival curve. Kaplan-Meier curves show the relationship between the aortic root dilation and late intervention. (***e***) Late intervention survival curve. Kaplan-Meier curves show the relationship between the right ventricular outflow tract obstruction and late intervention. RVOTO = right ventricular outflow tract obstruction; TGA-IVS = Transposition of the great arteries-Intact ventricular septum; TGA-TBA = Transposition of the great arteries-Taussig-Bing anomaly; TGA-VSD = Transposition of the great arteries-Ventricular septal defect.

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2019. Risk factors for root dilatation were complex transposition of the great arteries anatomy (Transposition of the great arteries-Ventricular septal defect, double-outlet right ventricle with subpulmonary Ventricular septal defect) and male gender. Risk factors for aortic valve regurgitation ≥ moderate were: complex transposition of the great arteries anatomy and neo-aortic growth. Per millimetre increase in aortic root dimension, there was a 9% increase in the hazard of aortic valve regurgitation ≥ moderate. However, Bicuspid pulmonary valve did not relate to the presence of root dilatation or aortic valve regurgitation, which is different from our view. Emanuela Angeli et al.[16] reported a long-term evaluation of the effects of the mitral pulmonary valve on new aortic valve regurgitation and aortic root dilation after arterial switch operation. In univariate analysis, weight at operation was the only independent variable that predicted increased aortic valve regurgitation ($P = 0.02$). Only the position of the great vessels (anteroposterior versus other position) was a higher risk of aortic root dilation for side-by-side or rightward position of the great arteries (univariate analysis: $P = 0.03$). Shinichiro Oda et al.[13] believed that major risk factors for NRD were double-outlet right ventricle and presence of neo-aortic valve insufficiency. Rui Lu et al.[9] summarised and analysed the results of new aortic valve regurgitation after arterial switch operation in 599 transposition of the great arteries children in the Pediatric Cardiac Surgery Center of Fuwai Hospital. They believe that previous pulmonary artery banding and aorto-pulmonary diameter mismatch are risk factors for severe aortic insufficiency, and no severe aortic regurgitation was found after neo-aortosinusoplasty in children with aorto-pulmonary diameter mismatch. Their conclusions are consistent with the conclusions of this study. We believe that aorto-pulmonary diameter mismatch and the previous pulmonary artery banding have changed the geometry of the aortic root and the sinotubular junction to varying degrees. The haemodynamics have changed, which is easy to cause turbulent flow, and the growth and development of the child itself are combined, with the growth over time, the probability of new aortic valve regurgitation and aortic root dilation occurrence is increasing. As for the relationship between low surgical weight and advanced new aortic valve regurgitation, it may be because the lower the surgical weight of the child, the more immature the pulmonary valve is, the texture is relatively brittle, and it is easy to be damaged during arterial switch operation. This requires us to perform more delicate surgical operations and pay attention to protecting the pulmonary valve when operating on low-weight children in the future.

In 2014, Arcieri et al.[17] proposed a V-shaped resection technique to reduce the mismatch between the new aortic root and the ascending aorta. Based on the same purpose, neo-aortic sinotubular junction reconstruction technique was used in 30 consecutive patients with transposition of the great arteries who had mismatched two major arteries in Fuwai Hospital since 2011. All patients with neoaortic sinotubular junction reconstruction did not develop severe new aortic valve regurgitation during the postoperative follow-up period, and the results were significantly better than those without neoaortic sinotubular junction reconstruction. The experience of Fuwai Hospital is that neo-aortic sinotubular junction reconstruction technique is easy to perform and does not significantly increase the aortic cross-clamp time and cardiopulmonary bypass time. neoaortic sinotubular junction reconstruction technique can significantly improve the incidence of long-term complications, and significantly reduce the incidence of late new aortic valve regurgitation and aortic root dilation after arterial switch operation.

Late intervention

Although survival has greatly improved, recurrent and new lesions remain and require reoperations or catheter interventions. According to previously published literature reports, the late reintervention rate ranges from 5 to 20%.[18–21] The late reintervention rate of this study was 10.84%, which was consistent with published reports. The long-term complications after arterial switch operation mainly include right heart system disease, left heart system disease, coronary artery dysfunction and arrhythmia. This cohort showed that right heart system intervention was the most common (6/18), arrhythmia intervention was the least common (3/18), and no coronary reintervention was seen, but one patient died of myocardial infarction due to left coronary embolism in late death patients without timely intervention.

Limitations

The most important limitation of this study is its retrospective nature. An additional limitation is the relatively small study size limiting the statistical robustness of any inference that may be drawn. In the future, longer follow-up and larger sample size multicentre clinical studies are needed to further evaluate our conclusion.

Conclusions

In conclusion, new aortic valve regurgitation, aortic root dilation, recurrent coarctation of the aorta, and right ventricular outflow tract obstruction are major indications for long-term reintervention. Aorto-pulmonary diameter mismatch, previous pulmonary artery banding, and trace new aortic regurgitation at discharge were common independent risk factors for late new aortic valve regurgitation and aortic root dilation. Low body weight was an independent risk factor specific to new aortic valve regurgitation and bicuspid native pulmonary valve was an independent risk factor specific to aortic root dilation. Older age at surgery and aortic root dilation are independent risk factors for late right ventricular outflow tract obstruction. Older age at surgery, surgery before 2014, late right ventricular outflow tract obstruction and late aortic root dilation are independent risk factors for late intervention. neoaortic sinotubular junction reconstruction technique may reduce the incidence of new aortic valve dysfunction after arterial switch operation, significantly reduce the incidence of new aortic valve regurgitation and aortic root dilation, and improve the incidence of late complications after arterial switch operation.

Supplementary material. The supplementary material for this article can be found at https://doi.org/10.1017/S1047951124000453.

Data availability statement. All data are incorporated into the article, and the data underlying this article are available in the article.

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Author contribution. **Zhangwei Wang:** Conceptualisation; Data curation; Formal analysis; Investigation; Methodology; Software; Validation; Visualisation; Writing—original draft. Kai Ma: Writing – review & editing. Shoujun Li: Writing – review & editing.

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