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A Prospective Observational Study on the Long-Term Fate of Neo-Aorta Following Arterial Switch Surgery

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Abstract

Introduction: For patients of all ages with transposition of the great arteries and its different subtypes, arterial switch surgery is the standard of care. While short-term mortality and morbidity have decreased significantly over time, long-term neoaortic regurgitation development is still a significant problem. Methodology: The study included all children who underwent primary ASO with or without integrated ECMO support, were operated on by a single surgeon at our facility, and finished at least five years of follow-up. During the course of the study, 35 patients were evaluated. The paediatric cardiologist performed the clinical examination and echocardiographic evaluation. Findings: The patients' median age at follow-up was 10 years (range: 5 - 13 years). Girls (n = 3, 8.5%), boys (n = 32, 91%). At presentation, 31 patients (88.5%) had TGA, intact ventricular septum; 4 patients (11.5%) had TGA, VSD; 4 patients (11.4%) had moderate AR; 10 patients (28.57%) had mild AR; and 21 patients (60%) had no or trivial AR. There was no discernible dilatation in the LV dimensions of these four patients. Conclusion: Aortic regurgitation has no effect on neo aortic growth, with the exception of the annulus. Therefore, an early return of transposed arteries to their normal anatomical position results in a competent aortic valve because systemic pressure causes the valve's cell signalling to be upregulated.

Keywords

ASO, TGA, NEO Aortic Regurgitation, Congenital Heart Disease

1. Introduction

For patients of all ages with transposition of the great arteries and its various subtypes, arterial switch surgery is the primary treatment. The great artery transposition anomaly is anatomically corrected by this procedure. This entails splitting the aorta and pulmonary arteries, moving the coronary buttons to the neoaorta, performing the Lecompte manoeuvre (moving the pulmonary artery anteriorly and the aorta posteriorly), and resuturing the great vessels to their corresponding roots. While short-term mortality and morbidity have decreased significantly over time, long-term neoaortic regurgitation development is still a significant problem.

Preoperative pulmonary valve regurgitation; acute angulation of the aortic arch following posterior translocation of the ascending aorta; impaired growth of the neoaorta; intrinsic weakness of native pulmonary artery and valve tissue in facing systemic pressure (although some have disputed this hypothesis); non-facing commissures; abnormal coronary artery anatomy; intrinsic weakness of native pulmonary artery and valve tissue in facing systemic pressure. Aortic transection with disruption of the vasa-vasorum may change the structure of the neoaorta; very large buttons for translocation of the coronary arteries may also cause distortion [1]-[3].

According to published studies, the prevalence of AR ranges from 6 to 84% [4]-[6]. This is dependent upon both the age at which the child is evaluated and the study population. Neo AR is typically a minor complication that calls for ongoing medication and monitoring. Reintervention frequency ranges from 0 to 3% [4]-[6].

2. Methods

Table 1. Characteristics of children on follow-up after primary Arterial Switch Operation (ASO) in infancy by a single surgical team.

	Surgery (N = 35)	Follow up (N = 35)	Remarks
Age	2 months (5d - 24mo)	10 years (5 - 13)	
Sex	Boys (n = 32, 91%): Girls (n = 3, 8.5%)		10:1
Body surface Area Body Mass Index	1.036 cm^2	16.1 kg/m^2	
Diagnosis	TGA, IVS (n = 31, 88.5%): TGA, VSD (n = 4, 11.5%)		8:1
Treatment	ASO + VSD closure in 5: ASO + VSD closure in 4		P value: 0.3825*
ECMO	Integrated ECMO circuit used- n = 10 ECMO support (n = 3)		

We prospectively profiled the neoaortic root in a group of infants with TGA and its subtypes, who underwent ASO (Arterial switch operation). We used echocardiograms to examine the functional effects on the neoaortic root following ASO. This is a cross sectional study wherein children who have been operated on by a single surgeon (AKB) at our centre and have completed 5 years after surgery (Arterial switch operation with or without ECMO support) are evaluated for severity of aortic regurgitation and dimensions of aortic root. Children who underwent additional procedures such as pulmonary valvotomy, LVOT resection, or coarctation of aorta repair were not included. The study was approved by the Institute Ethics Committee (IECPG-412/27.06.2019).

2019 saw the collection of baseline demographic data (as shown in **Table 1**), including contact validation and record verification. In 2020, we began contacting the kids for their evaluations, and the families' commutes from their hometowns to New Delhi took varying amounts of time. From February 2020 to January 2021, echocardiographic evaluation and follow-up were carried out.

A paediatric cardiologist performed the follow-up echocardiogram to assess the following: the degree of aortic regurgitation; the type of aortic regurgitation (eccentric jet or central jet); the dimensions of the aortic root (aortic annulus, sinus of valsalva, ST junction, ascending aorta); the size and function of the left ventricle; and the type of neo-aortic valve (tricuspid or bicuspid). The American Society of Echocardiography's (ASE) guidelines served as the foundation for the echo evaluations. Every evaluation lasted five to ten minutes. Every child was evaluated in both supine and left lateral positions. During the process, ECG leads were connected. 5 and/or 8 MHz probes were employed.

2.1. Classification of Severity of AR Based on ASE Criteria [7]

1) Trace (trivial): only a very small color-Doppler jet with minimal penetration into the LVOT, no or very small vena contracta, no measurable EROA/regurgitant volume or values well below mild thresholds; supportive signs of trivial severity (normal LV size and diastolic flow patterns).

2) Mild AR:

a) Color-jet width/LVOT diameter ratio < 25%.

b) Vena contracta < 0.3 cm.

c) Effective regurgitant orifice area (EROA) < 0.10 cm^2.

d) Regurgitant volume < 30 mL/beat.

e) Regurgitant fraction < 30%.

f) Holodiastolic flow reversal absent in descending aorta (or only intermittent).

3) Moderate AR:

a) Color-jet width/LVOT ratio 25% - 5%.

b) Vena contracta 0.3 cm - 0.6 cm.

c) EROA 0.10 cm - 0.29 cm^2.

d) Regurgitant volume 30 - 59 mL/beat.

e) Regurgitant fraction 30% - 49%.

f) Holodiastolic flow reversal may be present (partial).

There were 126 children's medical records available. Of these, 19 children were excluded because their parents' phone numbers were not available in the medical records, and 30 children's parents' phone numbers were either inaccurate or unreachable, so they were also excluded. Two children passed away after the procedure, and five children experienced in-hospital mortality. For the study and clinical follow-up, the remaining seventy kids were invited to visit the hospital. The operating team was informed to recruit children who meet the inclusion criteria and have visited the out-patient department for their clinical follow-up in order to address the issue of recruitment attrition.

The patient's copy of the discharge summary was then used to gather clinical information. 35 children participated in the study whose characteristics are described in **Table 1**; the remaining 35 were unable to visit the hospital because of the COVID-19 pandemic, which led to a nationwide lockdown until the study's record collection was completed. Although variables such as presence of vsd, bicuspid neoaortic valve, age at surgery and ecmo exposure was noted, significance of these with respect to AR severity could not be ascertained as sample size is too small.

Table 2 shows echocardiographic values of LV outflow orifice valve and their z scores, reference for which is from Petterson MD *et al.* [8].

Table 2. Echocardiographic values of the LV outflow orifice valve apparatus (Aortic Annulus, SOV, STJ), AA, LVED and their z scores indexed to body surface area.

N = 35	Size (mean ± SD) cm	Z scores	SD
Aortic annulus	18.35 ± 3.06	+1.08[@]	1.19
SOV	25.80 ± 3.16	+1.34	1.02
STJ	19.22 ± 3.77	+0.29	1.74
AA* (n = 33)	20.13 ± 3.83	+0.64	1.62
LVed		−1.24	1.25
[@]Aortic annulus z score when indexed to pulmonary valve annulus		+0.02	0.78

Table 3. Details of the LV outflow orifice valve apparatus and functional effects (regurgitation) across it.

Severity of AR	No AR in 17 (48.57%), Trivial AR in 4 (11.43%), Mild AR in 10 (28.57%)		Mod AR in 4 (11.43%)
Categorisation for comparison	**No, Trivial, Mild AR (n = 31)**	**Mod AR (n = 4)**	**P value**
Age at surgery	**5.14 months**	**5.65 months**	**0.9679**
Age at Follow-up	**10 years**	**10 years**	**0.9202**
Aortic annulus Z score	**0.91**	**2.425**	**0.0131**
Sinus of Valsalva Z score	**1.811**	**1.125**	**0.3504**
STJ Z score	**−0.05**	**0.0575**	**0.1615**
Ascending Aorta Z score	**0.38**	**1.45**	**0.5326**

Note: Left Ventricular outflow orifice = Aortic Annulus + Sinus of Valsalva (SOV) + Sinotubular Junction (STJ); Obs—4, Sum of Wgt—4, Mean—2.425, Std. Dev—0.7066116, Variance—0.4993, Skewness—0.446308; Obs—31, Sum of wgt—31, Mean—0.9112903, Std. Dev—1.132304, Variance—1.282112, Skewness—0.0585211.

Table 3 shows that four patients (11.4%) had moderate AR, ten patients (28.57%) had mild AR, and twenty-one patients (60%) had no or trivial AR. The

LV dimensions of these four patients were not significantly dilated. Analysis was done on the relationship between neoaortic root size and AR severity. We separated the severity of AR into two groups: no AR, mild AR, and trivial AR, and moderate AR. These two groups' annular Z scores were compared using Mann-Whitney U test. Only two of the 35 patients had a bicuspid aortic valve, according to echocardiography. These two individuals had mild AR. The first patient had dilated annulus (Aortic annulus Z score 2.14, Sinus of Valsalva Z score 4.31, Sinotubular junction Z score 5.73, and Ascending aorta Z score −4.9), while the second patient had dilated annulus (Annulus Z −0.65, Sinus of Valsalva 1.97, Sinotubular junction −3.75, Ascending aorta 1.85).

2.2. Statistical Analysis

Analysis was done in STATA 14 software. Continuous variables and their distribution were expressed as Mean +/− SD, Median or Mode. Chi square test was used for categorical variables. Mann whitney U test was used for continuous variables compared with severity. Kruskal Wallis (Non parametric tests) were used for testing significance. P value < 0.05 was found to be significant.

3. Discussion

The preferred procedure for patients with TGA is arterial switch surgery. Few facilities, like ours, have attempted to push the boundaries and perform the procedure on children as young as six weeks or older, despite the fact that it is not advised for children older than one month. These cases' outcomes have already been published [9].

One known postoperative complication is neoaortic valve regurgitation. The incidence of AR has been reported in various studies to range from 5% to 30% over a period of one to five years. The course of this AR varies widely; some have reported that its incidence has increased over time, remained constant, or even decreased. Neo AR has been attributed to a number of factors, including high afterload, high turbulence at the anastomosis site due to Aorta-PA size mismatch, complex rearrangement of sinuses and sino-tubular junctions, reflected pulse wave after Lecompte maneuver due to acute angulation of the aortic arch, etc. [4]-[6].

The incidence of neo-AR (more than trivial AR) in our case was 61% at discharge, 28% at six months, 9% at one year, and 4% at twenty-four months. Over the course of 36 months, this AR is probably going to vanish. At 12 months, the freedom from more than trivial AR was 90%, and at 36 months, it was expected to reach 100%. The acute angulation of the arch gradually expands and becomes obtuse as the child grows, improving the forward pulse wave and decreasing the reflected pulse wave, which is why the degree of neo-AR has improved. The neoaortic root pressure is lowered by this decrease in the reflected pulse wave. Consequently, the leaflets and neo-AR are less stretched [10].

Ten patients (28.57%) had mild AR, four patients (11.4%) had moderate AR, and twenty-one patients (60%) had no or minimal AR in the current study. None of the patients under study had dilated LV dimensions. Patients with no AR, trivial AR, and mild AR had their aortic roots compared to those with moderate AR. Patients with moderate AR had a significantly dilated aortic annulus compared to those with no to mild AR. The remaining parameters were similar for both groups.

The results of this study indicate that, in comparison to children of the same age, aortic roots in children who have experienced ASO grow normally. Because the aortic annulus was a pulmonary valve prior to the procedure, it is typically larger.

49% of the 172 patients in a study by Krzysztof W. Michalak *et al.* had developed neo-AR by the end of the 13.5-year follow-up period. The mean increase in the neo-AR grade was 0.64, with 85% having mild AR, 15% having moderate AR, and 1% having severe MR. Neo-AR was most likely to develop between the first and sixth postoperative years. Neo-AR risk factors, including associated VSD, age at surgery, and coronary anomalies, were not found to be significant contributors. On average, there were no differences in the measured aortic root dimensions between patients with and without neo-AR. By the end of the study, the root dimensions had grown from an average of 37% to 57% larger than the general population. However, the degree of aortic regurgitation was not found to be directly correlated with the size of the aortic root, indicating that the degree of dilatation is not a significant factor in the impairment of neoaortic valve function [2].

Similar findings to ours were reported by Bove *et al.*, who discovered no connection between aortic regurgitation and neo-aortic root dimensions [11]. Aortic root dimensions increased from a z-score of 2.6 to 3.6 after five years and 4.6 after ten years of follow-up in a series published by Schwartz *et al.* [12].

In the study by Mauro Lo Rito *et al.*, 332 patients had ASO; the median follow-up period was 16 years. At 10 and 20 years of follow-up, the freedom from moderate regurgitation was 97% and 80%, respectively. Aortic valve regurgitation necessitated reoperation for five patients [13].

Young patients who underwent surgery have demonstrated that the neoaortic root can tolerate systemic pressures, much like patients who underwent Ross procedures. At 15 years, 86% of participants in a multi institutional study by Jason W. Greenburg *et al.* were free from more than moderate aortic regurgitation [14].

This can be explained by the fact that progenitor cells for the aortic, pulmonary, and aortomitral curtain originate from the distal part of bulbuscordis and develop in the truncus arteriosus with assistance from the EMT (epi, myo, and endocardium). Therefore, when exposed to systemic pressure, the neoaortic valve is upregulated.

In a metaanalysis by Jacquemyn *et al.* of 6169 TGA patients after ASO describe the incidence and risk factors for aortic root complications, 30 studies have been included in the metaanalysis. The analysis shows mild neo-aortic regurgitation is common by adulthood (only 47.7% freedom from ≥ mild neo-aortic regurgitation at 20 years, cumulative incidence of 67.5% at 30 years); however, more significant neo-aortic regurgitation is uncommon (87.8% freedom from ≥ moderate neo-aortic regurgitation at 20 years, cumulative incidence of 21.4% at 30 years). Neo-aortic root dilatation is present in half of children and the majority of adults after ASO (34.9% freedom from neo-aortic root dilatation at 20 years) and appears to be progressive over time. The one reassuring part is that surgery to address the dilated aortic root is rare [15].

Limitations of the Research

Due to the difficulty of contacting patients for follow-up during the Covid pandemic, only a small number of patients were evaluated.

Improved aortic regurgitation analysis, such as with MRI or 3D echocardiography.

Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

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