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Two-stage arterial switch for late-presenting transposition of the great arteries†

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Abstract

OBJECTIVES: Ventricular retraining and arterial switch have been described in late-presenting transposition of the great arteries (TGA) in older infants who were unable to undergo neonatal arterial switch operation (ASO) and late survivors of atrial switch with systemic right ventricular dysfunction. There are little data available on patients presenting between these 2 groups. This study aims to review the early and mid-term outcomes of the management of late-presenting TGA with an unprepared left ventricle (LV) by a 2-stage arterial switch.

METHODS: The demographic, procedural and outcome data were obtained for all children who underwent LV retraining for late-presenting TGA between 2005 and 2017 at our institution. The primary outcomes were early mortality and extracorporeal membrane oxygenation (ECMO) after arterial switch.

RESULTS: Twenty patients were included during the study period, with a median age of 12 months (range 6 weeks–3.3 years). The median time of LV retraining was 48 (range 8–170) days. Indexed LV mass increased from 34 ± 19 g/m^2 before LV retraining to 106 ± 85 g/m^2 before arterial switch. There was 1 death (5%) after LV retraining. Three patients required ECMO support after arterial switch (15%) despite retraining. During follow-up, there was 1 late death, no late reinterventions or reoperations, and all surviving patients had normal or near-normal LV function at late follow-up.

CONCLUSIONS: LV retraining resulted in an increase in LV mass and enabled a 2-stage arterial switch to be carried out with acceptable early and mid-term outcomes. Two-stage arterial switch is a reasonable option for late-presenting TGA. A long-term follow-up is required to assess late LV function after preparation.

Keywords: Congenital heart disease • Transposition of the great arteries • Arterial switch • Ventricular preparation

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INTRODUCTION

Primary arterial switch operation is the gold standard in management of transposition of the great arteries (TGA) with intact ventricular septum or restrictive ventricular septal defect before 3 weeks of age, with outstanding early and late outcomes [1, 2]. The ability of the left ventricle (LV) to function under systemic pressures decreases after 2 weeks of age in TGA with an intact ventricular septum and depends on the preload and the afterload of the LV, namely the patency of the ductus arteriosus, the pulmonary vascular resistance, the size of the atrial septal defect and the presence of left ventricular outflow tract obstruction [3]. LV retraining in TGA with intact ventricular septum was first reported by Yacoub *et al*. [4] in 1977. The Boston group expanded on this approach, proposing the concept of rapid 2-stage arterial switch in young infants with an unprepared LV [5, 6]. LV retraining has also been reported in 2 settings of systemic right ventricles, at the other spectrum of childhood: first, in patients with systemic right ventricular failure after an atrial switch operation usually during late childhood [7–9] and second, in children with congenitally corrected TGA with an unprepared LV before anatomic repair, used in small children and adolescents [10–13]. Between these 2 extremes in presentation, there are relatively little data available on patients presenting between these 2 groups, particularly since patients with TGA and a systemic right ventricle have become a disappearing population with the introduction of the primary arterial switch operation in neonates and the ageing and natural attrition of patients after an atrial switch [11]. There are a significant number of patients worldwide, without access to care or for other reasons, who cannot benefit from primary neonatal arterial switch and are referred late in life for management. Furthermore, data regarding the response to retraining and outcomes after 2-stage arterial switch can be of interest to provide

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further data supporting LV retraining in other patient groups, such as congenitally corrected TGA before anatomic repair [12, 13]. This study aims to review the early and mid-term outcomes of the 2-stage arterial switch for patients with TGA presenting late beyond the neonatal period.

METHODS

Study design

This study is a retrospective review of all patients who underwent LV retraining for late-presenting TGA between 2005 and 2017 at our institution. The cardiac surgery database was queried for patients with TGA. Inclusion criteria were an anatomy of TGA amenable to an arterial switch operation and an unprepared LV, judged by a combination of a decreased LV mass (usually <35 g/m^2), a banana-shaped LV or a right-to-left interventricular septum indicating low LV pressure. Exclusion criteria were candidates who were deemed suitable for immediate arterial switch operation, age >10 years and the presence of other significant lesions precluding an arterial switch operation, such as left ventricular outflow tract obstruction or dysplastic semilunar valves; these patients were scheduled for a Rastelli, 'reparation à l'étage ventriculaire', Nikaidoh or double-root translocation. Baseline demographic, echocardiographic, surgical and follow-up data were reviewed. LV mass was calculated at echocardiography in TM mode as described previously [3]. The primary end points were early mortality and extracorporeal membrane oxygenation (ECMO) requirement after LV preparation and/or arterial switch operation. The study was approved by the local review board (Comité Cantonal de l'Ethique de la Recherche (CCER), no. 14–045R), and individual patient consent was waived.

Operative techniques

LV preparation was performed primarily through a left thoracotomy. The left subclavian artery was dissected free, and the left pulmonary artery was dissected up to the hilum. A bolus of 100 units/kg of heparin was administered. The distal left subclavian artery was clamped laterally using a Cooley clamp placed on the underside of the artery, and a longitudinal arteriotomy was performed on the inferior aspect of this artery. An end-to-side anastomosis was performed between an adequately sized (usually 4–5 mm in diameter) GoreTex (W. L. Gore & Associates Inc., Newark, DE, USA) graft and the subclavian artery. Shunt size was chosen based on body weight (4 mm for weight of 4–6 kg, 5 mm for weight of 6–10 kg and 6 mm for weight >10 kg) and tailored to the size of the pulmonary arteries. The side clamp was released, and good shunt flow was confirmed through the proximal anastomosis. The shunt was then flushed with heparinized saline and clamped. The left pulmonary artery was controlled, usually distally by placing vessel loops around the individual lobar arteries to allow for as much working space as possible and a vascular clamp proximally. A longitudinal arteriotomy was performed. The distal end-to-side anastomosis was done between the graft and the left pulmonary artery using continuous running suture as for the proximal anastomosis. The shunt and pulmonary artery were then unclamped, and haemostasis was verified. The pericardium was then opened anterior to the phrenic nerve. The coronary anatomy was inspected (to ensure feasibility of an arterial switch operation after retraining), and a limited plane was dissected free between the aorta and pulmonary artery. An umbilical tape, premeasured to a circumference of 20 mm + 1 mm/kg (following the Trussler's rule), was placed around the main pulmonary artery and secured using 6-0 polypropylene suture. The LV pressure was not routinely measured during the procedure. Inotropes were added as required during the postoperative course. In patients with severe systemic desaturation (due to insufficient mixing despite an adequately sized atrial shunt) who did not stabilize after anaesthesia induction, the same procedure was performed through a full sternotomy and on cardiopulmonary bypass. Patients were discharged home (for humanitarian patients to local foster care) and followed up in our cardiology outpatient clinic.

Left ventricle preparation follow-up and arterial switch

Subsequent assessment of suitability for arterial switch was performed using transthoracic echocardiography, rarely supplemented by cardiac catheterization. Progression to arterial switch was generally considered appropriate in patients with significant progression of LV mass (usually >35 g/m^2) with less than moderate LV dysfunction and less than moderate mitral regurgitation.

Statistical analysis

Statistical analyses were performed using the SPSS 23 software (SPSS Inc., Chicago, IL, USA). Data are presented as mean ± standard deviation or median (range) where appropriate. Continuous variables were analysed with the related samples using Wilcoxon signed rank test and categorical variables using the Fisher's exact test. All statistical tests were 2-tailed, and *P*-values of <0.05 were considered significant.

RESULTS

Study population

The study included 20 consecutive patients with TGA who underwent LV retraining during the study period. The median age of the patients was 12 months (range 6 weeks–3.3 years) at LV retraining. The majority of the patients were aged between 2 and 24 months at retraining (15, 75%). Baseline patient characteristics at LV retraining are summarized in Table 1. The mean indexed LV mass was 34.1 ± 19.1 g/m^2 before LV preparation (median 31.6, range 16.2–71.9 g/m^2). During the study time period, 3 late-presenting patients with TGA and intact ventricular septum (1 patient with subpulmonary stenosis) were deemed suitable for primary arterial switch and excluded from the study.

Left ventricle preparation

One patient was operated on through a median sternotomy to restrict a very large atrial septal defect to 4 mm on cardiopulmonary bypass; the remainder of the patients were operated on through a left thoracotomy. One other patient required coarctation repair at the time of LV preparation. The median shunt size was 4.5 (range 3.5–7) mm. All patients required adrenaline infusion (0.04 and 0.15 μg/kg/min) in the operating room, which was

Table 1: Baseline patient characteristics

Characteristics	Value
Age (months)	12 (1.5–40)
<2	2 (10)
2–6	5 (25)
6–18	8 (40)
18–24	2 (10)
24–36	0 (0)
>36	3 (15)
Weight (kg)	6.25 (2.2–10.7)
Body surface area (m^2)	0.33 (0.17–0.49)
Associated lesions	
Sinus venosus atrial septal defect	1 (5)
Aortic coarctation	1 (5)
Aberrant right subclavian artery	1 (5)
Prior procedures	
Rashkind balloon atrioseptostomy	7 (35)
LV mass index (g/m^2)	34.1 ± 19.1

Data are reported as *n* (%), median (range) or mean ± standard deviation as appropriate.
LV: left ventricular.

weaned progressively, if deemed feasible within the first 24 h. On postoperative echocardiogram, the median band gradient was 43 (range 21–75) mmHg. The median intensive care unit (ICU) length of stay was 7 (range 3–71) days. The course in the ICU was usually relatively complex, as described for rapid 2-stage arterial switch [14]. One patient required reoperation for band tightening; this patient then had a difficult postoperative course complicated by repeated hypotensive spells and sepsis, left mainstem bronchus compression and finally death after cardiac arrest 37 days after banding. One other patient presented with persistent low cardiac output requiring inotropic support, complicated by fungal sepsis. Five patients presented with postoperative pericardial effusion, which did not require late drainage.

Left ventricle response to retraining and arterial switch

All surviving patients were followed up using serial echocardiography. The indexed LV mass increased to a mean of 106.2 ± 85.8 g/m^2 or a median of 88.3 (range 32–345 g/m^2, $P = 0.002$ when compared with preoperative LV mass, Fig. 1). The time-dependent variation of LV mass between retraining and banding is summarized in Fig. 2 and showed moderate correlation ($R^2 = 0.26$).

The median time of LV retraining was 48 (range 8–170) days. Among the 19 survivors, all underwent an arterial switch operation, pulmonary artery band and shunt takedown. The coronary anatomy was usual for dextro-transposition of the great arteries (D-TGA) in 16 (84.2%) patients, 1 patient had the LAD from the right coronary artery (RCA) (5.2%) and 2 patients had a single coronary ostium from the left sinus (10.5%). Two patients required branch pulmonary artery plasty at the site of insertion of the shunt. One patient required immediate revision of the left coronary button for significant ischaemia on weaning from cardiopulmonary bypass. The mean aortic cross-clamp time was 86 ± 28 min, and cardiopulmonary bypass time was 115 ± 28 min. Four (21.1%) patients were electively left with an open chest after arterial switch. Three patients required ECMO cannulation after arterial switch; 2 patients presented with left ventricular failure, increased lactate and left atrial pressure, which progressed to severe hypotension and cardiac arrest despite increases in inotropes, requiring urgent chest reopening, internal resuscitation and ECMO cannulation on post-switch Day 1. The 1st patient was weaned successfully after 6 days on ECMO and the 2nd after 4 days, with delayed sternal closure. Both patients had an uneventful course after ECMO and recovered normal LV function. The 3rd patient presented with septic shock, LV dysfunction and required elective ECMO cannulation, which was successfully weaned after 8 days. He had an uneventful course after ECMO and recovered normal LV function. One further patient had to undergo urgent arterial switch operation, due to persistent acidosis and hypoxaemia due to shunt thrombosis 8 days after retraining, which required urgent cannulation under cardiopulmonary resuscitation. His indexed LV mass had progressed to 98 g/m^2 before switch. He required delayed sternal closure and multiple readmissions to the ICU for low cardiac output, despite normalization of his systolic LV function. The median ICU stay after arterial switch was 7.5 (range 2–122) days.

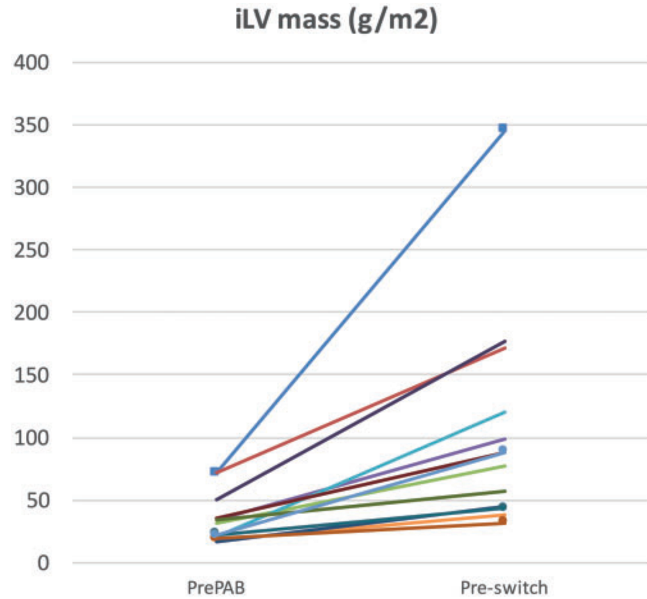

Figure 1: iLV mass variation between before preparation and before arterial switch. iLV: indexed left ventricular; PAB: pulmonary artery banding.

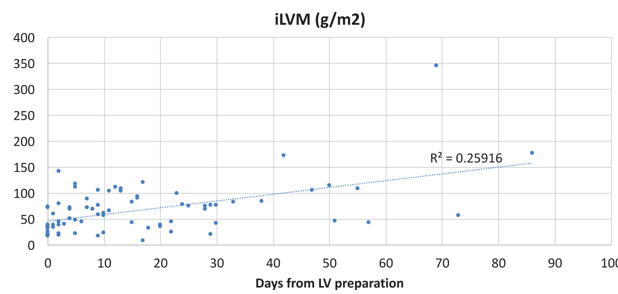

Figure 2: A time-dependent variation of indexed left ventricular mass between preparation (Time 0) and arterial switch.

Follow-up

All patients were followed up before return to their country of origin, with a median of 1.7 (range 0.5–48) months from arterial

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switch. Echocardiography revealed mild LV systolic dysfunction in 3 patients and normal LV systolic function in the remainder of the patients. During mid-term follow-up, no patients required a reoperation or reintervention. One patient died of sudden cardiac death shortly after discharge at home.

DISCUSSION

The arterial switch is the operation of choice for patients with TGA, as it restores the LV in the systemic position. Postnatal LV growth in a normal heart occurs in response to a combination of volume and pressure load, resulting in a rapid increase in LV mass. TGA and the absence of pressure load result in retardation of this increase in LV mass [15]. Decreasing LV volume load by balloon atrial septostomy, often required to improve mixing in TGA and stabilize a patient before arterial switch, decreases the LV mass significantly. In a retrospective study including 25 children with atrial septostomy at a median age of 4 days of life, LV mass decreased from a mean baseline of 48–25 g/m^2 by 15 days after balloon atrial septostomy or 1.5 g/m^2 per day during the first 2 weeks [16]. This regression was more pronounced in patients with atrial septostomy after 3 weeks of life ($P < 0.001$) [16].

Immature neonatal myocardium responds to pressure overload by hyperplasia, whereas between 3 and 6 months, the response changes to hypertrophy [15, 17]. These findings supported the use of a rapid 2-stage arterial switch in infants older than 3 weeks if there is evidence of regression of LV mass [3, 5, 6, 14]. In this neonatal and infant population, successful doubling of LV mass was reported as early as 7 days [6, 15], although the initial postoperative course was characterized by low cardiac output and multiple complications [3, 14], as reported in our patients.

Other options have emerged to manage these ‘unprepared’ infants, including a trial of pulmonary artery banding to assess suitability for a single-stage arterial switch. In a retrospective study including 5 patients with TGA and intact ventricular septum, with an age of 28 to 70 days [18], these patients had a pulmonary artery to systemic pressure ratio of 0.2–0.5, and echocardiography showed a banana-shaped LV and low LV wall thickness. These patients underwent a trial of pulmonary artery banding to systemic pressure for 15–30 min, during which they remained haemodynamically stable, and an arterial switch operation was performed. All patients were successfully weaned from cardiopulmonary bypass, although they all had prolonged inotropic dependence. Although it is elegant, and avoids the difficult post-retraining period and a rocky ICU course, and has shown outstanding results, the validity of such a short trial of acutely elevating the LV afterload to assess fitness for the arterial switch operation remains to be validated in more extensive experience. Finally, in the more recent era, primary arterial switch has been reported in infants up to 10 weeks of age, with outcomes similar to neonatal arterial switch, in terms of early mortality and requirement of mechanical circulatory support [2, 15, 19–22]. Recent data have confirmed the feasibility of primary arterial switch in late-presenting TGA with intact ventricular septum, avoiding the morbidity and mortality associated with 2-stage arterial switch, but at the risk of requiring ECMO or an LV assist device to support post-switch LV dysfunction [23–25].

At the other end of the age spectrum, late retraining has been reported in patients with a failing systemic right ventricle after atrial switch for TGA, first by Mee [7, 8] and then by other groups [9]. These studies have shown that, in patients as old as early adolescence, the morphological LV can be retrained sufficiently to allow for takedown of the atrial switch (Mustard or Senning) and performance of an arterial switch operation, with excellent outcomes in a very difficult patient group.

There are very little data available on retraining the LV before arterial switch between these 2 age extremes. Corno *et al.* [26] reported LV retraining in 6 children with a mean age of 8.3 (range 3–25) months, showing that retraining was feasible. Furthermore, although the long-term results of atrial switch procedures are considered poor with late systemic right ventricular dysfunction, baffle leaks and arrhythmias, more recent reports show excellent short to mid-term outcomes of atrial switch in the more recent era [27, 28]. Given these improvements and relatively low perioperative risk, and the lack of data on the long-term performance of a retrained LV after 2-stage arterial switch, atrial switch procedures remain a valid option in this patient population.

Beyond this, more attention has been directed towards a similar, but different group of patients: congenitally corrected TGA with an unprepared LV, who are being considered for anatomic repair. The Birmingham group reported their experience in 11 patients requiring LV retraining before anatomic repair, with similar outcomes in patients not requiring retraining, although retrained LVs had significantly more deterioration in LV function at an early stage [10, 11]. The Boston group reported 25 patients with congenitally corrected TGA who underwent LV retraining, with 1 early death after banding, and 18 who progressed to anatomic repair [12]. LV dysfunction was significantly more prevalent in patients who underwent anatomic repair older than 3 years ($P = 0.01$).

Our study reports our experience with LV retraining in patients with late- and very late-presenting TGA with an intact ventricular septum, who were predominantly between the ages of 2 and 24 months, extending to 3 years. This age group is significantly older than most prior series. Our study showed that despite late referral, LV retraining was possible, with time-dependent increase in LV mass. Despite a difficult postoperative course in the ICU, low cardiac output and significant morbidity, all but 1 of these patients underwent a successful arterial switch operation. Despite preparation and adequate preswitch evaluation, 3 of these patients required ECMO support early after arterial switch. Ventricular function recovered at late follow-up. Our approach for retraining, primarily through a left thoracotomy despite these patients being very hypoxaemic, allowed for a relatively distal shunt placement. This allowed us to choose a relatively larger shunt size, as flow is limited by the size of the subclavian artery and allows for growth. Shunt control and takedown at arterial switch was not an issue, and the shunt was easily mobilized in all patients. Furthermore, by avoiding a redo-sternotomy, the arterial switch and the extensive dissection of the aortic and pulmonary roots, and coronary arteries were relatively simple. Another issue in retraining, namely LV volume load and the role of atrial restriction, remains open, as we have had little experience with this approach. In 1 patient, the atrial septal defect was considered too large, and a planned shunt, band and atrial restriction were done. This patient had a very difficult postoperative ICU course, even more so than the patients we had previously managed without atrial restriction. Using the same principles, the Sankt Augustin group has proposed to ‘enhance’ LV retraining in congenitally corrected TGA by adding an atrial shunt in addition to a loose pulmonary band, to increase LV preload (in an inverted effect when compared with our TGA patients versus ccTGA) [13]. Beyond this experience, there are no reported data on the role of atrial septal restriction in TGA to augment LV preload, unless we extrapolate the results from secondary LV recruitment in borderline hypoplastic left hearts [29].

Limitations

This study is limited by the small sample size and the specific patient population included. This small sample size made any considerations on risk factors, limits of age to consider for LV retraining or factors suggestive of response to retraining impossible. In most developed countries patients with TGA are managed at birth or within a few weeks, and all patients included in this study were referred from foreign countries for management and cases like these are extremely rare in developed countries. In developing countries, there are many more patients who do not have access to neonatal care and could benefit from this 2-stage arterial switch. Finally, this contribution focuses on the LV retraining and early outcomes after 2-stage arterial switch; it lacks long-term follow-up, which is of paramount importance to assess whether the retrained LV maintains systolic function late after arterial switch.

CONCLUSIONS

In a challenging group of patients, 2-stage arterial switch can be performed with acceptable outcomes and a low rate of reintervention. LV retraining and arterial switch are reasonable options for late-presenting TGA, although a long-term follow-up is required to assess late LV function.

Conflict of interest: none declared.

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