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Transposition of the great vessels and intact ventricular septum: is there an age limit for the arterial switch? Personal experience and review of the literature

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Original Article

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Abstract

Objective: Prognosis of the transposition of the great arteries has completely changed since the introduction of the arterial switch. Time limit to perform this intervention is still controversial. The aim of this study is to demonstrate the early and late outcome of primary arterial switch operation beyond the age of months. *Methods:* We included all patients with the diagnosis of transposition of the great arteries with intact ventricular septum beyond the age of 8 weeks who underwent primary arterial switch operation. The procedures were performed by the same surgeon, in two different institutes. Patients who had transposition of the great arteries and associated anomalies (except atrial septal defect and persistent arterial duct) were excluded. Ventricular shape, geometry, and mass were not considered during the decision on procedure type. *Results:* In the study, 11 patients with the diagnosis of simple d-transposition of the great arteries beyond 8 weeks were undergone primary arterial switch operation with a mean age of 90.63 days (60–137 days), and 7 patients had a Rashkind procedure. All patients had squashed left ventricle shape with preserved function. The sternum was left open in 10 patients. Extracorporeal membrane oxygenation support was necessary in 45.45% of cases. The mean mechanical ventilation time was 7.27 days (1–16 days). No mortality was recorded until now. Post-operatory left ventricular function was preserved in 90.9% of the patients. Only one patient had mild myocardial dysfunction at the time of discharge. *Conclusions:* Primary arterial switch procedure can still be the best surgical option in patients with the diagnosis of transposition of the great arteries with intact ventricular septum beyond 8 weeks of age, providing that mechanical circulatory support and an expert cardiac intensive care unit service are available.

Transposition of the great vessels (transposition of the great arteries with intact ventricular septum) and intact ventricular septum (transposition of the great arteries with intact ventricular septum) is a rare congenital heart disease occurring in 3 per 10,000 of the neonates and is rapidly lethal (90% mortality in the first year of life without correction).[1] Prognosis of this pathology has completely changed after the introduction of the arterial switch procedure that must be undertaken in the early days of life while the left ventricle is still able to adapt to the conditions of systemic high pressure. The neonatal time period after which the arterial switch procedure is feasible is still controversial; some authors consider the cut-off of performing a primary switch to be 2 months of age.

In the last years, few European hospitals have developed a sort of collaboration programme with some developing countries for treating children with congenital heart defects. The major aspect of this agreement is transferring and treating patients of those developing countries in advanced cardiac centre abroad.

The necessity of early surgical intervention for those patients' population required early transfer of those patients to an advanced cardiac centre. The author has the opportunity to work in two different health institutes in northern Italy, which have this kind of collaboration agreement with those countries.

The reason for the late presentations of this group patients could be either clinical reason (prematurity, sick kids which needs medical therapy for other associated health problems) or just due to logistic reasons (ID, passport, visa paperwork, etc.).

The aim of this article is to demonstrate a personal experience of primary arterial switch in infants beyond the limit of 2 months. The author shares both immediate and long-term results in two different institutions where the author has worked.

Methods

We performed a retrospective review study of a consecutive series of patients with simple transposition of the great arteries older than 8 weeks of age operated on at Policlinico San Donato,

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Milan, between 2004 and 2017 and Istituto Giannina Gaslini, Genoa, between 2017 and 2018. Patients having ventricular septal defect, coarctation of the aorta, or other associated anomalies were excluded from this study. Patients who underwent atrial switch (Senning or Mustard) or double-stage arterial switch were not included in this study. Immediate outcome was observed carefully and documented. Mid-term and late outcome were reported as well.

Surgical technique

Primary arterial switch was the intervention of choice in all patients with simple transposition of great arteries (with intact ventricular septum). The decision to perform primary arterial switch procedure was taken regardless of the geometry, thickness, or function of the left ventricle.

Primary *arterial switch operation* performed with cardiopulmonary bypass under moderate hypothermia (28–32 °C). Patterns of the coronary arteries were documented intra-operatively. Two different types of cardioplegia were used (cold blood, 4 patients; custodial, 7 patients). Harvested coronary ostia bottom were re-implanted directly to the neoaortic root using surgical aortic punch. Lecompte manoeuvre was performed in all patients. Fresh autologous pericardium was used to reconstruct pulmonary artery trunk. Sternums were left open in all except one patient at the end of the primary arterial switch operation. Extracorporeal membrane oxygenation was used when weaning from cardiopulmonary bypass was unachievable, or in case of high left atrium pressure with low systemic blood pressure.

Intra-operative management was judged on few major haemodynamic values and blood test ranges, in addition to intra-operative echocardiogram studies.

Left atrial pressure in correspondence to systemic arterial pressure was an important indicator for the necessity of mechanical circulatory support. In most cases, left atrial pressure <20 mmHg with mean systemic arterial pressure of 45 mmHg was an acceptable condition to avoid mechanical circulatory support.

In addition, monitoring lactate and SVO_2 level were important indicators of cardiac function and output status. In borderline cases (variable left atrium pressure, variable systemic pressure), standby extracorporeal membrane oxygenation with already paced purse-string cannula sutures inside the open chest was our preferred plan.

The mean cardiopulmonary bypass time was 146.8 minutes and the mean cross clamp time was 72 minutes.

The mean time of sternum closure was 4.4 days (2–9 days). Mechanical circulatory support was necessary in five patients (45.45%) with a mean support time of 6.5 days (5–9 days). Inotropic support utilised in all patients for a period of 2 to 16 days with mean period of 8.54 days.

Intubation was maintained for a mean period of 7.27 days following arterial switch with median period of 4.5 days and ranging from 1 to 16 days. The mean period of in-hospital stay was 30.27 days (19–72). No mortality has been reported until the time of conducting this study.

Collecting data

All in-hospital admission data, including pre-operative records, echocardiogram reports, operative details, and post-operative period registries were collected from inpatient files. Mid-terms and late follow-up data were collected through local cardiologists overseas.

Nevertheless, our report's aim is to demonstrate early and late outcome after primary arterial switch procedure in those groups of patient.

We reported all observations collected, no significant analytic statistics could be led.

Review of the literature

We performed a literature search research on PubMed, with the exact terms [("d TGA" OR "d TGV," OR "transposition") AND "late arterial switch"], which resulted in 216 articles among which 29 were related to arterial switch. After examining those articles, eight articles were chosen as presenting examples of late arterial switch for transposition of the great arteries and intact ventricular septum.

Results

Between 2004 and 2018, 134 patients with the diagnosis of simple transposition of the great arteries underwent primary arterial switch procedure at Policlinico San Donato Hospital in Milan and Istituto Giannina Gaslini in Genoa. Among these patients, 11 patients had their operations after the age of 8 weeks (7 males, 4 females). All of 11 patients were coming from abroad.

There were two other patients coming from abroad with the diagnosis of simple transposition of the great arteries. The first patient was 18-month old with simple transposition of the great arteries and large atrial septal defect: Senning procedure was performed in this patient. The second patient was 9-month old: again Senning procedure was performed. In both cases, we did not consider arterial switch operation because of patients' age. We were not sure about the outcome of arterial switch operation after 6 months. No patients in the series underwent two-stage approach.

All of the patients were born at full term and had uneventful perinatal courses. Weight at the time of surgery ranged from 3270 to 5775 g. The mean age at primary arterial switch procedure was 90.63 days (ranging from 60to 137 days) (Table 1).

Previous atrial septectomy had been performed in seven patients (63.6%) (Table 2). No patient was diagnosed pre-natally.

All patients had small, squashed "banana-shaped" left ventricles at the time of arrival. We used Yacoub–Radley-Smith classifications for coronary anatomy descriptions. Among them, seven patients had type A coronary anatomy, one patient had type B, two patients had type E, and one patient had intra-mural left coronary artery (Table 3).

We have not collected the data of left ventricle mass and posterior wall thickness since we don't consider these echographic parameters as determinants of our choice of the arterial switch operation.

The mean cardiopulmonary bypass time was 146.8 minutes and the mean cross clamp time was 72 minutes. No mortality has been reported and the mean period of in-hospital stay was 30.27 days (19–72). Post-operative state has been summarised in Table 4.

Immediate post-operative check-up revealed a preserved left ventricular function in 90.9% of the patients. Only one patient had mild left ventricle dysfunction. Moderate aortic stenosis was noted in one patient with medium gradient of 25 mmHg. Only one patient had a severe stenosis at the bifurcation of the pulmonary artery with high right ventricular systolic pressure (70 mmHg); right ventricle outflow tract obstruction was successfully treated through percutaneous balloon dilatation in his home country (Table 5).

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Table 1. Pre-operative clinical data

Patient	Gender	Gestational age	Pre-natal diagnosis	Age at time of diagnosis (days)	Age at time of intervention (days)	Weight at time of intervention (g)	O_2 Saturation at time of intervention (%)
1.	Male	term	No	1	60	4700	65
2.	Male	term	No	2	94	5775	70
3.	Male	term	No	33	94	3455	70
4.	Female	term	No	80	112	4400	60
5.	Female	term	No	1	117	4000	75
6.	Male	term	No	90	118	5580	65
7.	Female	term	No	35	76	4800	80
8.	Female	term	No	20	60	3270	60
9.	Male	term	No	7	79	4800	80
10.	Male	term	No	10	61	3980	70
11.	Male	term	No	2	137	3480	75

Table 2. Atrial-septostomy (Rashkind) procedure

Patient	Rashkind	Age at time of Rashkind (days)
1.	Yes	3
2.	No	
3.	Yes	34
4.	No	
5.	Yes	60
6.	No	
7.	Yes	62
8.	Yes	7
9.	No	
10.	Yes	26
11.	Yes	12

Although all patients were coming from overseas, but follow-up data were transferred regularly to the institutes where surgeries were performed. Median follow-up time was 44 months (14–85). All patients were maintained good biventricular function throughout their follow-up period with good clinical status. No unexpected complications were reported during follow-up period.

Discussion

Transposition of the great arteries (transposition of the great arteries) is one of the frequent cyanotic congenital heart defects that require urgent surgical correction (arterial switch operation). Surgical outcome is mostly related to the timing of the operation. Arterial switch operation performed after the first week of life may be at risk of myocardial dysfunction related to absence of adaptation of the left ventricle to the overload of systemic pressure. Anderson et al have shown that mortality and the cost of hospitalisation increase every day after the 5th day of life.[2]

In the last years, many neonates and infants with the diagnosis of transposition of the great arteries were transferred from overseas to few Italian paediatric cardiac centres. Some of those patients were presenting for surgery at later age. The author (Pr Giuseppe Pomè G.P.) has the opportunity to work in two different health institutes in Northern Italy, which have this kind of collaboration agreement with overseas.

In this retrospective study, we aimed to report personal experience in (two different centres) the outcome of primary arterial switch operation for transposition of the great arteries with intact ventricular septum after the 8th week of life. We have reported 0% mortality, 45% of early mechanical circulatory assistance with extracorporeal membrane oxygenation with excellent long-term outcomes. A preserved post-operative myocardial function of the systemic ventricle in 90.9% of the cases was reported; one patient had reduced left ventricular function at the time of hospital discharge. This experience suggests in consequence that late arterial switch is a safe procedure and remains as the best surgical option for late presenting transposition of the great arteries with intact ventricular septum.

Our strategy was to opt for the primary arterial switch operation regardless of left ventricular shape, function, or coronary artery pattern. This strategy was based on both our experience in performing the arterial switch and experiences reported in the literature of successful primary arterial switch in patients after 1 month of life (Table 6). Our gained experiences based on the following:

1. Expanding the cut-off age for arterial switch operation beyond 3 weeks did not affect the late outcome of the surgery.
2. Left ventricle function recovery after the surgery was constant. This expanding cut-off from 3 weeks, 6 weeks, and then 2 months, etc., was always acceptable even for banana-shaped left ventricles or patients with depressed left ventricle function, but with more frequent uses of extracorporeal membrane oxygenation.
3. LV mass and posterior wall thickness was never considered when extending the cut-off age beyond 21 days in the centres strategy.[3] Actually these parameters were important in considering the pre-conditioning of the left ventricle while our strategy is based on the post-conditioning of the left ventricle so these parameters were not collected and not considered in our decision.

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Table 3. Pre-operative echocardiography data

Patient	Yacoub class	Intramural coronary artery	Persistent arterial duct	LV function	Banana shaped LV	Systemic-pulmonary collaterals	RV Function	Diameter of ASD	ASD Shunt
1.	B	No	No	Preserved	Yes	No	Preserved	7	2
2.	A	No	Yes	Preserved	Yes	No	Preserved	3	2
3.	A	No	Yes	Preserved	Yes	Yes	Preserved	5	1
4.	A	No	Yes	Preserved	Yes	No	Preserved	2	2
5.	A	No	Yes	Preserved	Yes	No	Preserved	5	2
6.	A	No	Yes	Reduced	Yes	Yes	Preserved	4	2
7.	A	No	No	Preserved	Yes	No	Preserved	8	2
8.	A	No	Yes	Preserved	Yes	No	Preserved	7	2
9.	E	No	No	Reduced	Yes	Yes	Preserved	9	1
10.	E	No	No	Preserved	Yes	Yes	Mildly reduced	4	1
11.	B	yes	No	Preserved	Yes	No	preserved	6	2

LV = left ventricle; RV = right ventricle; ASD = atrial septal defect

Table 4. Post-operative state

Pt.	Opened sternum	Sternal closure	ECMO	Inotropic assistance (days)	Inotropic drugs	Days of intubation	Complications	30 days or in-hospital death	In-hospital stay	Follow-up (month)
1.	Yes	5 days	Yes	5	Adrenalin + Milrinone	5	None	No	24	85
2.	Yes	3 days	No	6	Adrenalin + Milrinone + Levosimondan	3	None	No	19	47
3.	Yes	6 days	Yes	8	Adrenalin + Milrinone + Levosimondan	8	Sternal infection	No	47	51
4.	Yes	3 days	No	11	Adrenalin + Milrinone	3	None	No	21	65
5.	No	0	No	2	Milrinone	1	None	No	19	63
6.	Yes	9 days	Yes	14	Adrenalin + Milrinone + Levosimondan	14	Pneumonia	No	33	44
7.	Yes	2 days	No	4	Adrenalin + Milrinone	3	None	No	21	29
8.	Yes	2 days	No	5	Adrenalin + Levosimondan	4	None	No	21	40
9.	Yes	6 days	Yes	16	Adrenalin + Levosimondan	16	Chylothorax	No	72	41
10.	Yes	4 days	No	14	Adrenalin + Milrinone	13	None	No	24	35
11.	Yes	7 days	Yes	9	Adrenalin + Milrinone	10	None	No	32	14

ECMO = Extra corporeal membrane oxygenation

Table 5. Post-operative echocardiography

	LV function	RV Function	RV pressure	Significant aortic gradient	Significant pulmonary gradient
1.	Preserved	Preserved	25	No	No
2.	Preserved	Preserved	30	No	No
3.	Preserved	Preserved	20	No	No
4.	Preserved	Preserved	20	No	No
5.	Preserved	Preserved	20	Yes (25 mmHg)	No
6.	Preserved	Preserved	15	No	No
7.	Preserved	Preserved	15	No	Yes (20 mmHg)
8.	Preserved	Preserved	15	No	No
9.	Moderate reduction	Moderate reduction	32	No	No
10.	Preserved	Mild reduction	70	No	Severe stenosis of pulmonary bifurcation
11.	Preserved	preserved	25	No	No

LV = left ventricle; RV = right ventricle

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Table 6. Main results of studies reporting late arterial switch samples

Article	Sample	Mean age (extremes)	ECMO use	Duration of inotrope drugs	ICU stay	Mortality	Other findings
Foran et al[4]	37	12 days (21–60)	2.7%	5.2 ± 3.1 d	7.3 ± 4.4 d	2.7%	No significant difference between patients according to LV shape
Kang et al[5]	105	–28 days (21–185) –9 patients > 60 days	5.7% 22%	–	–	3.8% 0%	Primary switch is indicated until 6 months of life in selected cases
Sarris et al[6]	36 Multi-centric study	>8 weeks	–	–	–	3%	Age at the operation was a non-significant factor of mortality
Ismaïl et al[7]	27	37 ± 17 days	3.75%	85.3 ± 69.3 hours	9.7 ± 6.9 days	7%	–
Edwin et al[8]	6	49 days (31–66)	33.3%	–	20 ± 13.8 days	0%	–
Fricke et al[9]	23	>30 days 8 patients >60 days	–	–	–	4.3% 0%	–
Ma et al[10]	78	1.9 month (1–6.8)	–	–	–	2.6%	–
Bisoi et al[11]	109	69:4–84 days 27: 85–168 days 13: >169 days	14.7% immediate support 6.5% later support	–	–	Early 8.2% Late 2%	Mortality was compared between children in the age group of 6 to 12 weeks (n = 5 of 67) and children >12 weeks (n = 7 of 42) using log-rank test; no significant difference was found in the mortality between the two groups p = 0.13
Yildiz et al[12]	14	42 days (22–125) 2 patients >2 months	7.14%	–	12 days (3–48)	0%	–

After primary arterial switch operation and during weaning from cardiopulmonary bypass, close observation of the haemodynamic values is highly considered whether mechanical circulatory support is needed or not for weaning from cardiopulmonary bypass. The extracorporeal membrane oxygenation strategy is central canulation with left ventricle vent. The sternum is always left open. In borderline cases (left atrium pressure between 15 and 20) and moderate left ventricle dysfunction (ejection fraction 25–35%), strict clinical observation with serial lactate and mixed VO_2 levels will be checked in the first post-operative hours. In case of any haemodynamic compromises during early post-operative period, extracorporeal membrane oxygenation will be implanted in intensive care unit. Myocardial recovery is usually observed in 3rd to 5th days after the surgery.

Till now there are no clear criteria in the literature indicating the right timing of the arterial switch. The majority of studies indicate 21st day of life as a safe limit for performing primary arterial switch and the limit of 2 months as a possible borderline with an extracorporeal membrane oxygenation background (Table 6). Studies presenting patients operated beyond 2-month old have generally small samples, which can give only descriptive conclusions but not statistically valid guidelines.

Dr Bisoi in 2014 published a paper studying 109 arterial switch for late presenting D transposition of the great arteries. Mortality was compared between children in tow age groups of 6 to 12 weeks and children >12 weeks using log-rank test; no significant difference was found in the mortality between the two groups with p value = 0.13.[11] Besides, the approach in that article was not based on the left ventricle mass since it was judged as underestimating the ventricle function and it was not considered as a predictor of good clinical outcomes.[4,13,14]

Most authors propose a double-stage switch for patients aged more than 1 month. This technique aims to adapt the left ventricle for overload pressure.[15,16] In spite of its advantage, the pulmonary artery banding was reported to be technically difficult especially to find the right tightness of the bandage without leading to ventricular dysfunction.[13,17,18] Corno et al reported that half of patients operated for pulmonary artery banding were re-operated to adapt the size of the bandage.[15] Also the necessity of a systemic to pulmonary artery shunt in certain cases makes also this technique more complicated and even results in prolonged hospitalisation in the intensive care unit.[19]

Primary switch in patients aged more than 2 months with an extracorporeal membrane oxygenation background may be then a logical alternative to two-stage switch with a reduced number of surgical interventions.

In our experience, both not included patients with late simple TGA (9 months and 18 months) were considered too old to risk the operation of arterial switch. Actually, we were not sure about the outcome of ASO after 6 months of age. Also we have not found enough literature to consider the two-stage approach for this age.

Based on this experience, we propose the limit of 6 months as a cut-off for considering arterial switch in simple TGA with the background of extracorporeal membrane oxygenation as a method of left ventricular training.

Clinical guidelines have recently been established by the European Association for Cardio-Thoracic Surgery and the Association for European Paediatric and Congenital Cardiology about the management of patients with transposition of the great arteries with intact ventricular septum and recommended as a Class I Level B that the surgery of primary arterial switch must

be performed up to 3 weeks of life and as a Class IIa Level B to be performed until the age of 2 months.[20] The small samples and the lack of big studies lead the authors to advise a rapid two-stage arterial switch operation for left ventricle retraining. We consider that making the left ventricle face the systemic post-charge with extracorporeal membrane oxygenation assistance is itself a sort of retraining for the left ventricle.

Limits of the study

As the majority of the studies related to the arterial switch, it is difficult to collect a statistically significant sample of patients having that intervention after the age of 2 months.

A multi-centre prospective study should be performed to fix the borderlines of using the arterial switch in simple transposition of the great arteries.

Conclusions

We believe that the primary arterial switch procedure is still the best surgical option for late presenting transposition of the great arteries (after 8 weeks). Imaging studies are a helpful tool for intra-operative planning and expected outcome but it should not have influence on which surgical option needs to be chosen. Other research studies, no reported mortality, and mechanical circulatory (extracorporeal membrane oxygenation) availability are encouraging our belief that primary arterial switch is still a safe and best surgical procedure after the age of 2 months. Six months is in our experience a safe limit in this approach; we might extend the age limit, probably with some precautions in the future.

Conflict of interest. None.

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