ORIGINAL ARTICLE

Arterial Switch Operation: Long-term Outcome

Cirugía de switch arterial: evolución alejada

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ABSTRACT

Background: Arterial switch is the surgical procedure of choice for transposition of the great arteries. However, its outcome is not free from adverse events.
Objective: The aim of this study was to evaluate the mid- and long-term outcome of this surgery at our hospital.
Methods: The study analyzed 224 patients who underwent the Jatene operation at our institution with mean follow-up of 7.6 years (±5.4 years).
Results: The survival rate at 15 years was 98%, with all survivors currently in functional class I-II and with adequate ventricular function.
Thirty-nine patients (17.4%) evolved with significant pulmonary stenosis, mainly located at the supravalvular level (94.8%).
Twelve percent of patients developed aortic root dilation and 10.3% significant aortic regurgitation. The latter was associated with aortic root dilation (p=0.0000), prior left ventricular preparation (p=0.001) and aortic regurgitation in the immediate postoperative period (p=0.01).
Coronary artery lesions were detected in 5 patients (2.2%) and arrhythmias in 4 (1.8%).
Freedom from reintervention at 5, 10 and 15 years was 94%, 86% y 58%, respectively, with pulmonary stenosis as the leading cause for reintervention.
Mortality was 0.9% (2 patients) during follow-up, and it was associated with coronary artery involvement (p=0.0000) and development of arrhythmias (p=0.0000).
Conclusions:
The arterial switch operation has excellent long-term survival. The most frequent adverse event during follow-up was pulmonary stenosis. Significant aortic regurgitation was associated with neo-aortic root dilation, prior left ventricular preparation and aortic regurgitation in the immediate postoperative period. There was low incidence of coronary artery obstruction and arrhythmias, but these were associated with mortality.

Key words: Congenital Heart Defects - Cardiovascular Surgical Procedures - Arterial Switch operation - Jatene Surgical Procedure - Transposition of the Great Arteries - Long-term follow-up.

RESUMEN

Introducción: La cirugía de switch arterial es el procedimiento de elección para la transposición de los grandes vasos. Sin embargo, no está exenta de complicaciones en su evolución.
Objetivo: Analizar los resultados a mediano y largo plazo de la cirugía de switch arterial en nuestro hospital.
Material y métodos: Se analizaron 224 pacientes operados con cirugía de Jatene en nuestra institución con un seguimiento de 7,6 años (± 5,4 años).
Resultados: La sobrevida a los 15 años fue del 98%, encontrándose los pacientes en clase funcional I-II y con buena función ventricular.
Evolucionaron con estenosis pulmonar significativa 39 pacientes (17,4%), localizada principalmente a nivel supravalvular (94,8%).
El 12% desarrolló dilatación de la raíz aórtica y el 10,3%, insuficiencia aórtica significativa. Esta última se asoció con dilatación de la raíz aórtica (p = 0,0000), preparación previa del ventrículo izquierdo (p = 0,001) e insuficiencia aórtica en el posquirúrgico inmediato (p = 0,01).
Se evidenció lesión coronaria en 5 pacientes (2,2%) y arritmias en 4 (1,8%).
Permanecieron libres de reintervenciones a los 5, 10 y 15 años el 94%, 86% y 58%, respectivamente, siendo la estenosis pulmonar la indicación más frecuente.
La mortalidad en el seguimiento fue del 0,9% (2 pacientes) y se asoció con compromiso coronario (p = 0,0000) y con el desarrollo de arritmias (p = 0,0000).

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Conclusiones:
La cirugía de switch arterial tiene excelente sobrevida alejada. En la evolución, la estenosis pulmonar fue la complicación más frecuente. La insuficiencia aórtica significativa se asoció con dilatación de neorraíz, preparación previa del ventrículo izquierdo e insuficiencia aórtica en el posquirúrgico inmediato. La obstrucción coronaria y las arritmias tuvieron baja incidencia, pero se asociaron con mortalidad.

Palabras claves: Cirugía cardíaca - Cardiopatías congénitas - Cirugía de switch arterial - Cirugía de Jatene- Transposición de grandes vasos - Evolución posquirúrgica

Abbreviations

AR	Aortic regurgitation	**PS**	Pulmonary stenosis
AVB	Atrioventricular block	**SD**	Septal defect
DOL	Days of life	**TGA**	Transposition of the great arteries
LV	Left ventricular	**VT**	Ventricular tachycardia

INTRODUCTION

Transposition of the great arteries (TGA) is the most prevalent cyanotic congenital heart defect presenting in neonates and represents 5-7% of all heart diseases. (1)

In 1975, Jatene et al. described the arterial switch operation to treat this defect, consisting in the translocation of the great arteries above the sinuses with coronary reimplantation in the neoaorta. (2) Different from previous procedures (Senning in 1959 and Mustard in 1964), this surgical technique achieves anatomical correction restoring the left ventricle as a systemic chamber.

Thereafter, the aortic switch operation (with some later modifications as the Lecompte maneuver) has become the procedure of choice for this type of defect. (3-5)

Long-term outcome reports of this surgical technique describe complications as aortic regurgitation, pulmonary stenosis, aortic root dilation and coronary artery obstruction. (6-37)

This surgery is performed at our center since 1992. Thus, the purpose of the present work was to analyze the mid- and long-term outcome of our 20-year experience with aortic switch operation.

METHODS

A retrospective cohort study was performed including 224 patients operated on with the aortic switch technique at Hospital de Pediatría "Prof. Dr. Juan P. Garrahan" from January 1992 to December 2013, and who are currently attending control follow-up at our institution.

Patients who died in the immediate postoperative period or were lost to follow-up (57 patients) were excluded from the study.

The analysis of the surgical experience was divided into two periods: an initial phase (1992-2002) and a second phase (2002-2013).

Median age at the time of surgery was 22 days of life (DOL) (25-75% CI 11-54 DOL; range 1 DOL-10 years) and median weight was 3.5 kg (25-75% CI 3-4-kg; range 1.9-24 kg). Mean extracorporeal and clamping times were 188 min (±55.3) and 115.5 min (±35.29), respectively.

The anatomical variants identified in the patients were: simple transposition of the great arteries (n=122, 54.4%), complex transposition (n=77; 34.3%) and Taussig Bing anomaly (n=25; 11%). For the population analysis, the Taussig Bing anomaly was included as a complex variant.

Other cardiac anomalies associated with the disease were: aortic coarctation (n=13), LV outflow tract obstruction (n=2), multiple septal defect (SD) (n=1), straddling tricuspid valve with hypoplastic right ventricle (n=1) and left pulmonary artery agenesis (n=1).

One hundred and seventy-three patients (77.2%) had normal coronary artery pattern.

Diagnosis was made based on clinical, radiological, electrocardiographic, echocardiographic, and in some cases angiographic findings, and with multislice computed tomography.

Preoperative procedures were required in 47.7% patients (n=107); these consisted in the Rashkind procedure in 42.8% of patients (n=96) and surgeries in 8.9% (n=20).

The anatomical variants, surgical interventions prior to arterial switch and the main data about this procedure are described in Table 1.

Follow-up

All patients were followed-up at our institution from the time of hospital discharge until the end of the study, with mean follow-up of 7.6±5.4 years.

In all cases, follow-up evaluation consisted in physical exam, thorax teleradiography, electrocardiogram, color Doppler echocardiography, tissue Doppler echocardiography, Holter monitoring and exercise testing.

According to initial evaluation findings, some patients were requested other complementary diagnostic tests: stress echocardiography, new echocardiographic techniques (strain, strain rate, speckle tracking), cardiac nuclear magnetic resonance imaging, multislice computed tomography coronary angiography and/or cardiac catheterization.

The diagnosis of valve stenosis and regurgitation was based on echocardiographic data following current guidelines, (38, 39) considering as significant moderate and severe degrees. Similarly, two-dimensional (2D) and M mode echocardiography were used for the analysis of aortic root dimension, considering aortic root dilation when the diameter at the level of the sinuses of Valsalva was above Z=2 for the corresponding body surface area. (40)

Functional status was assessed following the New York Heart Association classification.

Left ventricular function was mainly assessed by M mode and 2D echocardiography and tissue Doppler imaging, using new echocardiographic techniques and/or magnetic resonance imaging only for discordant cases.

Statistical analysis

Microsoft Office Excel 2013™ was used to store data and the analysis was performed using Statistix 8.0™ statistical package.

Table 1. Preoperative characteristics of arterial switch operation. (n=224)

Anatomical variants:	n (%)
- Simple TGA, n (%)	112 (54.4)
- TGA+SD, n (%)	77 (34.3)
-with Ao C, n	4
-with LVOTO, n	2
- Taussig Bing, n (%)	25 (11)
-with Ao C, n	9
Other associated anomalies	
- Multiple SD, n	1
- Straddling tricuspid valve with hypoplastic RV, n	1
- Left pulmonary artery agenesis, n	1
Coronary artery patterns	
- Usual (S1: LCA – S2: RCA), n (%)	173 (77.2)
- Circumflex artery originates in RCA (S1: ADA – S2: Cx and RCA), n (%)	20 (9.2)
- Single coronary artery (S1: RCA, ADA and LCX), n (%)	7(3.1)
- Single coronary artery (S2: RCA, ADA and LCX), n (%)	14(6.2)
- Single coronary artery (S2: RCA, ADA and LCX with intramural course), n (%)	4(%)
- Inverted (S1 RCA – S2: LCA), n (%)	2(0.8%)
- Others, n (%)	4(1.6%)
Prior palliative interventional procedures	
- Rashkind	96 (42.8%)
- Prior surgeries	20 (8.9%):
- LV preparation:	18
- Pulmonary artery cerclage	9
- Pulmonary artery cerclage + SPA	9
- Systemic-pulmonary anastomosis	1
- Glenn + Blalock Hanlon septostomy	1
Arterial switch operation	
- Median age, days	22 (25%-75% CI=11-54 dol) range 1dol-10 years
- Median weight, kg	3.5 (25%-75% CI= 3-4) range 1.9 – 24
- Mean ECC time, min	188±55.3
- Clamping time, min	115.5±35.29
- Date of surgery:	
- Initial period (before 2002)/after 2000	82(36.6%)/142 (63.4%)

TGA: Transposition of the great arteries. SD: Septal defect. AoC: Aortic coarctation. LVOTO: Left ventricular outflow tract obstruction. RV: Right ventricle. CS1: coronary sinus 1. LCA: Left coronary artery. CS2: Coronary sinus 2. RCA: Right coronary artery. ADA: Anterior descending artery. LCX: Left circumflex artery. LV: Left ventricular. SPA: Systemic-pulmonary anastomosis. DOL: Days of life. ECC: Extracorporeal circulation.

Qualitative variables were expressed as absolute values and/or percentages of the total number of cases, and quantitative variables as mean and standard deviation or median and interquartile range (IQR) according to normal or non-normal data distribution.

Continuous variables were compared using Student's t test or the Mann–Whitney test as appropriate, and Fischer's exact test or the chi-square test for proportions. A p value <0.05 was considered statistically significant. The Kaplan-Meier method was used to calculate mid-and long-term survival.

Ethical considerations

The study was approved by the institutional Ethics Committee according to regulations in force for observational studies, and in compliance with the Declaration of Helsinki principles.

RESULTS

Survival

Survival at 5, 10 and 15 years was 98% (Figure 1A).

All surviving patients are in functional class I-II (99% in functional class I).

All patients had normal ventricular function, with 37% (±4.8%) mean LV shortening fraction.

Long-term complications

Pulmonary stenosis

The outcome, with mean follow-up of 7.6 years (±5.4

years), showed that 39 patients (17.4%) developed significant pulmonary stenosis, with mean gradient of 66 mmHg (±13.5) that was severe in 25 cases (11.2%)

The most common site of obstruction was supravalvular stenosis (n=37; 94.8%): related to the suture site (n=17; 43.6%), at the level of the pulmonary branches (n=5; 12.8%) and in combined forms (n=15; 38.4%) (Figure 2).

The development pf PS was associated with follow-up duration (p=0.0000) and the initial surgical stage (p=0.004).

Eighty percent of these patients (n=32) required reintervention.

Neo-aortic root dilation

Twenty-seven patients progressed with neo-aortic root dilation (12%) with mean Z score of 3.5 (±0.8; range 2.1-5), presenting with significant AR in 10 patients (p=0.0000) and severe in 4 (p=0.0008) (Figure 3).

Neo-aortic root dilation was associated with prior left ventricular preparation (p=0.009), initial surgical stage (p=0.002) and longer follow-up (p=0.0000).

Aortic regurgitation

Twenty-three patients (10.3%) presented with significant (≥ moderate) AR, which was severe in 8 cases (3.6%).

Univariate analysis showed that significant AR was associated with aortic root dilation (p=0.0000), prior LV preparation (p=0.001), older age at surgery (p=0.045), presence of AR in the immediate postoperative period (p=0.01) and longer follow-up (p=0.02). In addition, AR was associated with complex TGA (p=0.01).

In the multivariate analysis, significant AR was associated with neo-aortic root dilation (p=0.000), prior LV preparation (p=0.0087) and AR in the immediate postoperative period (p=0.0022).

Seven patients (30.4%) with AR required reoperation due to this cause.

Aortic stenosis

Nine patients (4%) developed LV outflow tract obstruction that was severe in 2 cases (0.9%).

The most frequent obstruction site was supravalvular in 5 patients (55.6%) and subvalvular in 4 (44.4%).

The 2 cases of severe aortic stenosis were supravalvular. Both were Taussig Bing anomaly (p=0.11) and presented unusual coronary artery reimplantations (p=0.0089).

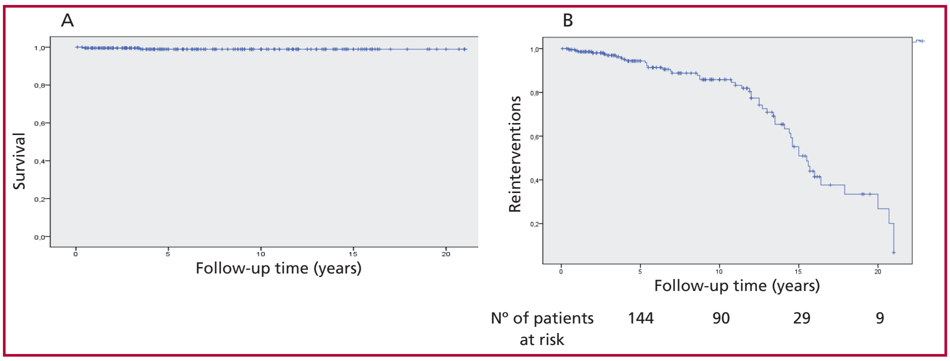

Fig. 1. Kaplan Meier curves. **A.** Survival and **B.** Reinterventions in the long-term follow-up.

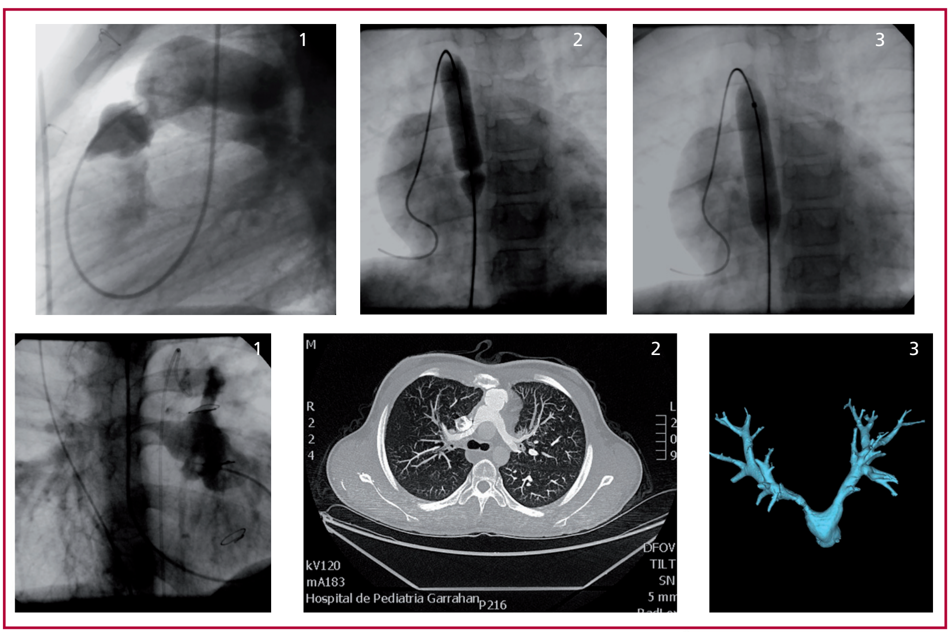

Fig. 2. Supravalvular pulmonary stenosis. **A.** at the suture site in the pulmonary trunk (during effective interventional cardiac catheterization). **B.** in pulmonary branches secondary to Lecompte maneuver. **B1:** at diagnostic cardiac catheterization. **B2:** at multislice computed tomography coronary angiography. **B3:** at three-dimensional reconstruction of multislice computed tomography coronary angiography.

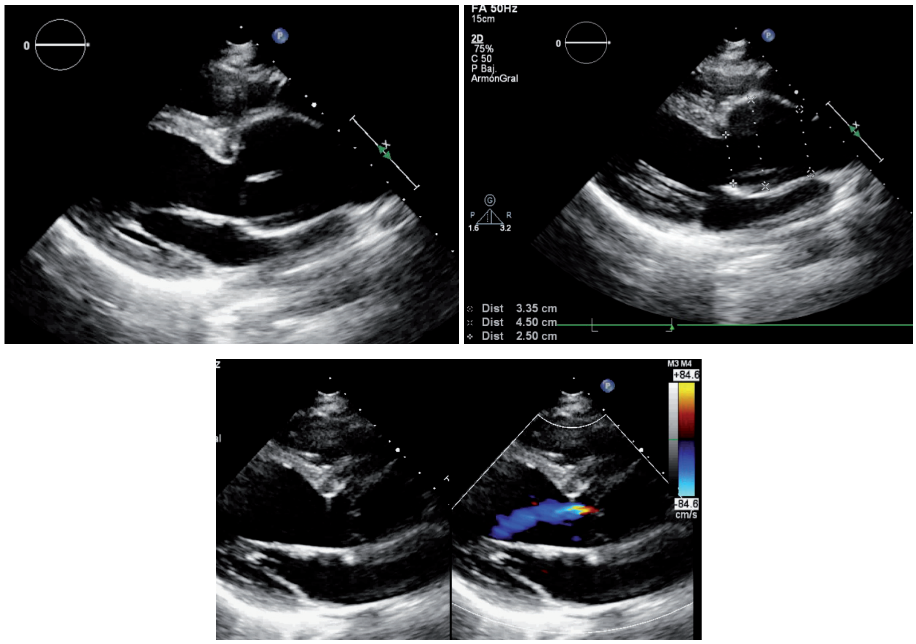

Fig. 3. Color Doppler echocardiographic images of a 17-year-old patient with history of simple TGA operated on at one year of age with arterial switch procedure, requiring prior left ventricular preparation. Sixteen years after the procedure he presents with neo-aortic root dilation (Z=4.5) and mild aortic regurgitation.

Coronary artery obstruction

Five patients presented evidence of coronary artery lesion (2.2%). Prior coronary pattern was normal in 2 cases (p=0.04) and they were all complex TGA (p=0.01).

In 3 patients coronary obstruction was found during cardiac catheterization. One patient died after reoperation for septal defect closure and pulmonary artery cerclage removal. The 2 remaining patients are asymptomatic, in FC I and with preserved cardiac function.

The other two coronary artery obstructions were diagnosed in the immediate postoperative period in patients with ventricular failure. One of them consisted in left coronary ostium obstruction, which was reoperated 12 days after the arterial switch procedure with effective coronary reimplantation and ventricular function recovery that remains normal at 15 years of postoperative follow-up. The remaining case was a more distal left coronary artery stenosis; the patient was compensated and discharged with moderate ventricular dysfunction and died 3 months after surgery due to ventricular tachycardia (VT) refractory to treatment and heart failure.

Arrhythmias

The incidence of arrhythmias during follow-up was 1.8% (n=4), consisting of VT in 3 patients and complete atrioventricular block (AVB) in 1 patient.

All these patients had complex TGA (p=0.02) and had been operated on in the initial period (p=0.007). One patient also had coronary artery lesion (p=0.001).

The AVB was progressive and was reoperated 47 months after the arterial switch procedure for cardiac pacemaker implantation.

Two cases of ventricular arrhythmia presented in the long-term outcome (15 and 17 years post arterial switch operation) in patients without hemodynamic substrate. In the first patient, the episode was non-sustained VT recorded during control Holter monitoring, which was managed with medical treatment. The second case was sustained VT requiring implantable cardioverter defibrillator.

The remaining case of VT occurred 3 months after the arterial switch procedure in a patient with left coronary artery stenosis.

Reinterventions

In the mid- and long-term outcome, 22.5% of patients (n=50) required some type of reintervention (interventional catheterization and/or reoperation).

At 5, 10 and 15 years, 94%, 86% and 58% of patients, respectively, remained free from reinterventions (Figure 1B).

Reinterventions were more frequent in patients with complex TGA and Taussig Bing anomaly (p=0.0004), prior LV preparation (p=0.04), surgery performed during the initial period (p=0.0004) and longer follow-up period (p=0.0000).

Interventional catheterizations

At 5, 10 and 15 years, 97%, 93% and 70 % of patients, respectively, remained free from interventional catheterizations.

Thirty interventional catheterizations were performed in 29 patients (12.9%) at mean postoperative time of 4.9±4.13 years, without mortality due to this procedure.

The main indication (80%) was pulmonary stenosis (n=24), leading to pulmonary angioplasty (n=20), angioplasty and stent implantation in pulmonary branches (n=4) and angioplasty of implanted stent in a pulmonary branch (n=1) (Figure 2A).

The remaining procedures were: angioplasty of aortic recoarctation (n=1), aorto-pulmonary collateral embolization (n=3) and SD closure with Amplatzer (n=1).

Need for interventional catheterization was higher in patients operated on in the initial surgical phase (p=0.0084) and with longer follow-up time (p=0.0000).

Reoperations

At 5, 10 and 15 years, 95%, 89% and 63 % of patients, respectively, remained free from reoperations.

Forty-seven reoperations were indicated in 37 patients (13.7%) at a mean postoperative interval of 5.5±4.3 years. Among the reoperated patients, 7 (18.9%) required a second and one (5.4%) a third reintervention, at a mean postoperative time of 10.8 (±4.6) and 10.5 years, respectively. Two patients have a right-sided programmed reoperation.

Reoperations are detailed in Table 2.

Sixty percent of surgical indications corresponded to right-sided conditions (isolated in 20 patients and combined in 8).

Univariate analysis showed that reoperations were associated with complex anatomical variants (p=0.0004), initial surgical period (p=0.0004) and longer follow-up period (p=0.000).

Mortality

Mortality during follow-up was 0.9%. Two patients with coronary artery lesions died at 3 months and 42 months after surgery.

Long-term mortality was associated with coronary artery involvement (p=0.0000) and arrhythmias (p=0.0000).

DISCUSSION

The aortic switch operation has radically modified the natural history of TGA, becoming the treatment of choice for this entity. This surgery is performed at our hospital since 1992, generating a considerable population of survivors operated on with this technique.

Table 2. Reoperations indicated in the long-term follow-up (47 reoperations in 37 patients)

Reoperations indicated (47)
On the right side (22)
- RVOT enlargement (12)
- RV-PA conduit implantation (2)
- RVOT enlargement + transannular patch (1)
- Infundibular resection and pulmonary valve commissurotomy (1)
- RVOT enlargement + SD closure (1)
- RV-PA conduit replacement (2)
- RV-PA conduit replacement + SD closure + PB plastic surgery (1)
- RV-PA conduit implantation + PB plastic surgery (1)
- Resection of subpulmonary stenosis (1).
On the left side (7)
- Prosthetic aortic valve replacement (2)
- Subaortic membrane resection (2)
- Ross Back surgery(1)
- Bentall surgery(1)
- Aortic valve replacement + tricuspid valve prosthesis replacement (1)
On both outflow tracts (7)
- Supravalvular aortic and pulmonary enlargement (3)
- Mechanical aortic valve replacement + RV-PA homograft implantation (1)
- Resection of subaortic stenosis and pulmonary valve annulus widening (1)
- Supravalvular aortic and LPB enlargement (1)
- Subaortic membrane resection + RVOT enlargement (infundibular resection + pulmonary valve annulus and PB enlargement (1)
Others (11)
- Septal defect closure (3)
- RVOT enlargement + SD closure (1)
- Left coronary artery reimplantation (1)
- Pacemaker implantation (1)
- Pacemaker battery replacement (1).
- Implantable cardioverter defibrillator implantation (1)
- Multiple SD closure + pulmonary cerclage removal (1)
- Mitral valve replacement (1)
- Tricuspid valve replacement with biological valve (1)

RVOT: Right ventricular outflow tract. RV: Right ventricular. PA: Pulmonary artery; PBr: Pulmonary branches. LPBr: Left pulmonary branches.

To optimize follow-up of these patients, we considered it was essential to know mid- and long-term surgical outcomes. Mid-term outcome results have already been published by our group. (11) Now, after 20-year experience with this surgery, we analyze the long-term outcome.

Survival at 15 years was 98%, and all patients are asymptomatic, in good *functional class* and with preserved *ventricular systolic function*, findings similar to those of other series. (4, 6-10, 13-15, 22)

The most prevalent long-term complication was *PS*, mainly at the supravalvular level (at the surgical suture site in the pulmonary trunk) and/or pulmonary branches (attributable to tension or stretching following the Lecompte maneuver).

Similarly to other reports, *neo-aortic root dilation* was recorded in 12% of patients. (9, 26) *Aortic regurgitation* was associated with complex TGA and Taussig Bing anomaly, prior LV preparation, aortic root dilation and presence of AR in the immediate postoperative period, indicating that it is a multifactorial process as also described recently in the literature. (9, 16, 25-28, 36, 37)

All these adverse effects were more frequent at longer follow-up.

Coronary artery stenosis was not frequent. It occurred in 2% of patients, although no multislice computed tomography coronary angiography, cine coronary angiography or myocardial perfusion studies with radioisotopes were routinely performed in these patients, as suggested by other groups. (29, 30) No patient presented with acute coronary syndrome and all had negative exercise testing for ischemia.

Arrythmias were a very infrequent complication but their presence was associated with mortality, same as coronary heart disease.

In agreement with the literature, (7-10) a significant rate of *reinterventions* (22%) was performed during the long-term follow-up. Complex forms of TGA presented higher rate of reinterventions and *pulmonary supravalvular stenosis* was the most frequent indication. (8, 10, 12, 23) However, progressive left-sided lesions, coronary artery obstructions and severe arrhythmias (12, 19, 30, 37) start to become more relevant in the long-term follow-up.

Finally, *mortality* in the long-term follow-up was low (0.9%) and was associated with coronary artery stenosis and severe ventricular arrhythmias.

Limitations

The work presents the inherent limitations of its retrospective and observational design. Although predetermined final endpoints, as PS, reoperations, AR and long-term mortality could be identified, other events such as prevalence of coronary artery stenosis might be underestimated, as they are not routinely studied with more specific tests in this group.

Most events were more frequent in patients operated on in the initial surgical phase, but they are also the group with longer outcome; therefore, patients who underwent the aortic switch operation during the second decade will require longer follow-up time to validate our findings.

CONCLUSIONS

The arterial switch operation has excellent long-term survival. Despite adverse events and need for reinterventions during follow-up, all patients are in very good functional class.

Arterial switch survivors, mainly those with complex forms, who are more prone to complications, require careful and systematic monitoring for a timely detection and treatment.

Conflicts of interest

None declared. (See authors' conflicts of interest forms in the website/Supplementary material).

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