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Mariana Amorim Ribeiro

Transposition of the Great Arteries: Review of Cases from a Reference Center

Transposição das Grandes Artérias: Revisão de Casos de um Centro de Referência

ABRIL, 2021

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TÍTULO DISSERTAÇÃO

Transposition of The Great Arteries: Review of Cases from a Reference Center

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ASSINALE APENAS UMA DAS OPÇÕES:

É AUTORIZADA A REPRODUÇÃO INTEGRAL DESTE TRABALHO APENAS PARA EFEITOS DE INVESTIGAÇÃO, MEDIANTE DECLARAÇÃO ESCRITA DO INTERESSADO, QUE A TAL SE COMPROMETE.	☐
É AUTORIZADA A REPRODUÇÃO PARCIAL DESTE TRABALHO (INDICAR, CASO TAL SEJA NECESSÁRIO, Nº MÁXIMO DE PÁGINAS, ILUSTRAÇÕES, GRÁFICOS, ETC.) APENAS PARA EFEITOS DE INVESTIGAÇÃO, MEDIANTE DECLARAÇÃO ESCRITA DO INTERESSADO, QUE A TAL SE COMPROMETE.	☐
DE ACORDO COM A LEGISLAÇÃO EM VIGOR, (INDICAR, CASO TAL SEJA NECESSÁRIO, Nº MÁXIMO DE PÁGINAS, ILUSTRAÇÕES, GRÁFICOS, ETC.) NÃO É PERMITIDA A REPRODUÇÃO DE QUALQUER PARTE DESTE TRABALHO.	☒

Faculdade de Medicina da Universidade do Porto, 09/04/2021

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DEDICATÓRIA

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ORIGINAL ARTICLE

Title

Transposition of the Great Arteries: Review of Cases from a Reference Center

Título

Transposição das Grandes Artérias: Revisão de Casos de um Centro de Referência

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Abstract

Introduction and Objectives: Dextro-transposition of the great arteries (d-TGA) is a common cyanotic congenital heart defect, with the aorta and the pulmonary trunk arising from the right and left ventricles, respectively. The arterial switch operation (ASO) allows for its anatomical correction with low morbi-mortality rates. Our main goal was to describe the characteristics and outcomes of patients with d-TGA treated in our center.

Methods: We performed a single-center retrospective cohort study of newborns with d-TGA admitted to our hospital between January 2016 and December 2020. We reviewed patient's medical records and collected data on their characteristics, surgery, and pre- and postoperative periods.

Results: We included 18 patients with d-TGA: nine patients had simple d-TGA, eight had d-TGA with ventricular septal defect (VSD) and one had complex d-TGA. ASO was performed in 17 patients and there was one preoperative death. The complications found in the early postoperative period were: 10 infection/sepsis, seven chylothorax, five neurological lesions, five dysrhythmia, four wound dehiscence, two acute kidney injury, two diaphragmic paralysis and one cardiac tamponade. There were three early reinterventions. In the late postoperative period, five (27.8%) patients had moderate-to-severe supravalvular pulmonary stenosis, with two needing reinterventions. There were four (22.0%) patients with aortic insufficiency and two (11.1%) with aortic root dilation.

Conclusions: The management of d-TGA cases in our hospital was comparable to other reference centers and resulted in low mortality, without any postoperative deaths. In the early and late postoperative period, morbidity was low and there were few reinterventions.

Keywords: Transposition of the Great Vessels; Arterial Switch Operation; Congenital Heart Defects; complications; mortality

Resumo

Introdução e Objetivos: A dextro-transposição das grandes artérias (d-TGA) é uma cardiopatia congénita cianótica, em que a aorta e o tronco pulmonar têm origem no ventrículo direito e esquerdo, respetivamente. A cirurgia de *switch* arterial permite a sua correção anatómica com morbimortalidade reduzida. O nosso principal objetivo foi descrever as caraterísticas e resultados dos doentes com d-TGA operados no nosso hospital.

Métodos: Realizamos um estudo de coorte retrospetivo unicêntrico dos recém-nascidos com d-TGA admitidos no nosso centro de referência entre janeiro de 2016 e dezembro de 2020. Revimos os registos clínicos dos doentes e colhemos dados sobre as suas caraterísticas, cirurgias e períodos pré e pós-operatórios.

Resultados: Incluímos 18 doentes com d-TGA: nove com d-TGA simples, oito com d-TGA e comunicação interventricular e um com cardiopatia complexa. Dezassete doentes foram submetidos a *switch* arterial e ocorreu uma morte pré-operatória. As complicações pós-operatórias precoces foram: 10 infeção/sépsis, sete quilotórax, cinco lesões neurológicas, cinco arritmias, quatro deiscências da ferida cirúrgica, duas lesões renais agudas, duas parésias diafragmáticas e um tamponamento cardíaco. Três doentes foram submetidos a reintervenção precoce. No período pós-operatório tardio, cinco (27.8%) doentes apresentaram estenose pulmonar moderada-severa, dos quais dois necessitaram de intervenção cirúrgica. Quatro (22,0%) doentes apresentavam insuficiência aórtica e dois (11,1%) dilatação da raiz da aorta.

Conclusões: O tratamento de doentes com d-TGA no nosso hospital foi comparável a outros centros de referência, apresentando uma baixa mortalidade, sem nenhuma morte pós-operatória. A nossa coorte revelou reduzida morbilidade e taxas de intervenção imediatamente após a cirurgia e no seguimento a curto e médio-prazo.

Palavras-chave: Transposição dos Grandes Vasos; Operação de *Switch* Arterial; Cardiopatia Congénita; complicações; mortalidade

Introduction

Dextro-transposition of the great arteries (d-TGA) is a congenital heart defect characterized by atrioventricular concordance and ventriculoarterial discordance, with the aorta arising from the morphological right ventricle and the pulmonary artery arising from the morphological left ventricle. Therefore, circulation is parallel: oxygenated blood runs through the left heart chambers and the pulmonary vessels; while deoxygenated blood runs through the right heart chambers and the systemic. Consequently, survival depends on adequate mixing circuits, which normally occurs through defects in the atrial or ventricular septa and/or through the ductus arteriosus [1, 2].

d-TGA represents 5-7% of all congenital heart defects [1, 3-5] and is the second most common cyanotic congenital heart disease (20%) [6, 7], with an estimated incidence of 1:3200 live births [2]. It can be further classified as simple or isolated d-TGA (without other cardiac abnormalities), d-TGA with ventricular septal defect (VSD) and complex d-TGA (accompanied by cardiac malformations such as left ventricle outflow tract obstruction, or aortic arch abnormalities). Abnormal coronary artery (CA) patterns are also present in many cases [1, 3].

Newborns with d-TGA will have some degree of hypoxemia, potentially leading to shock, end-organ-dysfunction, and death. Adjuvant therapies, such as intravenous prostaglandin E1 (PGE1) [1, 6], Rashkind balloon atrial septostomy (BAS), mechanical ventilation (MV), inotropic support (IS), and others, can be used to temporarily improve systemic blood oxygenation [1, 3, 5].

Definitive treatment can only be achieved by surgical correction of d-TGA [1, 6]. Currently, the gold-standard is the arterial switch operation (ASO), performed successfully for the first time by Jatene in 1975 [1, 5, 6]. In this procedure, the surgeon anatomically and physiologically corrects the malformation, by sectioning the aorta and pulmonary trunk and transposing them to the morphological left and right ventricles, respectively [1, 2].

Nowadays, ASO can be performed with good short-, mid- and long-term results [2, 8-11],with an overall long-term survival rate of 87-90% [4, 5] and freedom from reintervention at 10 years varying from 80% to 90% [10]. The most frequent late complications associated with ASO are supravalvular pulmonary stenosis, neo-aortic root dilation, aortic regurgitation, and coronary stenosis [1, 3-5, 11, 12].In recent years, some risk factors for a complicated perioperative period and late complications have been described. Examples include patient characteristics (prematurity,

surgical weight under 2500g, complex cardiac anatomy, CA abnormalities) and events during preoperative care (timing of ASO and need of adjuvant therapies after surgery) [3, 6, 8, 9, 13].

Our center performed ASO for the first time in 2016. With this study, we intended to characterize all patients who underwent surgical correction in our institution and their short- and mid-term outcomes. We also aimed to investigate possible risk factors for postoperative morbidity mortality and need for reintervention, with special emphasis on cardiac and coronary anatomy, and perioperative care. Ultimately, we hope this study will help us understand how our center compares to other reference centers for congenital heart diseases and improve the management and care of d-TGA patients in our institution.

Methods

Study design and data collection

This single-center retrospective cohort study was approved by the ethics committee and the administration board of Centro Hospitalar Universitário de São João (CHUSJ). We reviewed patient's electronic, and paper based medical records and collected data on patient characteristics, preoperative period, surgical intervention, and early and late postoperative periods. Data was anonymized and stored in a data base.

Participants

We included all patients with d-TGA admitted to CHUSJ between January 2016 and December 2020. We chose 2016 as the starting year for patient inclusion because it was the year in which our institution started to perform the ASO procedure. Before this, patients were admitted to our center for preoperative care, being transferred afterwards to another Portuguese surgical center. Thus, we excluded them from this analysis to guarantee data uniformity and a lower rate of missing data, at the cost of shorter follow-up times. In total, 18 patients meet the inclusion criteria.

Preoperative Period

If d-TGA had been prenatally diagnosed, pregnant women were followed in our hospital, so that the newborn could receive treatment immediately after birth. Otherwise, when diagnosis was suspected postnatally, patients were transferred to our center for cardiac evaluation.

All patients underwent transthoracic echocardiogram (TTE) for confirmation of d-TGA and to further establish cardiac and coronary anatomy. If necessary, patients would receive PGE1 infusion, Rashkind BAS, MV, non-invasive ventilation (NIV) and IS. We collected data on preoperative interventions, and parameters 24 hours before surgery (oxygen saturation, left and right systolic function).

Surgical Technique

ASO was the preferred technique for correction of d-TGA. Surgery was performed through a median sternotomy and depended on use of extracorporeal circulation (ECC) and periods of aortic clamping (AC). Patients were subjected to hypothermia (24-30 ºC) and Celsior cardioplegic solution was used for myocardial protection. The aorta was sectioned above the sinuses and the coronary artery buttons were excised. The pulmonary trunk was sectioned below

the level of its bifurcation, and a Lecompte maneuver was performed in all patients. The surgeon decided if additional maneuvers were necessary to translocate coronary arteries without tension, kinking or torsion, and they would be implanted in the neo-aortic root, followed by anastomosis of the aorta. The pulmonary artery was reconstructed with a bovine pericardial patch and anastomosed to the neo-pulmonary root. In the end, the delayed sternal closure (DSC) technique was performed in all patients using a bovine pericardial patch.

Early Postoperative Period

The early postoperative period was defined as the first 30 days after surgery or time before hospital discharge. Patients received analgesia with fentanyl and were mechanically ventilated. Extubation was to occur as soon as their clinical status would allow it. They also received IS with milrinone, dopamine and/or adrenaline, with doses adjusted to clinical response.

Major morbidity was defined as occurrence of cardiac tamponade, chylothorax, dysrhythmia, ischemic events, diaphragmatic paresis, infection or sepsis, acute kidney injury (AKI), need for peritoneal dialysis, necrotizing enterocolitis, neurological complications, or surgical wound dehiscence. Opioid withdrawal syndrome and pulmonary atelectasis were considered minor complications. We also evaluated the need for reintervention related to d-TGA or ASO, duration of MV or IS, time of DSC, need for extracorporeal membrane oxygenation (ECMO), length of stay in the neonatal intensive care unit (NICU) and hospital. Statistical analysis was performed to study the possible associations between patient characteristics, perioperative variables, and major complications as well as need for reintervention.

Late Postoperative Period

The late postoperative period began after the first 30 postoperative days or hospital discharge. Patients were followed in the Pediatric Cardiology outpatient department. At each visit, medical history and physical examination, an electrocardiogram (EKG) and TTE were performed.

We studied occurrence of late complications: supravalvular pulmonary stenosis, neo-aortic root dilation, aortic insufficiency, ischemic events, and dysrhythmias. The presence of symptoms and need for reintervention were also registered. We performed statistical analysis to study for associations between patient characteristics and perioperative variables and late postoperative complications and reinterventions.

Statistical Analysis

We used IBM SPSS version 27.0 software package for Windows to analyze data. Missing data were excluded from analysis. For the descriptive analysis qualitative variables were presented as absolute number and percentage; quantitative values were presented as mean and standard deviation (SD) if normally distributed or median and interquartile range (IQR) if otherwise. Normality of distribution was determined by the Kolmogorov-Smirnov test. For the risk factors analysis Fisher's exact test, student t-test or Mann-Whitney U were used and $p<0.005$ defined significance.

Results

Patient Characteristics

During the study period, our institution treated 18 patients with d-TGA in total, 14 of which were males (77.8%). The mean gestational age was 38 weeks (SD ± 2.0), with two preterm newborns (11.1%), with 33 and 35 weeks of gestation. The mean birth weight was 3190.8 g (SD ± 653.8), and there were three patients (16.7%) with low birth weight (<2500g) and one (5.6%) was macrossomic at birth (>4000g). The median APGAR score at the 1st minute was 8 (IQR 8-9), with two (11.1%) patients scoring less than 6. Patient characteristics and demographic data are presented in table 1.

Ten newborns (55.6%) had the diagnosis of d-TGA established prenatally, so they were delivery in our institution. The diagnosis of the remaining was after birth: seven (38.9%) had cyanosis and/or heart murmur detected before discharge from the nursery ward, five in the first 12 hours, one in the first day and the other in the second day of life. The remaining patient was only diagnosed at 35 days of life presenting with cardiogenic shock.

Definitive cardiac diagnosis included nine patients (50.0%) with simple TGA, eight (44.4%) with TGA and VSD and one (5.6%) with complex cardiac anatomy: d-TGA and total anomalous pulmonary venous return (TAPVR). One patient showed signs of pulmonary hypertension. Coronary anatomy was abnormal in 10 cases (55.6%) – four had a single CA, one of them with an intramural course; two had a circumflex CA arising from the right CA; one had the anterior descending and right CAs arising from the left-hand coronary sinus and the circumflex CA from the right-hand coronary sinus; one had an intramural left CA; one patient had the left CA arising from the non-facing sinus and myocardial bridging; and one had right CA arising from the non-facing sinus and the left CA originating from the proximal ascending aorta.

Three patients (16.7%) had extracardiac malformations – pyelocaliceal dilation, balanic hypospadias and cleft lip/cleft palate – and chromosomal abnormalities were identified in two (11.1%) – X-linked ichthyosis (Xp22.31) and marker chromosome 22q12.

Preoperative Period

Intravenous PGE1 infusion was administered preoperatively to 17 patients (94.4%), for a median of 13 days (IQR 9.8-22.8), and the only patient who did not received it had late diagnosis

and had a large VSD. BAS was performed in 15 patients (83.3%), at a median of one day (IQR 1 – 1) after diagnosis. One patient required a second BAS procedure 13 days after the first one.

Prolonged mechanical ventilation (>2 days) in the preoperative period was required for 10 patients (55.5%), with a median duration of six days (IQR 4 - 11), and two patients (11.1%) needed non-invasive ventilation during seven and 23 days after being extubated. In the 24 hours before surgery, the median peripheral oxygen saturation was 90.0% (IQR 84.0 – 94.0).

Inotropic support was necessary in five patients (27.8%) for a mean of 6.6 days (SD ± 3.6). Before surgery, left and right ventricular function were normal in almost all patients except one (5.6%) with mild left ventricular disfunction.

Eight patients (44.4%) had complications in the preoperative period: two (11.1%) infections (pneumonia and inguinal cellulitis), three (16.7%) sepsis, one (5.6%) acute kidney injury, one (5.6%) refractory shock before BAS and one (5.6%) patient needed cardiopulmonary resuscitation during septostomy.

There was one death in the preoperative period (5.6% mortality). It was a male patient with complex cardiopathy and low birth weight, without prenatal diagnosis, who presented cyanosis and was admitted to our hospital in the first day life. He received intravenous PGE1 and was taken to the catheterization room for urgent BAS but died before the beginning of the procedure. His chest radiograph showed bilateral pneumothorax and diffuse pulmonary infiltrates. The autopsy revealed d-TGA and supracardiac TAPVR and abnormal coronary artery pattern (right CA arising from the non-facing sinus and the left CA originating from the proximal ascending aorta)

The preoperative period variables are summarized in table 2.

Surgical Intervention

ASO was performed in 17 patients, at a median of 14 days (IQR 12-28.5) after diagnosis. All surgeries were performed in the neonatal period, except for one patient with late diagnosis of d-TGA, who was operated at 66 days of life. At surgery, median weight was 3210 g (IQR 3140 – 3505), and two newborns (11.8%) weighed less than 2500 g.

Mean total surgical time was 331.3 minutes (SD ± 98.0), with missing data for 6 patients. The median ECC time was 150 minutes (IQR 136.5 – 184.5) and median AC time was 79 minutes (IQR 69.5 – 87.5). Three patients (17.6%) required additional maneuvers for CA mobilization .

Intraoperative complications occurred in six patients (35.3%): three (17.6%) had atrioventricular block, one (5.9%) suffered a hepatic laceration, one (5.9%) had acute pulmonary edema and pulmonary hemorrhage and one (5.9%) had cardiorespiratory arrest and needed resuscitation. One patient (5.9%) was put on ECMO before leaving the operating room after ASO procedure, due to severe left ventricular disfunction. There were no intraoperative deaths.

Data related to surgical intervention are described in table 3.

Early postoperative period

All patients were on mechanical ventilation for a median of 7 days (IQR 6-11), and two patients (11.7%) required non-invasive ventilation for 1 and 7 days after being extubated. All patients needed inotropic support during a mean 7.9 days (SD ±3.8). The patient was weaned off ECMO 4 days after surgery. Delayed sternal closure was performed in all patients, with a median of 4 days (IQR 2-5.5).

Immediately after surgery, the left ventricular function was evaluated by transthoracic echocardiogram and was normal for twelve patients (70.6%), mildly depressed in three patients (17.6%), moderately depressed in one patient (5.9%) and severely depressed in another patient (5.9%). The median lactate levels were 2.8 mmol/L (IQR 1.4 – 4.2) and median troponin levels were 29 709.8 ng/L (13 901.1 – 40 381.5 ng/L). After the first 24 hours, median troponin levels dropped to 13 201.8 ng/L (6 832.0 – 15 742.3 ng/L).

The median length of stay in the NICU was 22 days (IQR 16.5-31) after surgery, and the median total length of hospital stay was 50 days (IQR 34-64).

Major complications were present in 14 patients (82.3%). Acute kidney injury occurred in two patients (11.8%), but there was no need for peritoneal dialysis. Ten patients (58.8%) had either infection or sepsis. Heart rhythm abnormalities were present in four patients (29.4%): one had junctional ectopic tachycardia (JET) and episodes of supraventricular tachycardia (SVT), one had frequent atrial and ventricular premature contractions, and three had atrioventricular block, of which only one (5.9%) required implantation of a permanent epicardial pacemaker. Cardiac tamponade occurred in one patient (5.9%) and chylothorax in seven (41.2%). Two patients (11.8%) suffered diaphragmatic paralysis. In terms of neurological conditions, one (5.9%) patient had a convulsive crisis and was later diagnosed with epilepsy, one patient (5.9%) had a grade III intraventricular hemorrhage (IVH) and required the placement of an Ommaya reservoir and three

patients (17.6%) had thalamic lesions visible in transfontanellar ultrasound. Additionally, four patients (23.5%) had surgical wound dehiscence. We also registered four (23.5%) pulmonary atelectasis, one of which associated with pneumonic pleural effusion (5.9%), and 12 patients (70.6%) suffered from opioid withdrawal syndrome. No patients had ischemic events in this period.

Early reinterventions were performed in three patients (17.6%), and one of them underwent two procedures: two (11.8%) patients needed to have their surgical wound revised because of dehiscence, one (5.9%) needed drainage of the cardiac tamponade and later a diaphragmatic plication. There were no early postoperative deaths.

The early postoperative outcomes are presented in table 4.

We performed a risk factor analysis for occurrence of major early postoperative complications and need for reinterventions, but we could not find any statistically significant associations (results presented in Supplementary Tables 1 and 2).

Late Postoperative Period

The 17 patients had follow-up in the Pediatric Cardiology outpatient department, with a duration of follow-up between 2 and 51 months (mean 28.8 months, SD ±13.9). During this period, 15 patients (88.2%) remained asymptomatic (class I of the Ross Classification of Pediatric Heart Failure). The other two patients both suffered from fatigue while feeding or during exertion (class II). Additionally, one of them suffered from growth retardation and the other had frequent respiratory tract infections. Left ventricular function was normal in all patients, but there were three (17.6%) with mild right ventricular dysfunction. In the late follow-up period, two patients (17.7%) maintained rhythm abnormalities already identified in the early postoperative period: one had supraventricular tachycardia episodes and the other frequent premature atrial and ventricular contractions.

Supravalvular pulmonary stenosis was the most frequent complication during the follow-up period. We found moderate pulmonary stenosis in three patients (17.7%) and severe pulmonary stenosis in two (11.8%). The second most frequent complication was aortic regurgitation found in four patients (23.5%), with two having mild regurgitation and the remaining moderate regurgitation. The least frequent complication was aortic root dilation, which was found in two patients (11.8%).

In total, two patients (11.8%) needed re-intervention after hospital discharge. They received main pulmonary artery plasty at nine and 27 months after ASO. The younger patient also underwent closure of residual VSD and excision of accessory tissue form the mitral valve in the same procedure.

The late postoperative outcomes are presented in table 7.

The risk factor analysis for occurrence of moderate-to-severe pulmonary stenosis was statistically significant for lower gestational age and lower birth and surgical weight (table 6). Need for reintervention in the late postoperative period was associated with lower gestational age, lower surgical weight and need for early postoperative reintervention (table 7). We also performed a risk factor analysis for development of aortic insufficiency and aortic root dilation but could not find any statistically significant associations (results presented in Supplementary Tables 3 and 4).

There was no mortality in the late postoperative period of this study. Overall survival in our study population was 94,4%, with a post-operative survival at 5 years of 100%.

Table 1 - Characteristics and demographic data of the 18 patients included in this study

Patient Characteristics	Total = 18
Male [a]	14 (77.8)
Gestational age (weeks) [b]	38 (± 2.0)
Preterm [a]	2 (11.1)
APGAR 1st minute [c]	8 (8 – 9)
Birth weight (g) [b]	3190.8 (± 653.8)
Low birth weight [a]	3 (16.7)
Prenatal diagnosis [a]	10 (55.6)
Time until postnatal diagnosis (days) [c]	0 (0 – 1)
<12 hours [a]	5 (27.8)
<24 hours [a]	1 (5.6)
<48 hours [a]	1 (5.6)
>30 days [a]	1 (5.6)
Definitive cardiovascular diagnosis [a]	
Simple d-TGA	9 (50.0)
d-TGA with VSD	8 (44.4)
Complex CHD	1 (5.6)
Coronary anomalies [a]	10 (55.6)
Pulmonary hypertension [a]	1 (5.6)
Extracardiac malformations [a]	3 (16.7)
Chromosomal abnormalities [a]	2 (11.1)

CHD: congenital heart disease

Data are presented as: [a] - number and percentage; [b] - mean and standard deviation; and [c] - median and interquartile range.

Table 2 – Preoperative period variables of 18 patients

Preoperative Period Variables	Total = 18
PGE 1	
Number [a]	17 (94.4)
Duration (days) [c]	13 (9.8 - 22.8)
BAS	
Number [a]	15 (83.3)
Time until BAS (days) [c]	1 (1-1)
Prolonged MV (>2 days)	
Number [a]	11 (61.1)
Duration (days) [c]	6 (4-11)
Need for NIV [a]	2 (11.1%)
Inotropic support	
Number [a]	5 (27.8)
Duration (days) [b]	6.6 (± 3.6)
Parameters 24 hours before surgery	
SatO2 (%) [c]	90.0 (84.0 – 94.0)
LV systolic disfunction [a]	
Mild disfunction	1 (5.6)
RV systolic dysfunction [a]	0
Complications (total) [a]	8 (44.4)
Infection	2 (11.1)
Sepsis	3 (16.7)
Acute kidney injury	1 (5.6)
Cardiogenic shock	1 (5.6)
Cardiopulmonary resuscitation	1 (5.6)
Mortality [a]	1 (5.6)

BAS: balloon atrial septostomy; LV: left ventricle; MV: mechanical ventilation; NVI: non-invasive ventilation; PGE1: prostaglandin E1

Data are presented as: [a] - number and percentage; [b] - mean and standard deviation; and [c] - median and interquartile range.

Table 3 – Surgical intervention data

Intraoperative Period Variables	Total = 17
Age at surgery (days) [c]	14 (12 – 28.5)
Surgical weight (g) [c]	3210 (3140 – 3505)
Duration of surgery (min) [b]	331.3 (± 98.0)
Duration of ECC (min) [c]	150 (136.5 – 184.50)
Duration of AC (min) [c]	79 (69.50 – 87.50)
Additional CA maneuvers [a]	3 (17.6)
Complications [a]	6 (35.3)
Mortality [a]	0

AC: aortic clamping; CA: coronary artery; ECC: extracorporeal circulation

Data are presented as: [a] - number and percentage; [b] - mean and standard deviation; and [c] - median and interquartile range.

Table 4 - Early postoperative period outcomes for 17 patients

Early Postoperative Period Outcomes	Total = 17
Supportive measures	
Duration of MV (days)	7 (6 – 11)
Need for NIV	2 (11.7)
Duration of IS (days)	7.9 (± 3.8)
Need for ECMO	1 (5.9)
Duration of DSC (days)	4 (2 – 5.5)
Immediate postoperative parameters	
<24h LV systolic disfunction	
Normal	12 (70.6)
Mild disfunction	3 (17.)
Moderate disfunction	1 (5.9)
Severe disfunction	1 (5.9)
<24h Lactate (mmol/l)	2.8 (1.4 – 4.2)
<24h Troponin (ng/L)	29 709.8 (13 901.1 – 40 381.5)
>24h Troponin (ng/L)	13 201.827 (6 832.0 – 15 742.3)
Major complications (total)	14 (82.3)
Infections/Sepsis	10 (58.8)
Chylothorax	7 (41.2)
Dysrhythmia	5 (29.4)
Device implantation	2 (11.8)
CNS lesions	5 (29.4)
Seizures	1 (5.9)
Thalamic lesions	3 (17.6)
IVH	1 (5.9)
Wound dehiscence	4 (23.5)
Acute kidney injury	2 (11.8)
Diaphragmic paralysis	2 (11.8)
Cardiac tamponade	1 (5.9)
Ischemia	0
Other events	
Pulmonary atelectasis	4 (23.5)
Pneumonic pleural effusion	1 (5.9)
Opioid Withdrawal syndrome	12 (70.6)
Length of stay	
Postoperative neonatology stay (days)	22 (16.5-31)
Total hospital stay (days)	50 (34-64)
Reinterventions	3 (17.6)
Mortality	0

CNS: central nervous system; DSC: delayed sternal closure; ECMO: extracorporeal membrane oxygenation; IS: inotropic support; IVH: intraventricular hemorrhage; LV: left ventricle; MV: mechanical ventilation; NVI: non-invasive ventilation
Data are presented as: [a] - number and percentage; [b] - mean and standard deviation; and [c] - median and interquartile range.

Table 5 - Late postoperative outcomes of 17 patients

Late Postoperative Period	Total = 17
Duration of follow-up (months) [b]	28.77 (± 13.9)
Symptoms [a]	2 (11.8)
Ross Classification [a]	
Class I	15 (88.2)
Class II	2 (11.8)
LV systolic disfunction [a]	0
RV systolic disfunction [a]	3 (17.6)
Mild	
Pulmonary stenosis [a]	16 (95.1)
Mild	11 (64.7)
Moderate	3 (17.6)
Severe	2 (11.8)
Aortic Insufficiency [a]	4 (23.5)
Mild	2 (11.8)
Moderate	2 (11.8)
Aortic Dilation [a]	2 (11.8)
Dysrhythmia [a]	3 (17.7)
Reinterventions [a]	2 (11.8)
Mortality [a]	0

LV: left ventricle; RV: right ventricle

Data are presented as: [a] - number and percentage; and [b] - mean and standard deviation.

Table 6 - Risk factor analysis for moderate or severe pulmonary stenosis (PS)

	With PS	Without PS	
	n=5	n=12	p
Patient Characteristics			
Gestational age [b]	36.2 (± 2.2)	39.3 (±1 .2)	**0.004***
Preterm [a]	2 (40.0)	0	0.074
Birth weight [b]	2607.9 (± 564.6)	3500 (± 478.1)	**0.001***
Low birth weight [a]	2 (40.0)	0	0.074
d-TGA with VSD [a]	2 (40.0)	6 (50.0)	1.000
Coronary anomalies [a]	2 (40.0)	7 (58.3)	0.620
Pulmonary hypertension [a]	0	1 (8.3)	1.000
Intraoperative variables			
Age at surgery (days)[c]	14.0 (11.0 – 28.0)	17.5 (12.25 – 31.0)	0.672
Surgical weight (g) [c]	2830.0 (2222.5 - 3172.5)	3397.5 (3173.8 - 3645.0)	**0.007***
Total duration of surgery (min)[b]	326.0 (± 175.0)	333.6 (± 64.7)	0.948
Duration of ECC (min) [c]	144.0 (116.0 – 155.0)	153.5 (141.5 – 201.6)	0.171
Duration of AC (min) [c]	78.0 (67.5 – 79.5)	82.5 (69.6 – 106.0)	0.187
Additional CA maneuvers [a]	0	3 (25.0)	0.515
Intraoperative Complications [a]	2 (40.0)	4 (33.3)	1.000
Early postoperative period			
Duration MV (days) [c]	7.0 (6.5 – 13.5)	7.5 (6.0 – 10.6)	0.630
Duration IS (days) [c]	7.0 (4.0 -11.0)	7.5 (6.0 10.6)	0.750
Duration DSC (days) [c]	4.0 (3.0 -11.0)	3.0 (2.0 – 5.5)	0.333
Complications [a]	5 (100)	9 (75.0)	0.515
Reintervention [a]	2 (40.0)	1 (8.3)	0.191

AC: aortic clamping; CA: coronary artery; DSC: delayed sternal closure; ECC: extracorporeal circulation; IS: inotropic support; MV: mechanical ventilation; VSD: ventricular septal defect

Data are presented as: [a] - number and percentage; [b] - mean and standard deviation; and [c] - median and interquartile range.

Table 7 - Risk factor analysis for late postoperative reinterventions

	With Reintervention	Without Reintervention	
	n=2	n=15	p
Patient characteristics			
Preterm [a]	1 (50.0)	1 (6.7)	0.228
Gestational age [a]	35.5 (± 3.5)	38.8 (± 1.7)	**0.031***
Low birth weight [a]	1 (50.0)	1 (6.7)	0.228
d-TGA with VSD [a]	2 (100)	6 (40.0)	0.206
Coronary anomalies [a]	2 (100)	7 (46.7)	0.471
Pulmonary hypertension [a]	0	1 (6.7)	1.000
Intraoperative variables			
Age at surgery (days) [c]	32.5 (29.0 – 36.0)	14.0 (12.0 – 27.0)	0.073
Surgical weight (g) [c]	3650.0 (2105.0 - 5195.0)	3210.0 (3145.0 - 3500.0)	**<0.001***
Total duration of surgery (min)[b]	268.0 (± 124.5)	347.1 (± 93.4)	0.336
Duration of ECC (min) [c]	181.5 (160.0 203.0)	149.0 (133.0 – 173.0)	0.180
Duration of AC (min) [c]	101.5 (72.0 - 131.0)	79 (67.0 87.0)	0.654
Additional CA maneuvers [a]	1 (50.0)	2 (13.3)	0.331
Intraoperative complications [a]	1 (50.0)	5 (33.3)	1.000
Early postoperative variables			
Duration of MV (days) [c]	12.0 (11.0 – 13.0)	7.0 (6.0 – 10.0)	0.112
Duration of IS (days) [c]	12.5 (12.0 – 13.0)	7.0 (5.0 – 9.0)	0.051
Duration of DSC (days) [c]	5.5 (5.0 – 6.0)	3.0 (2.0 – 4.0)	0.171
Complications [a]	2 (100)	12 (80.0)	1.000
Need for reintervention [a]	2 (100)	1 (6.7)	0.022

AC: aortic clamping; CA: coronary artery; DSC: delayed sternal closure; ECC: extracorporeal circulation; IS: inotropic support; MV: mechanical ventilation; VSD: ventricular septal defect

Data are presented as: [a] - number and percentage; [b] - mean and standard deviation; and [c] - median and interquartile range.

Discussion

In the year of 2016, our hospital started to autonomously perform the ASO procedure. In this five-year single-center retrospective study, we described the characteristics and outcomes of the first patients surgically treated in our institution. During this period, 18 patients with d-TGA were admitted, nine of which had simple d-TGA, eight had d-TGA with VSD and one had complex cardiac anatomy. In our study, the type of d-TGA did not prove to be a risk factor for early or late reintervention or mortality, unlike reported in other studies [3, 9, 14], with the lack of association possibly explained by the small sample size.

Similarly, anomalous coronary patterns, which were found in 10 newborns, were not significantly associated with worse outcomes. This was true even for the three patients who needed additional maneuvers for coronary artery relocation. Many authors previously found that coronary anatomy, especially single and intramural coronary arteries led to worse outcomes after ASO, both in the early and late postoperative periods [5, 14-16]. However, in recent years, other studies could not find this association as well, suggesting that the improvement in surgical techniques for coronary reimplantation could explain this difference [3, 9, 13, 17, 18]. Given these contradictory results, more studies are needed to clarify whether coronary anatomy remains a factor contributing to higher morbimortality after ASO.

In Portugal, all pregnant women undergo a minimum of three obstetric ultrasounds. If there is a suspicion or an increased risk of congenital heart disease due to maternal or fetus' factors, patients are referred to perform a fetal echocardiogram. After confirmation of the cardiac diagnosis, the follow-up will be maintained at our institution and, if necessary, the delivery as well, in order to offer immediate post-natal care. We found a 55.6% rate of prenatal detection of d-TGA, comparable to prenatal detection rates reported in literature, which vary greatly between 14 to 78% [19-22]. In our analysis, the absence of prenatal diagnosis was not a statistically significant risk factor for worse outcomes, although the only death occurred in a patient who was diagnosed postnatally. On the other hand, it has been reported in literature that prenatal detection of d-TGA is associated with lower morbidity and mortality in the early and late follow-up periods. [16, 19, 22-24].

Newborns with d-TGA can rapidly become hypoxemic after birth due to inadequate mixing of systemic and pulmonary blood, which can be enhanced by PGE1 infusion and BAS [1, 5, 16, 19, 23, 25]. In our series, most newborns received PGE1 infusion (94.4%) and BAS (83.3%). Some

patients also needed additional supporting measures to guarantee appropriate tissue oxygenation and avoid acidosis: mechanical ventilation in 55.5%, non-invasive ventilation in 11.1%, and inotropic support in 27.8%.

The ASO (with or without the Lecompte maneuver) and additional correction of concomitant defects is the current gold-standard of treatment [1, 5, 16]. Nowadays, the timing of surgery is still a topic of discussion [5, 16, 23, 25]. On one hand, delaying the performance of ASO allows transition from fetal to neonatal life, with decrease of pulmonary vascular resistance and improvement of renal, lung and liver functions [5]. Patients can also initiate enteral feeding and weight gain before surgery. In fact, patients weighting less than 2500g are prone to complications and mortality in the early perioperative period, with those under 2000 - 2200g having the highest risk [5, 16, 26]. In our study, patients weighted a median of 3210g (IQR 3140 – 3505), and two weighted less than 2500g. We could not find a significant association between surgical weight and worse early postoperative outcomes, but we found associations with development of moderate-to-severe supravalvular pulmonary stenosis and need for reintervention in the late postoperative study. On the other hand, delaying ASO can have deleterious effects on patient outcomes, especially for those with intact ventricular septum due to deconditioning of the left ventricle, which will not be able to support a systemic workload after surgical correction [16, 23, 25]. Furthermore, preoperative therapeutic adjuvants like PGE1 infusion, BAS, ventilation, and inotropic support are not innocuous during long periods. Most experts agree that surgery should be performed between 3 days and 3 weeks after birth [5, 16, 23, 25]. In our hospital, patients had a median age at surgery of 14 days (IQR 12 - 28.5 days), thus some patients were above the advised 3 weeks of age. According to clinical guidelines [16], ASO should not be postponed for weight gain purposes only, since delaying the repair of d-TGA was associated to higher rates of early morbimortality than operating on patients weighing less than 2500g Nonetheless, in our study we found that lower surgical weight was a risk factor for worse late postoperative period outcomes, while older age at surgery was not significantly associated with worse outcome.

There is no consensus on the best treatment of late d-TGA, especially in what concerns timing and best surgical approach. Some authors consider that after 3-4 weeks primary ASO should be contraindicated, and patients should receive a two-stage procedure: a left ventricular training procedure at first (like pulmonary artery banding), followed by a second stage ASO

procedure. In contrast, some centers report that it is possible to safely perform primary ASO in patients until 8 weeks or even older, although these patients might require longer duration of postoperative mechanical ventilation or additional supporting measures. [5, 16, 23, 25] However, there are still many gaps in the evidence surrounding this topic, especially concerning the long-term consequences of both approaches.

In patients with severe myocardial dysfunction, ECMO might be necessary in addition to inotropic support to maintain an adequate hemodynamic status [16]. In our center, only one patient required ECMO support before leaving the operating room. His native anatomy was d-TGA with VSD and normal coronary anatomy, with ASO being performed at 12 days of life (ECC and AC duration of 394 and 85 minutes, respectively). Despite a complicated early postoperative period, he was weaned off ECMO after 4 days and there was no need for cardiac reintervention. He did, however, need an Ommaya reservoir for grade III intraventricular hemorrhage, which could have been related to heparinization during ECMO [27]. At 3 months of age, he was asymptomatic with no late cardiac complications, despite maintaining antiarrhythmic therapy with beta-blocker due to previous SVT episodes. Thus, regardless of its risks, ECMO has good potential for supporting patients with low cardiac output syndrome in the postoperative period.

Our hospital performed delayed sternal closure after ASO routinely, with a median duration of 4 days. This is not the case for many centers, that only performs it electively. However, it has not been proven that this approach is associated with lower morbidity when compared to routine procedure [5, 16]. Our study did not establish a significant association between DSC duration and complications or reintervention either in the early or the late periods after ASO.

We found several major early postoperative complications, but we did not find any significant risk factors for their occurrence, probably due to our small sample size. On the other hand, in literature, it has been shown that patient characteristics such as prematurity, low birth and surgical weight, associated VSD, coronary anomalies and genetic conditions were associated with higher morbidity after ASO. It has also been suggested that preoperative MV, older age at surgery, and longer duration of surgery and ECC were risk factors for a complicated early postoperative period [3, 6-9, 13]. The most frequent early postoperative complication was infection or sepsis, which some authors relate to prolonged MV duration [5, 16]. Other complications found in

this study were chylothorax, neurological lesions, dysrhythmias, wound dehiscence, acute kidney injury, diaphragmic paralysis and cardiac tamponade.

Three of our patients (17.6%) needed early reinterventions, two of them due to wound dehiscence whereas the other needed to have a cardiac tamponade drained and later a diaphragmatic plication. We found a higher rate than the 9.9% reported by Fricke, *et. al* [9] in a cohort of 618 patients. However, their definition of reintervention only includes heart or great vessel procedures, thus excluding from their analysis wound debridement. This way, our higher rate of reintervention is explained by this difference in definition. In fact, if we adopted their classification our early reintervention rate would be 5.9%, as there is only one patient who fits these criteria.

Moderate or severe supravalvular pulmonary stenosis was the most frequent late complication of ASO (29.4%). In literature, a rate of 1-42% has been reported [3, 11, 15, 16]. Similarly, to what has been previously described, we found that lower birth and surgical weight and younger age at surgery surgical are significant risk factors for this complication [16]. It has also been associated with other patient-related (mismatch between vessel and valvular anulus, side-by-side great arteries, rapid somatic growth, etc.) and surgery-related factors (technique used for reconstruction, distortion, stretching and tension of the trunk and its branches after Lecompte maneuver, use of prosthetic material for sinus reconstruction, etc.) [16, 28, 29]. This complication is the most common cause for late reintervention [3, 5, 15, 16, 29], which was need in two patients (11.8%). We found that lower gestational age, lower surgical weight and need for reintervention in the early postoperative period were risk factors for reintervention in the late postoperative period. Our reintervention rate is comparable to those reported in literature (10-20%) [4, 10-12, 16, 29].

Aortic insufficiency was found in four patients (22.2%), two with mild and two with moderate degree of severity, which is comparable to the 16 - 44% at mid-term follow-up found in literature [3, 9, 11, 15, 30]. Our analysis could not identify statistically significant risk factors for aortic insufficiency, but other authors have identified higher age at surgery, size discrepancy between the aorta and pulmonary trunk, use of trap-door technique for coronary artery transfer and rapid development of aortic root dilation could be related with this complication. The mechanism that leads to valve regurgitation is hypothesized to be associated with the systemic burden imposed in a native pulmonary valve after ASO, and the complex suture lines created by coronary artery

transfer to the aortic root. [15, 16]. Aortic root dilation was found in two patients (11.1%), one of them associated with moderate aortic insufficiency. Although we could not identify risk factors related to this complication, it has been associated with previous pulmonary artery banding, male sex, and presence of VSD or aortic arch abnormality. Pathophysiology is likely multifactorial, with hemodynamic and anatomical factors contributing to its development. Progression of aortic dilation occurs through childhood and likely during adulthood as well [31]. Therefore, surveillance of patients for this complication is important, and more studies to clarify mechanisms of disease, predictors and preventive measures for this condition are fundamental.

We could not identify any early or late coronary lesions or ischemic events in our cohort. Nevertheless, this largely asymptomatic complication can lead to sudden cardiac death as its inaugural presentation, remaining the biggest mortality cause during follow-up [5, 15]. Abnormal coronary arteries, especially single and intramural patterns, as well as their relative position to the great vessels and bicuspid aortic valve have been established risk factors for coronary lesions [15, 16].

All patients in our center submitted to an ASO procedure are still alive, and we only registered one fatality (5.6%), which occurred in the preoperative period. Thus, we are well within the 87–90% mid-term survival rates reported in several studies from other reference centers, including a meta-analysis comprising 2115 patients [4, 5, 11].

Our research had several limitations. First, our study sample was small and there was a reduced number of events, which led to reduced power to detect significant differences between groups. Second, this was a single-center retrospective cohort study, affecting the external validation of our results. Furthermore, five years are not enough to understand our center's long-term outcomes, thus a future analysis should be performed. Because there are still many unanswered questions about d-TGA and its management that should be clarified by future large, multicentric prospective studies.

In conclusion, with this study we show that our institution has comparable results to other reference centers for congenital heart diseases, despite having only recently started performing this surgery autonomously. There were some complications and reinterventions in the early postoperative period, but there was no surgical mortality. Besides, our complication rate at mid-term was similar to those reported in literature. Furthermore, our study has helped consolidate

some risk factors for worse late outcomes: pulmonary stenosis was associated with lower gestational age and lower birth and surgical weight; and late reintervention was associated with lower gestational age, lower surgical weight and need for early reintervention.

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ANEXOS

ÍNDICE DE ANEXOS

ANEXO I – Tabelas Suplementares

Supplementary Table 1 - Risk factors analysis for major early postoperative complications

	Complicated	Not Complicated	
	n=14	n=3	**p**
Patient characteristics			
Preterm [a]	2 (14.3)	0	1.000
Low birth weight [a]	2 (14.3)	0	1.000
Prenatal diagnosis [a]	9 (64.3)	1 (33.3)	0.537
d-TGA with VSD [a]	6 (42.9)	2 (66.7)	0.576
Coronary anomalies [a]	7 (50.0)	2 (66.7)	1.000
Pulmonary hypertension [a]	1 (7.1)	0	1.000
Extracardiac malformations [a]	2 (14.3)	0	1.000
Chromosomal abnormalities [a]	1 (7.1)	1 (33.3)	0.331
Preoperative variables			
Need for septostomy [a]	13 (92.9)	2 (66.7)	0.331
Need for MV [a]	8 (57.1)	3 (100)	0.515
Need for NIV [a]	1 (7.1)	1 (33.3)	0.331
Need for IS [a]	3 (21.4%)	2 (66.7)	0.191
Preoperative complications	6 (42.9%)	2 (66.7)	0.576
Intraoperative variables			
Age at surgery (days) [c]	14.00 (11.5 – 27.3)	32.00 (14 – 66)	0.100
Surgical weight (g) [c]	3128.5 (3058.8 - 3498.6)	3500.0 (3210.0 - 3690.0)	0.186
Total duration of surgery (min)[b]	341.38 (± 104.32)	291 (± 79.20)	0.548
Duration of ECC (min) [c]	149.5 (129.5 – 169.0)	173 (140 - 334)	0.378
Duration of AC (min) [c]	79 (70.6 – 85.5)	88 (53 - 165)	0.528
Additional CA maneuvers [a]	2 (14.3)	1 (33.3)	0.465
Intraoperative complications [a]	4 (28.6)	2 (66.7)	0.515
Early postoperative variables			
Duration of MV (days) [c]	7.5 (6.0 - 11.5)	7 (5 -11)	0.565
Duration of IS (days) [c]	7.5 (5.6 – 11.3)	7 (3 – 10)	0.657
Duration of DSC (days) [c]	4 (2 - 5.5)	2 (2 - 9)	0.797

AC: aortic clamping; CA: coronary artery; DSC: delayed sternal closure; ECC: extracorporeal circulation; IS: inotropic support; MV: mechanical ventilation; NIV: non-invasive ventilation; VSD: ventricular septal defect

Data are presented as: [a] - number and percentage; [b] - mean and standard deviation; and [c] - median and interquartile range.

Supplementary Table 2 - Risk factor analysis for reintervention in the early postoperative period

	With Reintervention	Without Reintervention	
	n=3	n=14	**p**
Patients characteristics			
Preterm [a]	1 (33.3)	1 (7.1)	0.331
Low birth weight [a]	1 (33.3)	1 (7.1)	0.331
Prenatal diagnosis [a]	3 (100)	7(50)	0.228
d-TGA with VSD [a]	2 (66.7)	6 (42.9)	0.576
Coronary anomalies [a]	2 (66.7)	7 (50)	1.000
Pulmonary hypertension [a]	0	1 (7.1)	1.000
Extracardiac malformations [a]	0	2 (14.3)	1.000
Chromosomal abnormalities [a]	0	2 (14.3)	1.000
Preoperative period			
Need for septostomy [a]	3 (100)	12 (85.7)	1.000
Need for MV [a]	3 (100)	8 (57.1)	0.515
Need for NIV [a]	0 (0)	2 (14.3)	1.000
Need for IS [a]	1 (33.3)	4 (28.6)	1.000
Preoperative complications [a]	1 (33.3)	7 (50.0)	1.000
Intraoperative variables			
Age at surgery (days) [c]	29.0 (12 - 36)	14.0 (11.5 – 27.3)	0.343
Surgical weight (g) [c]	3135.0 (2105.0 - 5195.0)	3210.0 (3148.6 - 3502.5)	0.528
Total duration of surgery (min)[b]	268.0 (± 124.5)	347.1 (± 93.4)	0.336
Duration of ECC (min) [c]	160.0 (113 - 160)	177.9 (138.3 – 178.6)	0.801
Duration of AC (min) [c]	72.0 (63 – 131)	79.5 (75.3 – 87.3)	0.614
Additional CA maneuvers [a]	1 (33.3)	2 (14.3)	0.465
Intraoperative complications [a]	1 (33.3)	5 (35.7)	1.000
Early postoperative variables			
Duration of MV (days) [c]	11.0 (7.0 – 13.0)	7.0 (6 – 10.3)	0.224
Duration of IS (days) [c]	12.0 (3.0 – 13.0)	7.0 (5.6 – 9.3)	0.447
Duration of DSC (days) [c]	5.0 (4.0 – 6.0)	3.0 (2 – 4.6)	0.177

AC: aortic clamping; CA: coronary artery; DSC: delayed sternal closure; ECC: extracorporeal circulation; IS: inotropic support; MV: mechanical ventilation; NIV: non-invasive ventilation; VSD: ventricular septal defect

Data are presented as: [a] - number and percentage; [b] - mean and standard deviation; and [c] - median and interquartile range.

Supplementary Table 3 - Risk factor analysis for aortic insufficiency (AI)

	With AI	Without AI	
	n=4	n=13	p
Patient Characteristics			
Preterm [a]	0	2 (15.4)	1.000
Low birth weight [a]	0	2 (15.4)	1.000
d-TGA with VSD [a]	2 (50.0)	6 (46.2)	1.000
Coronary anomalies [a]	4 (100)	5 (38.5)	0.082
Pulmonary hypertension [a]	1 (25.0)	0	0.235
Intraoperative variables			
Age at surgery (days) [c]	17.5 (11.0 – 29.6)	14.0 (12.0 – 28.5)	0.955
Surgical weight (g) [c]	3405.0 (3232.5 - 3645.0)	3165.0 (2982.5 - 3497.5)	0.126
Total duration of surgery (min)[b]	353.5 (± 9.2)	325.6 (± 110.3)	0.743
Duration of ECC (min) [c]	148.0 (116.0 – 167.3)	152.0 (136.5 – 199.5)	0.497
Duration of AC (min) [c]	79.5 (68.5 – 86.0)	79.0 (69.5 – 99.5)	1.000
Additional CA maneuvers [a]	0	3 (100)	0.541
Intraoperative complications [a]	1 (25.0)	5 (38.5)	1.000
Early postoperative variables			
Duration of MV (days) [c]	7.5 (6.3 – 10.3)	7.0 (6.0 – 12.0)	0.954
Duration of IS (days) [c]	7.5 (5.3 – 9.6)	7.0 (4.5 – 11.5)	0.864
Duration of DSC (days) [c]	3.0 (2.0 – 7.8)	4.0 (2.0 – 5.5)	0.954
Complications [a]	3 (75.0)	11 (86.6)	1.000
Need for reintervention [a]	0	3 (23.1)	0.541

AC: aortic clamping; CA: coronary artery; DSC: delayed sternal closure; ECC: extracorporeal circulation; IS: inotropic support; MV: mechanical ventilation; VSD: ventricular septal defect

Data are presented as: [a] - number and percentage; [b] - mean and standard deviation; and [c] - median and interquartile range.

Supplementary Table 4 - Risk factor analysis for aortic root dilation (AD)

	With AD	Without AD	
	n=2	n=15	p
Patient characteristics			
Preterm [a]	1 (50.0)	1 (6.7)	0.228
Low birth weight [a]	1 (50.0)	1 (6.7)	0.228
Prenatal diagnosis [a]	2 (100)	8 (80.0)	0.485
d-TGA with VSD [a]	2 (100)	6 (40.0)	0.206
Coronary anomalies [a]	2 (100)	7 (46.7)	0.471
Pulmonary hypertension [a]	0	1 (6.7)	1.000
Intraoperative variables			
Age at surgery (days) [c]	25.0 (21.0 – 29.0)	14.0 (12.0-28.0)	0.369
Surgical weight (g) [c]	2807.5 (2105.0 - 3510.0)	3210.0 (3245.0 - 3500.0)	0.655
Total duration of surgery (min)[b]	180 (-) [d]	348.1 (± 87.4)	0.105
Duration of ECC (min) [c]	133 (106.0 – 160.0)	150 (140.0 – 196.0)	0.456
Duration of AC (min) [c]	68.5 (65.0 – 72.0)	80 (78.0 – 88.0)	0.135
Additional CA maneuvers [a]	0	3 (20.0)	1.000
Intraoperative complications [a]	0	6 (40.0)	0.515
Early postoperative variables			
Duration of MV (days) [c]	8.5 (6.0 -11.0)	7.0 (6.0 – 11.0)	0.940
Duration of IS (days) [c]	9.5 (6.0 -13-0)	7.0 (5.0 – 10.0)	0.549
Duration of DSC (days) [c]	3.5 (2.0 – 5.0)	4.0 (2.0 – 6.0)	0.879
Complications [a]	2 (100)	12 (80.0)	1.000
Need for reintervention [a]	1 (50.0)	2 (13.3)	0.331

AC: aortic clamping; CA: coronary artery; DSC: delayed sternal closure; ECC: extracorporeal circulation; IS: inotropic support; MV: mechanical ventilation; VSD: ventricular septal defect

Data are presented as: [a] - number and percentage; [b] - mean and standard deviation; and [c] - median and interquartile range.

[d] – SD was impossible to calculate due to data only being available for one patient.

ANEXO II – STROBE Statement –

Checklist of items that should be included in reports of *cohort studies*

	Item No	Recommendation	Page No
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract **"We performed a single-center retrospective cohort study …"** (*b*) Provide in the abstract an informative and balanced summary of what was done and what was found **"We performed a single-center retrospective cohort study of newborns with d-TGA admitted to our hospital between January 2016 and December 2020. We reviewed patient's medical records and collected data on their characteristics, surgery, and pre- and postoperative periods. We included 18 patients with d-TGA: nine patients had simple d-TGA, eight had d-TGA with ventricular septal defect (VSD) and one had complex d-TGA. There was one preoperative death. ASO was performed in 17 patients. The complications found in the early postoperative period were: 10 infection/sepsis, seven chylothorax, five neurological lesions, five dysrhythmia, four wound dehiscence, two acute kidney injury, two diaphragmic paralysis and one cardiac tamponade. There were three early reinterventions. In the late postoperative period, five (27.8%) patients had moderate-to-severe supravalvular pulmonary stenosis, with two needing reinterventions. There were four (22.0%) patients with aortic insufficiency and two (11.1%) with aortic root dilation."**	**2**
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported **"Dextro-transposition of the great arteries (d-TGA) is a congenital heart defect characterized by atrioventricular concordance and ventriculoarterial discordance, with the aorta arising from the morphological right ventricle and the pulmonary artery arising from the morphological left ventricle."** **"d-TGA represents 5-7% of all congenital heart defects [1, 3-5] and is the second most common cyanotic congenital heart disease (20%) [6, 7], with an estimated incidence of 1:3200 live births [2]."** **"Newborns with d-TGA will have some degree of hypoxemia, potentially leading to shock, end-organ-dysfunction, and death. Adjuvant therapies, such as intravenous prostaglandin E1 (PGE1) [1, 6], Rashkind balloon atrial septostomy (BAS), mechanical ventilation (MV), inotropic support (IS), and others, can be used to temporarily improve systemic blood oxygenation [1, 3, 5]."** **"Definitive treatment can only be achieved by surgical correction of d-TGA [1, 6]. Currently, the gold-standard is the arterial switch operation (ASO), performed successfully for the first time by Jatene in 1975 [1, 5, 6]."** **"Our center performed ASO for the first time in 2016."**	**3 - 4**
Objectives	3	State specific objectives, including any prespecified hypotheses **"With this study, we intended to characterize all patients who underwent surgical correction in our institution and their short- and mid-term outcomes. We also aimed to investigate possible risk factors for postoperative morbidity mortality and need for reintervention, with special emphasis on cardiac and coronary anatomy, and perioperative care. Ultimately, we hope this study will help us understand how our center compares to other reference centers for congenital heart diseases and improve the management and care of d-TGA patients in our institution."**	**4**
Methods			
Study design	4	Present key elements of study design early in the paper **"This single-center retrospective cohort study was approved by the ethics committee and the administration board of Centro Hospitalar Universitário de São João (CHUSJ)."** **"We included all patients with d-TGA admitted to CHUSJ between January 2016 and December 2020."**	**5**

Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection **"We included all patients with d-TGA admitted to CHUSJ between January 2016 and December 2020."** **"We reviewed patient's electronic, and paper based medical records and collected data on patient characteristics, preoperative period, surgical intervention, and early and late postoperative periods."** **"The early postoperative period was defined as the first 30 days after surgery or time before hospital discharge."** **"The late postoperative period began after the first 30 postoperative days or hospital discharge."**	**5 - 6**
Participants	6	(*a*) Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up **"We included all patients with d-TGA admitted to CHUSJ between January 2016 and December 2020. We chose 2016 as the starting year for patient inclusion because it was the year in which our institution started to perform the ASO procedure. Before this, patients were admitted to our center for preoperative care, being transferred afterwards to another Portuguese surgical center. Thus, we excluded them from this analysis to guarantee data uniformity and a lower rate of missing data, at the cost of shorter follow-up times."** **"We reviewed patient's electronic, and paper based medical records and collected data on patient characteristics, preoperative period, surgical intervention, and early and late postoperative periods."** Methods of follow-up – **Não aplicável, dado tratar-se de um estudo retrospetivo** (*b*) For matched studies, give matching criteria and number of exposed and unexposed **Não aplicável, uma vez que não se trata de um estudo com emparelhamento**	**5**
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable **"… collected data on patient characteristics, preoperative period, surgical intervention, and early and late postoperative periods."** **"Preoperative period: (…) If necessary, patients would receive PGE1 infusion, Rashkind BAS, MV, non-invasive ventilation (NIV) and IS. We collected data on preoperative interventions, and parameters 24 hours before surgery (oxygen saturation, left and right systolic function)."** **"Early Postoperative Period: (…) Major morbidity was defined as occurrence of cardiac tamponade, chylothorax, dysrhythmia, ischemic events, diaphragmatic paresis, infection or sepsis, acute kidney injury (AKI), need for peritoneal dialysis, necrotizing enterocolitis, neurological complications, or surgical wound dehiscence. Opioid withdrawal syndrome and pulmonary atelectasis were considered minor complications. We also evaluated the need for reintervention related to d-TGA or ASO, duration of MV or IS, time of DSC, need for extracorporeal membrane oxygenation (ECMO), length of stay in the neonatal intensive care unit (NICU) and hospital."** **"Late Postoperative Period: (…) We studied occurrence of late complications: supravalvular pulmonary stenosis, neo-aortic root dilation, aortic insufficiency, ischemic events, and dysrhythmias. The presence of symptoms and need for reintervention were also registered."**	**5 - 6**
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group. **"We reviewed patient's electronic, and paper based medical records and collected data on patient characteristics, preoperative period, surgical intervention, and early and late postoperative periods."** **"All patients underwent transthoracic echocardiogram (TTE) for confirmation of d-TGA and to further establish cardiac and coronary anatomy."**	**5**
Bias	9	Describe any efforts to address potential sources of bias	**5**

		"We included all patients with d-TGA admitted to CHUSJ between January 2016 and December 2020. We chose 2016 as the starting year for patient inclusion because it was the year in which our institution started to perform the ASO procedure. Before this, patients were admitted to our center for preoperative care, being transferred afterwards to another Portuguese surgical center. Thus, we excluded them from this analysis to guarantee data uniformity and a lower rate of missing data,"	
Study size	10	Explain how the study size was arrived at **"We included all patients with d-TGA admitted to CHUSJ between January 2016 and December 2020."**	**5**
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why **"…quantitative values were presented as mean and standard deviation (SD) if normally distributed or median and interquartile range (IQR) if otherwise. Normality of distribution was determined by the Kolmogorov-Smirnov test."**	**7**
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding **"For the descriptive analysis qualitative variables were presented as absolute number and percentage; quantitative values were presented as mean and standard deviation (SD) if normally distributed or median and interquartile range (IQR) if otherwise. Normality of distribution was determined by the Kolmogorov-Smirnov test. For the risk factors analysis Fisher's exact test, student t-test or Mann-Whitney U were used and p<0.005 defined significance."** (*b*) Describe any methods used to examine subgroups and interactions **Não aplicável neste estudo** (*c*) Explain how missing data were addressed **"Missing data were excluded from analysis."** (*d*) If applicable, explain how loss to follow-up was addressed **Não aplicável neste estudo** (*e*) Describe any sensitivity analyses **Não aplicável neste estudo**	**7**
Results			
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed **"During the study period, our institution treated 18 patients with d-TGA in total, …"** **"There was one death in the preoperative period…"** **"ASO was performed in 17 patients,…"** **"The 17 patients had follow-up in the Pediatric Cardiology outpatient department…"** (b) Give reasons for non-participation at each stage **Todos os participantes elegíveis foram incluídos na análise** (c) Consider use of a flow diagram **Todos os participantes elegíveis foram incluídos na análise**	**7 - 12**
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders **Table 1 - Characteristics and demographic data of the 18 patients included in this study** **Table 2 – Preoperative period variables of 18 patients** **Table 3 – Surgical intervention data** (b) Indicate number of participants with missing data for each variable of interest **"Mean total surgical time was 331.3 minutes (SD ± 98.0), with missing data for 6 patients."** (c) Summarise follow-up time (eg, average and total amount) **Não aplicável, devido a tratar-se de um estudo retrospetivo.**	**7 - 15**
Outcome data	15*	Report numbers of outcome events or summary measures over time **Table 4 - Early postoperative period outcomes for 17 patients**	**7 - 18**

		Table 5 - Late postoperative outcomes of 17 patients	
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included **"We performed a risk factor analysis for occurrence of major early postoperative complications and need for reinterventions, but we could not find any statistically significant associations (results presented in Supplementary Tables 1 and 2)."** **"The risk factor analysis for occurrence of moderate-to-severe pulmonary stenosis was statistically significant for lower gestational age and lower birth and surgical weight (table 6). Need for reintervention in the late postoperative period was associated with lower gestational age, lower surgical weight and need for early postoperative reintervention (table 7). We also performed a risk factor analysis for development of aortic insufficiency and aortic root dilation but could not find any statistically significant associations (results presented in Supplementary Tables 3 and 4)."** **"Overall survival in our study population was 94,4%, with a post-operative survival at 5 years of 100%."** **Table 6 - Risk factor analysis for moderate or severe pulmonary stenosis (PS)** **Table 7 - Risk factor analysis for late postoperative reinterventions** **Não foram realizados ajustes para fatores confundidores.** (*b*) Report category boundaries when continuous variables were categorized **Não aplicável, nenhuma variável contínua foi categorizada** (*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period **Não aplicável, uma vez que este estudo não avaliou o risco relativo ou absoluto**	**11, 12, 19, 20**
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses **Não aplicável, não foram realizadas estas análises no estudo**	**X**
Discussion			
Key results	18	Summarise key results with reference to study objectives **"In the year of 2016, our hospital started to autonomously perform the ASO procedure. In this five-year single-center retrospective study, we described the characteristics and outcomes of the first patients surgically treated in our institution. During this period, 18 patients with d-TGA were admitted, nine of which had simple d-TGA, eight had d-TGA with VSD and one had complex cardiac anatomy."** **"Similarly, anomalous coronary patterns, which were found in 10 newborns"** **"We found a 55.6% rate of prenatal detection of d-TGA, (…) In our analysis, the absence of prenatal diagnosis was not a statistically significant risk factor for worse outcomes, although the only death occurred in a patient who was diagnosed postnatally."** **"In our series, most newborns received PGE1 infusion (94.4%) and BAS (83.3%). Some patients also needed additional supporting measures to guarantee appropriate tissue oxygenation and avoid acidosis: mechanical ventilation in 55.5%, non-invasive ventilation in 11.1%, and inotropic support in 27.8%."** **"In our study, patients weighted a median of 3210g (IQR 3140 – 3505), and two weighted less than 2500g. We could not find a significant association between surgical weight and worse early postoperative outcomes, but we found associations with development of moderate-to-severe supravalvular pulmonary stenosis and need for reintervention in the late postoperative study.** **"In our hospital, patients had a median age at surgery of 14 days (IQR 12 - 28.5 days), thus some patients were above the advised 3 weeks of age. Nonetheless, older age at surgery was not associated with worse outcomes."** **"In our center, only one patient required ECMO support before leaving the operating room."** **"Our hospital performed delayed sternal closure after ASO routinely, with a median duration of 4 days."** **"We found several major early postoperative complications, but we did not find any significant risk factors for their occurrence, probably due to our small sample size."** **"The most frequent early postoperative complication was infection or sepsis, which**	**21-25**

		some authors relate to prolonged MV duration [5, 16]. Other complications found in this study were chylothorax, neurological lesions, dysrhythmias, wound dehiscence, acute kidney injury, diaphragmic paralysis and cardiac tamponade." **"Three of our patients (17.6%) needed early reinterventions, two of them due to wound dehiscence whereas the other needed to have a cardiac tamponade drained and later a diaphragmatic plication."** **"Moderate or severe supravalvular pulmonary stenosis was the most frequent late complication of ASO (29.4%). (…) we found that lower birth and surgical weight and younger age at surgery surgical are significant risk factors for this complication (…) This complication is the most common cause for late reintervention [3, 5, 15, 16, 29], which was need in two patients (11.8%). We found that lower gestational age, lower surgical weight and need for reintervention in the early postoperative period were risk factors for reintervention in the late postoperative period."** **"Aortic insufficiency was found in four patients (22.2%), two with mild and two with moderate degree of severity, (…) Our analysis could not identify statistically significant risk factors for aortic insufficiency, (…) Aortic root dilation was found in two patients (11.1%), one of them associated with moderate aortic insufficiency. Although we could not identify risk factors related to this complication, …"** **"All patients in our center submitted to an ASO procedure are still alive, and we only registered one fatality (5.6%), which occurred in the preoperative period."**	
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias **"Our research had several limitations. First, our study sample was small and there was a reduced number of events, which gave us reduced power to detect significant differences between groups. Second, this was a single-center retrospective cohort study, affecting the external validation of our results. Furthermore, five years are not enough to understand our center's long-term outcomes, thus a future analysis should be performed. Because there are still many unanswered questions about d-TGA and its management that should be clarified by future large, multicentric prospective studies."**	**25**
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence **"In our study, the type of d-TGA did not prove to be a risk factor for early or late reintervention or mortality, unlike reported in other studies [3, 9, 14], with the lack of association possibly explained by the small sample size."** **"Many authors previously found that coronary anatomy, especially single and intramural coronary arteries led to worse outcomes after ASO, both in the early and late postoperative periods [5, 14-16]. However, in recent years, other studies could not find this association as well, suggesting that the improvement in surgical techniques for coronary reimplantation could explain this difference [3, 9, 13, 17, 18]."** **"In our analysis, the absence of prenatal diagnosis was not a statistically significant risk factor for worse outcomes, although the only death occurred in a patient who was diagnosed postnatally. On the other hand, it has been reported in literature that prenatal detection of d-TGA is associated with lower morbidity and mortality in the early and late follow-up periods [16, 19, 22-24].** **"According to clinical guidelines [16], ASO should not be postponed for weight gain purposes only, since delaying the repair of d-TGA was associated to higher rates of early morbimortality than operating on patients weighing less than 2500g Nonetheless, in our study we found that lower surgical weight was a risk factor for worse late postoperative period outcomes, while older age at surgery was not significantly associated with worse outcome."** **"We found several major early postoperative complications, but we did not find any significant risk factors for their occurrence, probably due to our small sample size. On the other hand, in literature, it has been shown that patient characteristics such as prematurity, low birth and surgical weight, associated VSD, coronary anomalies and genetic conditions were associated with higher morbidity after ASO. It has also been suggested that preoperative MV, older age at surgery, and longer duration of surgery and ECC were risk factors for a complicated early postoperative period [3, 6-9, 13].** **"We found a higher rate than the 9.9% reported by Fricke, et. al 9 in a cohort of 618 patients. However, their definition of reintervention only includes heart or great**	**21-26**

		vessel procedures, thus excluding from their analysis wound debridement. This way, our higher rate of reintervention is explained by this difference in definition. In fact, if we adopted their classification our early reintervention rate would be 5.9%, as there is only one patient who fits these criteria." **"Similarly, to what has been previously described, we found that lower birth and surgical weight and younger age at surgery surgical are significant risk factors for this complication [16]. It has also been associated with other patient-related (mismatch between vessel and valvular anulus, side-by-side great arteries, rapid somatic growth, etc.) and surgery-related factors (technique used for reconstruction, distortion, stretching and tension of the trunk and its branches after Lecompte maneuver, use of prosthetic material for sinus reconstruction, etc.) [16, 28, 29]. (…) Our reintervention rate is comparable to those reported in literature (10-20%) [4, 10-12, 16, 29].** **"Aortic insufficiency was found in four patients (22.2%), two with mild and two with moderate degree of severity, which is comparable to the 16 - 44% at mid-term follow-up found in literature [3, 9, 11, 15, 30]. Our analysis could not identify statistically significant risk factors for aortic insufficiency, but other authors have identified higher age at surgery, size discrepancy between the aorta and pulmonary trunk, use of trap-door technique for coronary artery transfer and rapid development of aortic root dilation could be related with this complication."** **"Although we could not identify risk factors related to this complication, it has been associated with previous pulmonary artery banding, male sex, and presence of VSD or aortic arch abnormality."** **"All patients in our center submitted to an ASO procedure are still alive, and we only registered one fatality (5.6%), which occurred in the preoperative period. Thus, we are well within the 87–90% mid-term survival rates reported in several studies from other reference centers, including a meta-analysis comprising 2115 patients [4, 5, 11]."** **"In conclusion, with this study we show that our institution has comparable results to other reference centers for congenital heart diseases, despite having only recently started performing this surgery autonomously. There were some complications and reinterventions in the early postoperative period, but there was no surgical mortality. Besides, our complication rate at mid-term was similar to those reported in literature. Furthermore, our study has helped consolidate some risk factors for worse late outcomes: pulmonary stenosis was associated with lower gestational age and lower birth and surgical weight; and late reintervention was associated with lower gestational age, lower surgical weight and need for early reintervention."**	
Generalisability	21	Discuss the generalisability (external validity) of the study results **"…this was a single-center retrospective cohort study, affecting the external validation of our results."**	X
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based **Não aplicável, este estudo não foi financiado.**	

*Give information separately for exposed and unexposed groups.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at http://www.strobe-statement.org.

ANEXO III – Normas de Publicação na Revista Portuguesa de Cardiologia

Revista Portuguesa de Cardiologia

AUTHORS INFORMATION PACK

GUIDE FOR AUTHORS

INTRODUCTION

The Portuguese Journal of Cardiology, the official journal of the Portuguese Society of Cardiology, was founded in 1982 with the aim of keeping Portuguese cardiologists informed through the publication of scientific articles on areas such as arrhythmology and electrophysiology, cardiovascular surgery, intensive care, coronary artery disease, cardiovascular imaging, hypertension, heart failure and cardiovascular prevention.The Journal is a monthly publication with high standards of quality in terms of scientific content and production. Since 1999 it has been published in English as well as Portuguese, which has widened its readership abroad.

Please, take into account that as of January 2021, *Revista Portuguesa de Cardiologia* will require new article submissions to be written in English language.

The Journal accepts the following categories of articles:

Research (Original Investigation and Meta-Analysis), **Review and Education** (Narrative Reviews, Systematic Reviews -without meta-analysis, Guidelines, Case Reports, Images in Cardiology and Snapshots), **Opinion** (Current Perspective), **Correspondence** (Editorial Comment, Letters to the Editor, Research Letter and Observation)

Types of article

Manuscripts submitted for publication should be prepared in accordance with the "Recommendations for the Conduct, Reporting, Editing, and Publication of Scholarly Work in Medical Journals" of the International Committee of Medical Journal Editors (ICMJE). This document is available at http://www.icmje.org/recommendations/.

Summary table of *Revista Portuguesa de Cardiologia* types of article characteristics.

Original Investigation

Original Investigation articles cover areas of clinical or basic research: Clinical trial, Meta-analysis, Intervention study, Cohort study, Case-control study, Epidemiologic assessment, Survey with high response rate, Cost-effectiveness analysis, Decision analysis, Study of screening and diagnostic tests, Other observational studies) . They should have a maximum of 5000 words, with a total of up to 15 tables and/or figures, and should be structured as follows: Abstract (maximum 250 words; divided into Introduction and Objectives, Methods, Results and Conclusion(s)); 3-10 keywords; Introduction; Objectives; Methods; Results; Discussion; Conclusion(s); Acknowledgements, if any; References (up to 75); and figure legends, if any. Follow EQUATOR Reporting Guidelines.

Review Articles and Systematic Reviews

Review Articles should have a maximum of 5000 words, with a total of up to 15 tables and/or figures, and should be structured as follows: Abstract (maximum 250 words; unstructured); 3-10 keywords; Introduction; thematic sections at the discretion of the authors; Conclusion(s); Acknowledgements, if any; References (up to 100); and figure legends, if any.

Systematic Reviews should be structured as Introduction, Methods, Results, Discussion and Conclusion(s). The subject should be clearly defined. The objective of a systematic review should be to produce an evidence-based conclusion. The Methods should give a clear indication of the literature search strategy, data extraction, grading of evidence and analysis.

Systematic Reviews should not normally exceed 4000 words, with a total of up to 6 tables and/or figures and up to 100 references.

Authors are strongly recommended to consult the PRISMA statement (http://www.prisma-statement.org/), which is intended to help improve the reporting of systematic reviews and meta-analyses. We encourage authors to develop a systematic review protocol (e.g. following PRISMA-P) and register with PROSPERO.

Guidelines

It is recommended to consult the AGREE II instrument for which items should be reported that highlighted particular quality aspects of guideline development. In general, published statements intended to guide clinical care (e.g., guidelines, practice parameters, recommendations, consensus statements and position papers) should describe the clinical problem to be addressed, the mechanism by which the statement was generated, a review of the evidence for the statement (if available), and the statement on practice itself.

To minimize confusion and to enhance transparency, such statements should begin with the following questions, followed by brief comments addressing each question:

- What other guideline statements are available on this topic?
- Why was this guideline developed?
- How does this statement differ from existing guidelines?
- Why does this statement differ from existing guidelines?

The statement should have an unstructured abstract of up to 350 words, 3 to 10 keywords and can include up to 4000 words, a total of up to 6 tables and/or figures and up to 100 references.

Case Reports

Authors should use the CARE guidelines as a guiding framework. Case reports should not exceed 1500 words of body text, with up to 15 references and four tables or figures. They must include an abstract (unstructured, maximum 250 words) and bulleted statements (maximum 70 words) in answer to the following questions: What's already known about this topic? and What does this study add?
Please see the Ethics section of the Instructions regarding preservation of patients' privacy. Case Reports must have no more than 5 authors.

Images in Cardiology

Images in Cardiology should have a maximum of 250 words, without Abstract, keywords, tables, or division into sections and up to 5 references may be included.

Snapshots

This section is intended for the publication of rare or educational cases or novel techniques in cardiology. The text should not exceed 500 words and up to 3 figures with brief captions and up to 5 references may be included. Snapshots must have no more than 3 authors.

Current Perspective

This type of manuscript is submitted upon invitation by the Editorial Board. It may cover a broad diversity of themes focusing on cardiology and healthcare: current or emerging problems, management and health policies, history of medicine, society issues and epidemiology, among others. An author who wishes to propose a manuscript in this section is requested to send an abstract to the Editor-in-Chief including the title and Author list for evaluation. The text should not exceed 1200 words, and up to 10 references, two tables or two figures are allowed. An abstract is not required.

Editorial Comment

Editorials are submitted at the invitation of the Editor. They should not exceed 1500 words and can contain up to 20 references and 1 table and 1 figure. They do not have an Abstract or keywords.

Letters to the Editor

Letters to the Editor on articles previously published in the Journal will be considered up to 8 weeks after the publication of the article in question. They should not exceed 800 words and can contain up to 2 figures but without Abstract, keywords or tables. They should have no more than 3 authors.

Research Letter

Research Letters are concise, focused reports of original research. These should not exceed 600 words of text and 6 references and may include up to 2 tables or figures. Online supplementary material is not allowed. Research Letters may have no more than 7 authors.

Observation

Observations consisting of short reports of 1 or 2 complicated, unique cases should not exceed 600 words of text (not including acknowledgment, tables, figures, acknowledgments, and references) and 6 references and may include up to 2 tables or figures. Online supplementary material is not allowed. Observations may have no more than 7 authors.

If the patient(s) described in these manuscripts is identifiable, a Patient Permission form must be completed and signed by the patient(s) and submitted with the manuscript. Omitting data or making data less specific to deidentify patients is acceptable but changing any such data is not acceptable.

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Language

This journal is published in Portuguese and in English language.

The title (and abstract and key words if applicable) must be submitted in both English and Portuguese.
Articles submitted to the Journal should be clearly written in Portuguese (from Portugal) and/or English of a good standard. Text may be edited to maintain linguistic quality and to conform with standard American English.

ADVANCE NOTICE FOR AUTHORS
Please, take into account that as of January 2021, *Revista Portuguesa de Cardiologia* will require new article submissions to be written in English language.

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You can use this list to carry out a final check of your submission before you send it to the journal for review. Please check the relevant section in this Guide for Authors for more details.
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BEFORE YOU BEGIN

Ethics in publishing

Please see our information pages on Ethics in publishing and Ethical guidelines for journal publication.

Studies in humans and animals

If the work involves the use of human subjects, the author should ensure that the work described has been carried out in accordance with The Code of Ethics of the World Medical Association (Declaration of Helsinki) for experiments involving humans. The manuscript should be in line with the Recommendations for the Conduct, Reporting, Editing and Publication of Scholarly Work in Medical Journals and aim for the inclusion of representative human

populations (sex, age and ethnicity) as per those recommendations. The terms sex and gender should be used correctly.

The privacy rights of human subjects must always be observed. A statement must be included to the effect that the study was conducted in accordance with the amended Declaration of Helsinki, that the local institutional review board or independent ethics committee approved the protocol, and that written informed consent was obtained from all patients. The name of the committee, the name of the chairperson of the committee (or the person who approved the protocol), the date of approval and the approval number should follow this statement in the Methods section. For multicenter studies, a list of the relevant approvals may be provided in a separate document to be published as supplementary material.

All animal experiments should comply with the ARRIVE guidelines and should be carried out in accordance with the U.K. Animals (Scientific Procedures) Act, 1986 and associated guidelines, EU Directive 2010/63/EU for animal experiments, or the National Institutes of Health guide for the care and use of Laboratory animals (NIH Publications No. 8023, revised 1978) and the authors should clearly indicate in the manuscript that such guidelines have been followed. The sex of animals must be indicated, and where appropriate, the influence (or association) of sex on the results of the study.

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All authors must disclose any financial and personal relationships with other people or organizations that could inappropriately influence (bias) their work. Examples of potential competing interests include employment, consultancies, stock ownership, honoraria, paid expert testimony, patent applications/registrations, and grants or other funding. A conflict of interest may exist when an author (or the author's institution or employer) has financial or personal relationships or affiliations that could influence (or bias) the author's decisions, work, or manuscript. All authors are required to report potential conflicts of interest including specific financial interests relevant to the subject of their manuscript.

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Submission declaration and verification

Submission of an article implies that the work described has not been published previously (except in the form of an abstract or as part of a published lecture or academic thesis, see 'Multiple, redundant or concurrent publication' section of our ethics policy for more information), that it is not under consideration for publication elsewhere, that its publication is approved by all authors and tacitly or explicitly by the responsible authorities where the work was carried out, and that, if accepted, it will not be published elsewhere in the same form, in English or in any other language, including electronically without the written consent of the copyright-holder. To verify originality, your article may be checked by the originality detection service Crossref Similarity Check.

Authorship

Each author should have participated sufficiently in the work to take public responsibility for appropriate portions of the content. One or more authors should take responsibility for the integrity of the work as a whole, from inception to published article. According to the guidelines of the International Committee of Medical Journal Editors (ICMJE), authorship credit should be based on the following 4 criteria:

1. substantial contributions to conception or design of the work, or the acquisition, analysis, or interpretation of data for the work; and
2. drafting of the work or revising it critically for important intellectual content; and
3. final approval of the version to be published; and
4. agreement to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

Changes to authorship. Role of the corresponding author

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The ICMJE defines a clinical trial as any research project that prospectively assigns human participants to intervention or comparison groups to study the cause-and-effect relationship between an intervention and a health outcome. Interventions include but are not limited to drugs, surgical procedures, devices, behavioral treatments, educational programs, dietary interventions, quality improvement interventions, process-of-care changes, and the like.

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Omitting data or making data less specific to deidentify patients is acceptable, but changing any such data is not acceptable. Only those details essential for understanding and interpreting a specific case report or case series should be provided. Although the degree of specificity needed will depend on the context of what is being reported, specific ages, race/ethnicity, and other sociodemographic details should be presented only if clinically or scientifically relevant and important. Cropping of photographs to remove identifiable personal features that are not essential to the clinical message may be permitted as long as the photographs are not otherwise altered. Please do not submit masked photographs of patients. Patients' initials or

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PREPARATION

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It is important that the file be saved in the native format of the word processor used. The text should be in single-column format. Keep the layout of the text as simple as possible. Most formatting codes will be removed and replaced on processing the article. In particular, do not use the word processor's options to justify text or to hyphenate words. However, do use bold face, italics, subscripts, superscripts etc. When preparing tables, if you are using a table grid, use only one grid for each individual table and not a grid for each row. If no grid is used, use tabs, not spaces, to align columns. The electronic text should be prepared in a way very similar to that of conventional manuscripts (see also the Guide to Publishing with Elsevier). Note that source files of figures, tables and text graphics will be required whether or not you embed your

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Divide your article into clearly defined sections. Each subsection is given a brief heading. Each heading should appear on its own separate line. Subsections should be used as much as possible when cross-referencing text: refer to the subsection by heading as opposed to simply 'the text'. Use generic names of drugs (first letter: lowercase) whenever possible. Registered trade names (first letter: uppercase) should be marked with the superscript registration symbol ® or ™ when they are first mentioned.

The Journal recommends the guidelines for publication of the EQUATOR network (http://www.equator-network.org), including the CONSORT statement and its extensions for randomized trials (http://www.consort-statement.org/), STROBE for observational (cohort, case-control and cross-sectional) studies (http://www.strobe-statement.org/), STARD for diagnostic accuracy studies (http://www.stard-statement.org/), PRISMA for systematic reviews and meta-analyses (http://www.prisma-statement.org/), SQUIRE for quality improvement studies (http://www.squire-statement.org/) and CARE for case reports (http://www.care-statement.org/). Reporting of the statistical aspects of studies should be in accordance with the Statistical Analyses and Methods in the Published Literature (SAMPL) guidelines (http://www.equator-network.org/reporting-guidelines/sampl/).

Introduction

State the objectives of the work and provide an adequate background, avoiding a detailed literature survey or a summary of the results.

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Provide sufficient details to allow the work to be reproduced by an independent researcher. Methods that are already published should be summarized, and indicated by a reference. If quoting directly from a previously published method, use quotation marks and also cite the source. Any modifications to existing methods should also be described.

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Results should be clear and concise.

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This should explore the significance of the results of the work, not repeat them. A combined Results and Discussion section is often appropriate. Avoid extensive citations and discussion of published literature.

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The main conclusions of the study may be presented in a short Conclusions section, which may stand alone or form a subsection of a Discussion or Results and Discussion section.

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Submission of an article must include a cover letter with the following information:

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• ***Word count*** of the manuscript text.

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A structured abstract, by means of appropriate headings, should provide the context or background for the research and should state its purpose, basic procedures (selection of study subjects or laboratory animals, observational and analytical methods), main findings (giving specific effect sizes and their statistical significance, if possible), and principal conclusions. It should emphasize new and important aspects of the study or observations.

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The headings will consist of: Introduction and Objectives, Methods, Results and Conclusion(s))

Keywords

Immediately after the abstract, provide the keywords, using British spelling and avoiding general and plural terms and multiple concepts (avoid, for example, 'and', 'of'). Be sparing with abbreviations: only abbreviations firmly established in the field may be eligible. Keywords

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Acknowledgements

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Laboratory values are expressed using conventional units of measure, with relevant Système International (SI) conversion factors expressed secondarily (in parentheses) only at first mention. Articles that contain numerous conversion factors may list them together in a paragraph at the end of the Methods section. In tables and figures, a conversion factor to SI should be presented in the footnote or legend. The metric system is preferred for the expression of length, area, mass, and volume. For more details, see the Units of Measure conversion table on the website for the AMA Manual of Style.

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Tables and Figures. Image manipulation

Restrict tables and figures to those needed to explain and support the argument of the article

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• Size the illustrations close to the desired dimensions of the published version.
• Submit each illustration as a separate file.
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Number all figures (graphs, charts, photographs, and illustrations) in the order of their citation in the text. The number of figures should be limited. Avoid complex composite or multipart figures unless justified.
See Categories of Articles for limits on the number of figures and/or tables according to article type.

Ensure that each illustration has a caption. Supply captions separately, not attached to the figure. A caption should comprise a brief title (**not** on the figure itself) and a description of the illustration. Keep text in the illustrations themselves to a minimum but explain all symbols and abbreviations used written out in full and in alphabetical order. Different panels in a figure should be identified by capital letters (Figure 1A, Figure 2C, Figure 3A and B, etc. in the text and (A), (B), (C-E), etc. in the captions).

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Text graphics may be embedded in the text at the appropriate position. See further under Electronic artwork.

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All abbreviations used in the table must be written out in full, in alphabetical order, in the table legend immediately below the table. Footnotes may be used if necessary, indicated by superscript lower-case letters ([a], [b], [c] etc.) in the table and in the legend. Asterisks (*, **, *** etc.) may be used to indicate p values only. If a table contains a reference cited in the text, it should be cited with the name of the first author and "et al." followed by the reference number without space (e.g. Millard et al.[9]).

References

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Please ensure that every reference cited in the text is also present in the reference list (and vice versa). Any references cited in the abstract must be given in full. Unpublished results and personal communications are not recommended in the reference list, but may be mentioned in the text. If these references are included in the reference list they should follow the standard reference style of the journal and should include a substitution of the publication date with

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Reference links

Increased discoverability of research and high quality peer review are ensured by online links to the sources cited. In order to allow us to create links to abstracting and indexing services, such as Scopus, CrossRef and PubMed, please ensure that data provided in the references are correct. Please note that incorrect surnames, journal/book titles, publication year and pagination may prevent link creation. When copying references, please be careful as they may already contain errors. Use of the DOI is highly encouraged.

A DOI is guaranteed never to change, so you can use it as a permanent link to any electronic article. An example of a citation using DOI for an article not yet in an issue is: Ribeiro J. Left ventricular noncompaction and Fabry disease: An unlikely association. Rev Port Cardiol. 2019. https://doi.org/10.1016/j.repc.2019.12.001. Please note the format of such citations should be in the same style as all other references in the paper.

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As a minimum, the full URL should be given and the date when the reference was last accessed. Any further information, if known (DOI, author names, dates, reference to a source publication, etc.), should also be given. Web references can be listed separately (e.g., after the reference list) under a different heading if desired, or can be included in the reference list.

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This journal encourages you to cite underlying or relevant datasets in your manuscript by citing them in your text and including a data reference in your Reference List. Data references should include the following elements: author name(s), dataset title, data repository, version (where available), year, and global persistent identifier. Add [dataset] immediately before the reference so we can properly identify it as a data reference. This identifier will not appear in your published article.

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Reference style

Text: Indicate references by superscript numbers in the text. The actual authors can be referred to, but the reference number(s) must always be given.
List: Number the references in the list in the order in which they appear in the text.
Examples:
Reference to a journal publication:
17. Reis L, Paiva L, Costa M, Silva J, Teixeira R, Botelho A, et al. Registry of left atrial appendage closure and initial experience with intracardiac echocardiography. Rev Port Cardiol. 2018;**37**:763-72. https://doi.org/10.1016/j.repc.2018.03.009.

Reference to a journal publication with an article number:
2. Van der Geer J, Hanraads JAJ, Lupton RA. The art of writing a scientific article. *Heliyon*. 2018;**19**:e00205. https://doi.org/10.1016/j.heliyon.2018.e00205.

Reference to a book:
30. Cohn PF. Silent myocardial ischemia and infarction. 3rd ed. New York: Mansel Dekker; 1993.

Reference to a chapter in an edited book:
23. Nabel EG, Nabel GJ. Gene therapy for cardiovascular disease. In: Haber E, editor. Molecular cardiovascular medicine. New York: Scientific American;1995.p.79-96.
Reference to a website:
12. Portuguese Registry on Acute Coronary Syndromes (ProACS). Available at: http://www.clinicaltrials.gov/identifier NCT01642329 [accessed 26 October 2013].
Reference to a dataset:
[dataset] 5. Oguro M, Imahiro S, Saito S, Nakashizuka T. Mortality data for Japanese oak wilt disease and surrounding forest compositions, Mendeley Data, v1; 2015. https://doi.org/10.17632/xwj98nb39r.1.

Note shortened form for last page number. e.g., 51–9, and that for more than 3 authors the first 6 should be listed followed by 'et al.' For further details you are referred to 'Uniform Requirements for Manuscripts submitted to Biomedical Journals' (J Am Med Assoc 1997;**277**:927–34)(see also Samples of Formatted References).

Journal abbreviations source

Journal names should be abbreviated according to the PubMed list.

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ANEXO IV – Parecer da Comissão de Ética do Centro Hospitalar Universitário de São João

Parecer da Comissão de Ética do

Centro Hospitalar Universitário de São João / Faculdade de Medicina da Universidade do Porto

Título do Projeto: Transposição das grandes artérias: revisão de casos de um centro de referência

Nome da Investigadora Principal: Mariana Amorim Ribeiro

Onde decorre o Estudo: No Serviço de Cardiologia Pediátrica do CHUSJ. Apresentou declaração do Dr. Jorge Moreira.

Objetivos do Estudo:

Com este estudo de investigação pretende-se caraterizar os doentes com transposição das grandes artérias admitidos e intervencionados no Centro Hospitalar Universitário de São João nos últimos 10 anos, bem como os seus resultados clínicos a curto e médio prazo.

Pretende-se investigar possíveis fatores de risco e fatores preditores de piores resultados pós-operatórios, bem como comparar este centro com outros centros de referência para patologias cardíacas congénitas.

Estudo realizado no âmbito do Mestrado Integrado em Medicina, sob orientação da Dra. Ana Luísa Correia Rodrigues Costa e do Dr. João Nuno Sarmento.

Conceção e Pertinência do estudo:

A transposição das grandes artérias é uma patologia cardíaca congénita muito comum. Segundo a literatura atual, é possível uma correção cirúrgica desta patologia com bons resultados a curto e longo prazo. No entanto, a associação entre certos fatores de risco (caraterísticas dos doentes e do período pré-operatório) e piores resultados pós-operatórios ainda não está bem estabelecida. Para além disso, existe crescente interesse em descrever preditores de maior incidência de eventos adversos no período pós-operatório.

Com este estudo pretende-se contribuir com novas informações que ajudem a clarificar estes tópicos. Por outro lado, pretende-se comparar o CHUSJ com outros centros de referência para patologias cardíacas congénitas, de modo a melhorar a abordagem a doentes com transposição das grandes artérias.

Estudo retrospetivo dos últimos 10 anos. Estão definidos os critérios de inclusão, bem como as variáveis a recolher nos processos clínicos. *Nestas variáveis, inclui-se a data e local de nascimento, bem como a raça do participante. Deverá ser justificada a recolha da data e local de nascimento, uma vez que estes dados fragilizam a protecção de dados (bastaria a idade do participante e, eventualmente, o distrito de nascimento? e porquê o dado raça?)*

Benefício/risco: Não aplicável

Confidencialidade dos dados:
Não serão registados dados que permitam a identificação dos doentes.
Apresentou um pedido de reutilização de registos clínicos para Investigação e Desenvolvimento ao RAI.

Respeito pela liberdade e autonomia do sujeito de ensaio: Não aplicável

***Curriculum* da investigadora**: Adequado à investigação.

Data previsível da conclusão do estudo: março de 2021

Conclusão: Proponho um parecer favorável à realização deste projeto de investigação, desde que clarificada a questão expendida em itálico neste parecer.

Porto, 18 de dezembro de 2020

O Relator da CE, Doutor Pedro Brito

Pedro Brito

Parecer aprovado por votação electrónica dos membros da CE
2020-12-18

Todas as questões foram satisfatoriamente respondidas e ajustadas ao formulário, pelo que o parecer favorável se torna definitivo.
2020.12.31

Unidade de Investigação

Tomei conhecimento. Nada a opor. À DC.

11 de Janeiro de 2021

A Coordenadora da Unidade de Investigação

(Prof.ª Doutora Ana Azevedo)

SÃO JOÃO

n.º 478 / 2020

DIRECÇÃO CLÍNICA

2021 / 1 / 12

PEDIDO DE AUTORIZAÇÃO

Realização de Investigação

Exmo. Senhor Presidente do Conselho de Administração do Centro Hospitalar de São João

CONSELHO DE ADMINISTRAÇÃO - REUNIÃO DE 21 / 01 / 14

Presidente do Conselho de Administração

(Prof. Doutor Fernando Araújo)

Diretora Clínica (Prof.ª Doutora Maria João Baptista) | Enfermeira Diretora (Enf.ª Filomena Cardoso) | Vogal Executivo (Dr. Luís Porto Gomes) | Vogal Executivo (Dr.ª Sofia Leal)

Nome do Investigador Principal:

Mariana Amorim Ribeiro

Título da Investigação:

Transposição das Grandes Artérias: revisão de casos de um centro de referência

Pretendendo realizar no(s) Serviço(s) de:

Cardiologia Pediátrica

a investigação em epígrafe, solicito a V. Exa., na qualidade de Investigador/Promotor, autorização para a sua efetivação.

Para o efeito, anexo toda a documentação referida no dossier da Comissão de Ética do Centro Hospitalar de São João/ Faculdade de Medicina da Universidade do Porto respeitante à investigação, à qual enderecei pedido de apreciação e parecer.

Com os melhores cumprimentos. *O Investigador/ Promotor*

Porto, 08 *de* dezembro *de* 2020 .

Mariana Ribeiro
assinatura

Centro Hospitalar São João
Centro de Epidemiologia Hospitalar
8 / 1 / 2021

CES-IM005-0

SÃO JOÃO

U.PORTO FMUP FACULDADE DE MEDICINA UNIVERSIDADE DO PORTO

Questionário para submissão de Investigação

Exmo. Sr. Presidente da Comissão de Ética do Centro Hospitalar de São João/ Faculdade de Medicina da Universidade do Porto,

Pretendendo realizar a investigação infracitada, solicito a V. Exa., na qualidade de Investigador, a sua apreciação e a elaboração do respetivo parecer. Para o efeito, anexo toda a documentação requerida.

IDENTIFICAÇÃO DO ESTUDO

Título da investigação: Transposição das Grandes Artérias: revisão de casos de um centro de referência

Nome do investigador: Mariana Amorim Ribeiro

Endereço eletrónico: mariana.amorim.ribeiro@gmail.com **Contacto telefónico:** 961012076

Caracterização da investigação:

☒ Estudo retrospetivo ☐ Estudo observacional ☐ Estudo prospetivo

☐ Inquérito ☐ Outro. Qual? ____

Tipo de investigação:

☐ Com intervenção ☒ Sem intervenção

Formação do investigador em boas práticas clínicas *(GCP)*: ☐ Sim ☒ Não

Promotor *(se aplicável)*: ____

Nome do orientador de dissertação/tese *(se aplicável)*: Ana Luísa Correia Rodrigues Costa

Endereço eletrónico: analuisacrcosta@gmail.com

Local/locais onde se realiza a investigação: Serviço de Cardiologia Pediátrica - Centro Hospitalar Universitário São João

Data prevista para início: 01 / 01 / 2021 Data prevista para o término: 28 / 03 / 2021

PROTOCOLO DO ESTUDO

Síntese dos objetivos:

Com este estudo de investigação pretendemos caraterizar os doentes com transposição das grandes artérias admitidos e intervencionados no Centro Hospitalar Universitário de São João nos últimos 10 anos, bem como os seus resultados clínicos a curto e médio prazo.
Pretende-se investigar possíveis fatores de risco e fatores preditores de piores resultados pós-operatórios, bem como comparar o nosso centro com outros centros de referência para patologias cardíacas congénitas.

Fundamentação ética (ganhos em conhecimento/inovação; ponderação benefícios/riscos):

A transposição das grandes artérias é uma patologia cardíaca congénita muito comum. Segundo a literatura atual, é possível uma correção cirúrgica desta patologia com bons resultados a curto e longo prazo. No entanto, a associação entre certos fatores de risco (caraterísticas dos doentes e do período pré-operatório) e piores resultados pós-operatórios ainda não está bem estabelecida. Para além disso, existe crescente interesse em descrever preditores de maior incidência de eventos adversos no período pós-operatório.
Com este estudo pretendemos contribuir com novas informações que ajudem a clarificar estes tópicos.
Por outro lado, pretendemos comparar o Centro Hospitalar Universitário de São João com outros centros de referência para patologias cardíacas congénitas, de modo a melhorar a nossa abordagem a doentes com transposição das grandes artérias.

LISTA DE DOCUMENTOS ANEXOS

- [x] Pedido de autorização ao Presidente do Conselho de Administração do Centro Hospitalar de São João *(se aplicável)*
- [ ] Pedido de autorização à Diretora da Faculdade de Medicina da Universidade do Porto *(se aplicável)*
- [x] Protocolo do estudo
- [x] Declaração do Diretor de Serviço onde decorre o estudo
  (sendo um estudo na área de enfermagem deve anexar também a concordância da chefia de enfermagem)
- [ ] Profissional de ligação
- [x] Informação dos orientadores
- [ ] Informação ao participante
- [ ] Modelo de consentimento
- [ ] Instrumentos a utilizar *(inquéritos, questionários,escalas, p.ex.)*: _____
- [x] Curriculum Vitae abreviado *(máx. 3 páginas)*
- [ ] Protocolo financeiro
- [ ] Outros:

COMPROMISSO DE HONRA E DECLARAÇÃO DE INTERESSES

Declaro por minha honra que as informações prestadas neste questionário são verdadeiras. Mais declaro que, durante o estudo, serão respeitadas as recomendações constantes da Declaração de Helsínquia (1960 e respetivas emendas), e da Organização Mundial da Saúde, Convenção de Oviedo e das "Boas Práticas Clínicas" (GCP/ICH) no que se refere à experimentação que envolve seres humanos. Aceito, também, a recomendação da CES de que o recrutamento para este estudo se fará junto de doentes que não tenham participado em outro estudo, nos últimos três meses. Comprometo-me a entregar à CES o relatório final da investigação, assim que concluído.

Porto, 08 *de* dezembro *de* 2020

Nome legível: Mariana Amorim Ribeiro

Mariana Amorim Ribeiro
assinatura

Parecer da Comissão de Ética do Centro Hospitalar de São João/ FMUP Emitido na reunião plenária da CE de 18 / 12 / 2020

Agradecimentos

.Centro Hospitalar **São João**.

CONSIDERADOS QUE FORAM COMO SATISFATÓRIOS OS ESCLARECIMENTOS PRESTADOS PELO(A) INVESTIGADOR(A). A CES APROVA POR UNANIMIDADE O PARECER DO RELATOR, PELO QUE NADA TEM A OPOR À REALIZAÇÃO DESTE PROJETO DE INVESTIGAÇÃO.

31/12/2020

Prof. Doutor Filipe Alves
Presidente da Comissão de Ética

Prof. Doutor [illegible]
Presidente da [illegible]

478. 2

RESPONSÁVEL PELO ACESSO À INFORMAÇÃO

SÃO JOÃO

Pedido de Reutilização de Registos Clínicos para Investigação e Desenvolvimento (I&D)

Número do Pedido
21006077
(A preencher pelo Gabinete de Apoio ao RAI)

Exmo. Senhor
Responsável pelo Acesso à Informação
(Artigo 9.º da Lei n.º 26/2016, de 22 de agosto)
Dr. Rui de Vasconcellos Guimarães

SÃO JOÃO

AUTORIZADO
RAI - Responsável pelo Acesso à Informação do Centro Hospitalar de São João
(Art. 9º, Lei 26/2016, de 22/8)
07/01/2021

1. Identificação do(s) Investigador(es) *Preenchimento Obrigatório*

1.1. Investigador Principal *No caso de haver mais do que um investigador mencionar nas observações*

Nome Mariana Amorim Ribeiro
Contacto telefónico 961012076
Endereço eletrónico mariana.amorim.ribeiro @ gmail.com

1.2. Investigador(es) Associado(s)

Número Total: 2

Nome Ana Luísa Correia Rodrigues Costa
Contacto telefónico 918752553
Endereço eletrónico analuisacrcosta @ gmail.com

Nome João Nuno Meneses Antunes Barreto Sarmento
Contacto telefónico 918375572
Endereço eletrónico joaoantunessarmento @ gmail.com

Nome
Contacto telefónico
Endereço eletrónico @

1.3. Afiliação Institucional do Investigador Principal

1.3.1. Grupo Profissional

☐ Médico(a) ☐ Enfermeiro(a) ☐ Docente ☒ Estudante
☐ Outro. Qual?

1.3.2. Documento de identificação pessoal ou profissional

☒ Cartão de Cidadão ☐ Bilhete de Identidade ☐ Cédula Profissional
☐ Cartão de Docente ☐ Cartão de Estudante ☐ Outro. Qual?

Número de Documento 150743411

2. Enquadramento e Identificação do Trabalho de Investigação e Desenvolvimento *Preenchimento Obrigatório*

2.1. Enquadramento da investigação

☒ Projeto ou trabalho académico de investigação e desenvolvimento:
☐ Não conferidor de grau
☒ Conferidor de grau: ☐ Licenciatura ☒ Mestrado ☐ Doutoramento

04 01 2021

RAI-IM002-0

3. Observações *Preenchimento Facultativo*

4. Aceitação dos Termos e Condições da Reutilização

Cumulativamente com as obrigações decorrentes da lei já citada *(n.º 2 e 3 do art.º 21 e o n.º 1 e 2 do art.º 12, ambos da Lei n.º 26/2016, de 22 de Agosto)* ao submeter o presente pedido concordo e fico ainda vinculado, juridicamente, aos seguintes termos e condições:

- Comprometo-me a manter confidencial toda a informação à qual vou ter acesso;
- Após explicação do RAI do CHUSJ, embora a Lei 26/2016, de 22 de agosto, imponha como requisito a anonimização sem possibilidades de reversão, tal desiderato, é não só uma impossibilidade matemática já comprovada, como ainda resulta num prejuízo para a investigação, face à quantidade e qualidade da informação a retirar à fonte, razão pela qual, concordando com o RAI, assumimos como compromisso a pseudo anonimização, o que impõe uma avaliação e gestão do risco, num quadro ético-jurídico que aceitamos e nos comprometemos a colaborar;
- Não vou elaborar registos, suscetíveis de identificar ou tornar identificável a identidade das pessoas a quem os mesmos dizem respeito;
- Comprometo-me a consultar os processos clínicos nos termos e locais que me forem indicados para o efeito;
- Além do presente pedido para reutilizar registos clínicos, dirigido ao RAI, comprometo-me a obter os necessários pareceres quer do Encarregado da Proteção de Dados, quer da Comissão de Ética do Hospital, quer ainda do Centro de Epidemiologia Hospitalar;
- Comprometo-me a citar as fontes, sempre que publicitar o trabalho de investigação, independentemente de requerer a Certidão de Reutilização (***DAtaREuseCertificate for Research*** – **DARE**).
- Tomei conhecimento, que a violação de qualquer dos compromissos aqui assumidos, resultará no apuramento de responsabilidades disciplinares, civis e penais e ainda, à impossibilidade futura de aceder a informação de saúde para fins de investigação.

5. Decisão do investigador sobre requerer a DAta REuse Certificate for Research – DARE *Preenchimento Obrigatório*

☒ **Pretendo** desde já requerer a Certidão de Reutilização **(DARE)** cujo sentido, valor e significado consultei em *http://portal-chsj.min-saude.pt/pages/710*.

☐ **Não pretendo** requerer a Certidão de Reutilização **(DARE)** cujo sentido, valor e significado consultei em *http://portal-chsj.min-saude.pt/pages/710*.

Na circunstância do requerente não indicar nenhuma opção, presumimos que pretende requerer o DARE.

6. Assinatura

Nota 1: Se o presente pedido for submetido eletronicamente ou faz assinatura digital qualificada; ou posteriormente vem ao Centro Hospitalar de São João exibir o seu documento de identificação pessoal; ou no âmbito do seu espaço de liberdade e como manifestação expressa do seu consentimento envia cópia do referido documento, neste caso, concluído o processo ser-lhe-á devolvida ou eliminada a cópia do documento de identificação pessoal, conforme as indicações que dê.
Nota 2: Se o presente pedido for entregue presencialmente, assina e exibe o documento de identificação a quem recebe o pedido.

Data 2020 - 12 - 08

Mariana Amorim Ribeiro
Investigador Principal

Em caso de dúvida no preenchimento contacte através dos endereços eletrónicos
rai.reutilizacao.id@chsj.min-saude.pt **ou** ruiguimaraes@chsj.min-saude.pt
ou pelos números de telemóvel 962 204 194 **ou** 918 880 299

SUBMETER

APÊNDICE

Protocolo do Projeto de Investigação

Research Project Protocol

Transposition of the Great Arteries: Review of Cases from a Reference Center

Centro Hospitalar Universitário de São João - Serviço de Cardiologia Pediátrica

Primary Investigator:

Mariana Amorim Ribeiro (mariana.amorim.ribeiro@gmail.com)

Advisors:

Ana Luísa Correia Rodrigues Costa (analuisacrcosta@gmail.com)

João Nuno Meneses Antunes Barreto Sarmento (joaoantunessarmento@gmail.com)

1. Project Title

Transposition of the Great Arteries: Review of Cases from a Reference Center

2. Introduction

Transposition of the Great Arteries (TGA) is a congenital heart defect characterized by atrioventricular concordance and ventriculoarterial discordance. In patients affected by this condition, the aorta arises from the morphological right ventricle and the pulmonary artery arises from the morphological left ventricle. In other words, patients have a parallel circulation in which oxygenated blood runs through a circuit involving the left heart chambers and the pulmonary vessels, while the right heart chambers and the systemic vessels form another circuit that carries deoxygenated blood. As such, patient survival depends on adequate mixing of blood from both circuits, which normally occurs through the atrial or ventricular septums and through the ductus arteriosus [1, 2].

TGA is the second most common cyanotic congenital heart disease, accounting for 20% of all cases [3, 4]. Furthermore, it represents 5 to 7% of all congenital heart defects [1, 5-7], with an estimated incidence of 1 per 3200 live births [2]. In half of TGA cases there are no other cardiac abnormalities (simple or isolated TGA), but in remaining, TGA is accompanied by other cardiac malformations (complex TGA), the most common being ventricular septal defect (VSD), left ventricle outflow tract obstruction (LVOTO), double outlet right ventricle (DORV), aortic arch abnormalities and abnormal coronary artery patterns [1, 5].

Patients affected by TGA will have some degree of hypoxemia, potentially leading to shock, end-organ-dysfunction, and death. Adjuvant therapies, such as intravenous prostaglandin E1 [1, 3], Rashkind balloon atrial septostomy, mechanical ventilation, inotropes, and others, can be used to temporarily improve systemic blood oxygenation [1, 3, 7]. Nevertheless, definitive treatment can only be achieved by surgical correction of the heart defect [1, 3] .

The gold-standard for surgical correction of TGA is the arterial switch operation (ASO), performed successfully for the first time by Jatene in 1975 [1, 3, 7]. In this procedure, the surgeon anatomically and physiologically corrects the malformation, by sectioning the aorta and pulmonary trunks and transposing them to the morphological left and right ventricles, respectively [1, 2].

Nowadays, ASO can be performed with good short- and long-term results. Early mortality is estimated to be 2.8% and late mortality 0.9% [2, 8-10], with an overall survival rate at 20 years of nearly 90% [7] and freedom from reintervention at 10 years varying from

80% to 90% [10]. The most frequent late complications associated with ASO are supravalvular pulmonary stenosis, neo-aortic root dilation, aortic regurgitation, and coronary stenosis [1, 5-7, 11].

In recent years, some risk factors for a complicated perioperative period and late complications have been described. Some examples are patient characteristics, such as prematurity, low weight at time of surgery, complex cardiac anatomy and coronary artery abnormalities and variations in preoperative care such as timing of ASO and need of adjuvant therapies [3-5, 8, 9, 12].

However, uncertainty about the accuracy of these risk factors remains, and the association between perioperative characteristics and postoperative outcomes is still under investigation. There is also an interest in finding factors that can predict a worse postoperative outcome.

3. Aim

The purpose of this this study is to characterize patients treated in our institution and their short- and mid-term outcomes. We intend to investigate possible risk factors associated with worse perioperative outcomes, with special emphasis on cardiac and coronary anatomy, pre-operative and intra-operative care and their influence in morbidity, mortality and need for reintervention. We also intend to find possible predictors of postoperative prognosis in patients undergoing anatomical correction of TGA.

Furthermore, this study might help understand how our center compares to other reference centers for congenital heart diseases and to improve the management and care of TGA patients our institution.

4. Methods

4.1. Participants

We intend to perform a single-center retrospective cohort study, including all the patients diagnosed with transposition of the great arteries that were admitted and underwent surgical correction in our center in the past 10 years.

4.2. Study Design

To conduct this study, we intend to collect the following data:

- Patient demographics: (date and place of birth, sex, race/ethnic group, APGAR score, and weight at birth)

- Congenital defects (cardiac and non-cardiac malformations) and Coronary Anatomy
- Preoperatory period (hemodynamic status, adjuvant therapies and adverse outcomes)
- Surgical intervention (type of surgery and surgical technic)
- Early postoperative period (hemodynamic status, need for organic support and adverse outcomes)
- Post-discharge follow-up (morbidity, mortality and re-interventions).

The data will be collected from Electronical Medical Records of Centro Hospitalar Universitário de São João, after we obtain approval from the Ethics Committee.

All the information collected will be anonymized and safely stored, in order to guarantee their confidentiality.

4.3. Statistical Analysis

We intend to analyze the collected data with a statistical software, such as SPSS. First, we will perform a descriptive analysis of our data. In addition, we will use statistical hypothesis tests to compare between groups. We defined a significance value of 0.05, under which the differences between groups will be considered statistically significant.

5. References

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