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## Impact of pulmonary artery reduction during arterial switch operation: 14 years follow-up

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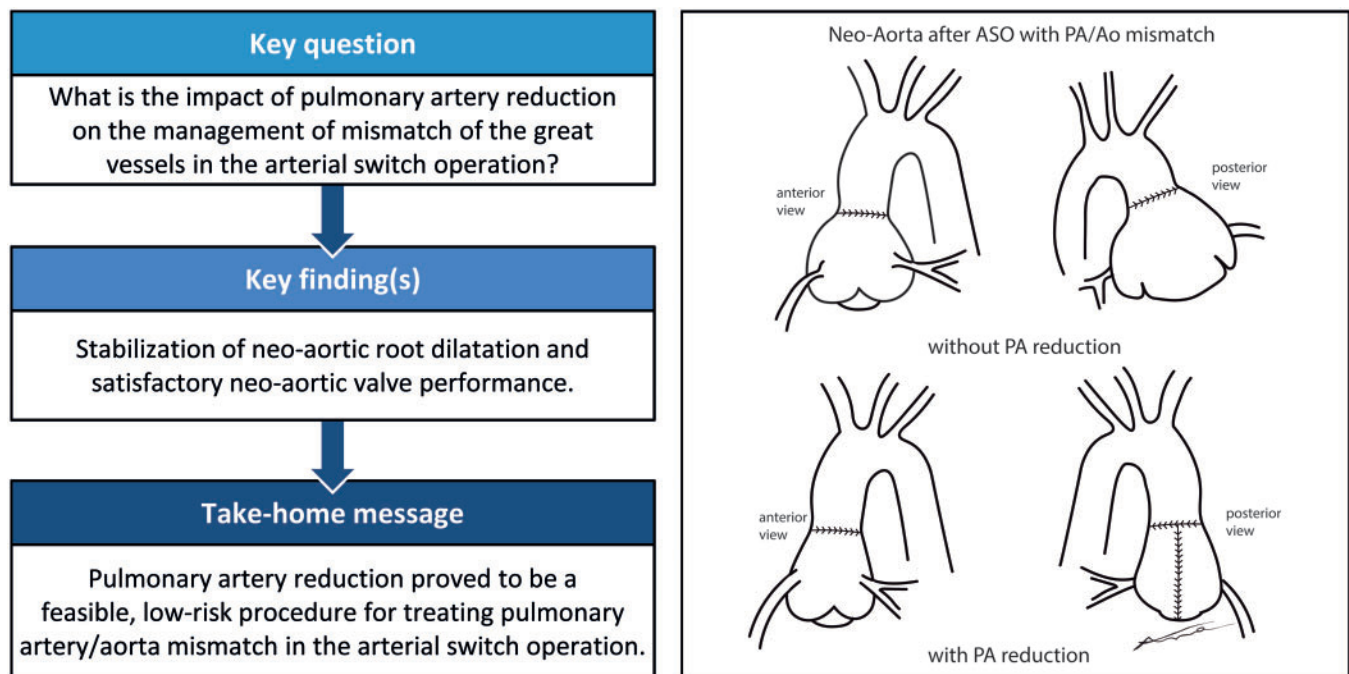
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### Abstract

**OBJECTIVES:** Pulmonary artery/aorta (PA/Ao) size discrepancy plays an important role in the development of neo-aortic root growth and valve regurgitation. Since 2004, we started using PA reduction to manage severe great vessels root mismatch at the time of arterial switch operation. The purpose of this study is to evaluate the impact of this technique in the mid- and long-term follow-up.

**METHODS:** Patients considered to have severe PA/Ao mismatch (>2:1 ratio) underwent resection of a 3- to 4-mm flap of the posterior PA wall. Patients submitted to this technique were followed up with clinical and image examinations. Echocardiographic findings were reviewed, and Z-scores were recorded to evaluate the incidence and progression of neo-aortic root dilatation and valve regurgitation.

Presented at the 33rd Annual Meeting of the European Association for Cardio-Thoracic Surgery, Lisbon, Portugal, 3–5 October 2019.

**RESULTS:** The median (Q1–Q3) follow-up time was 8 years (3–11). Before arterial switch operation, the median (Q1–Q3) Z-score of the PA annulus was 2.90 (2.75–3.75). At the latest follow-up, the median Z-score of the neo-aortic annulus was 1.34 (0.95–1.66). The mean difference between the Z-scores of PA annulus and neo-aortic annulus was 1.56 ( $P < 0.0001$ ). The mean value of the sinus of Valsalva was  $+0.29 \pm 1$ , that of sinotubular junction was  $+0.71 \pm 0.6$  and that of ascending Ao was  $+1.09 \pm 0.7$ . There was no severe dilatation of the neo-aortic annulus, neo-aortic root or ascending Ao during follow-up. Neo-aortic valve regurgitation was none or mild in 93% of patients.

**CONCLUSIONS:** PA reduction proved to be a feasible and low-risk procedure to approach PA/Ao mismatch in arterial switch operation. Mid- and long-term follow-up showed a tendency towards stabilization of the neo-aortic root dilatation and satisfactory valve performance after the procedure. Further investigation is required with a larger population and longer-term follow-up.

**Keywords:** Transposition of the great arteries • Arterial switch operation • Pulmonary artery/aorta mismatch • Pulmonary artery reduction • Neo-aortic dilatation • Neo-aortic regurgitation

## ABBREVIATIONS

Ao	Aorta
ASO	Arterial switch operation
BSA	Body surface area
NYHA	New York Heart Association
PA	Pulmonary artery
SD	Standard deviation
TGA	Transposition of the great arteries
VSD	Ventricular septal defect

## INTRODUCTION

The arterial switch operation (ASO) has become the surgical procedure of choice to repair transposition of the great arteries (TGA) in neonates and infants, with excellent early and mid-term results and satisfactory overall survival and functional status [1].

Complications related to the coronary arteries and right ventricular outflow tract are well known, and due to progressive technical refinement and increased surgical experience, its incidence has decreased significantly [2]. On the other hand, reports about progressive neo-aortic root dilatation and neo-aortic valve regurgitation in the long-term follow-up are raising concern for late reintervention in the patients submitted to ASO [3].

In our experience, and in accordance to other studies, we found that significant pulmonary artery/aorta (PA/Ao) size discrepancy plays an important role in the development of disproportionate neo-aortic root growth and neo-aortic valve regurgitation after ASO, especially in patients with complex variants of TGA and aortic arch anomalies association [4, 5]. Since 2004, we started using PA reduction to manage severe PA/Ao mismatch at the time of ASO. The purpose of this study is to evaluate the impact of this technique in the mid- and long-term follow-up of these patients.

## MATERIALS AND METHODS

### Patients

From January 1998 until December 2018, 425 patients underwent ASO in our institute. Since February 2004, 34 patients were submitted to PA reduction during ASO, with 32 hospital survivors. A total of 31 patients were followed up postoperatively with clinical examination and echocardiographic studies until December 2018. One patient, who resided outside of the state,

**Table 1:** Patient characteristics

Variables	n = 31
Gender, n (%)	
Male	16 (51.6)
Female	15 (48.4)
Type of TGA, n (%)	
Taussig–Bing	6 (19.4)
TGA + VSD	20 (64.5)
Simple TGA	5 (16.1)
Age at ASO (days), median (Q1–Q3)	26.0 (13.0–73.0)
Associated anomaly, n (%)	
None	14 (34.1)
Aortic arch hypoplasia	3 (7.3)
Aortic coarctation	9 (21.9)
Aortic arch interruption	2 (4.9)
Bicuspid pulmonary valve	3 (7.3)
Dextrocardia	2 (4.9)
Juxtaposed atrial appendages	2 (4.9)
Persistent fifth aortic arch	1 (2.4)
Persistent left superior vena cava	1 (2.4)
Ostium secundum atrial septum defect	1 (2.4)
Situs inversus	2 (4.9)
Straddling tricuspid valve	1 (2.4)

ASO: arterial switch operation; TGA: transposition of the great arteries; VSD: ventricular septal defect.

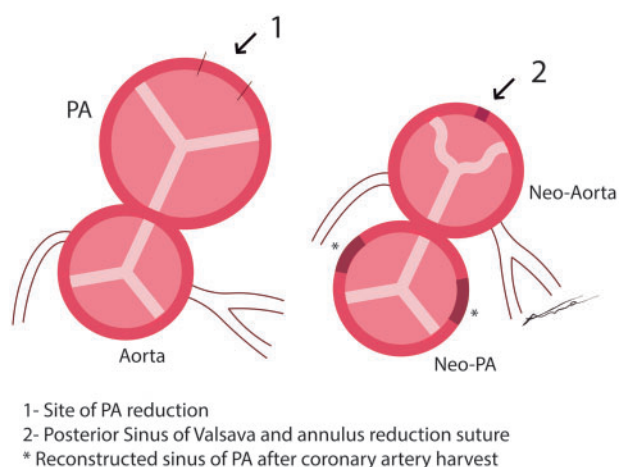
was lost for follow-up examinations and excluded from our study.

The median (Q1–Q3) age at the time of ASO was 26 (13–73) days. The median (Q1–Q3) age at the last follow-up was 8 years (3–11). Sixteen (51.6%) patients were male, and 15 (48.4%) patients were female. Twenty-six (76.47%) patients had complex TGA [TGA + ventricular septal defect (VSD) or Taussig–Bing anomaly], and 12 (35.29%) patients had associated cardiac anomalies related to the Ao (interrupted aortic arch, coarctation of the Ao or hypoplastic aortic arch) (Table 1). Detailed patients characteristics are available in the Supplementary Material (Table S1).

### Surgical technique

The ASO was performed by a single cardiac surgeon, using the usual technique adopted in our institution and previously described [6].

Surgery was performed under standard moderate hypothermic cardiopulmonary bypass, except in cases with aortic arch interruption, where a brief period of total circulatory arrest was necessary for aortic arch reconstruction. Single anterograde infusion of crystalloid cardioplegia was used. Coronary reimplantation



**Figure 1:** Schematic illustration of great vessels before and after PA reduction during arterial switch operation (ASO). The image on the left shows the position of the great vessels during ASO, PA/aorta mismatch and an indication of pulmonary reduction site. The image on the right shows the aspect of great vessels during ASO, after pulmonary reduction, with posterior sinus of Valsalva reduction suture and leaflets redundancy in the neo-aorta as well as reconstruction of sinus of Valsalva in the neopulmonary artery. PA: pulmonary artery.

was performed in the corresponding pulmonary sinus of Valsalva, after marking the anastomosis site with the distended Ao and using a button technique in all patients. The approach for VSD closure (right atrium, PA or Ao) was chosen after transection of the great vessels and coronary mobilization, depending on best site for surgical exposure; LeCompte manoeuvre was used in the great majority of patients (except in patients with side-by-side great vessels relationship); mean  $\pm$  standard deviation (SD) duration of extracorporeal circulation was  $108 \pm 11$  min, and that of cross-clamping time  $75 \pm 10$  min.

PA reduction was indicated when PA/Ao ratio was  $>2:1$  and was achieved by the resection of a 3- to 4-mm rectangular fragment from the edge of the posterior wall to within the annulus of the pulmonary valve (Fig. 1), after extensive mobilization of PA and coronary arteries and complete transection of the great vessels. Resection was performed at the posterior sinus of Valsalva (non-coronary sinus) in all but 3 patients with bicuspid pulmonary valve (in these patients, resection was executed in the larger sinus, away from the site of coronary reimplantation). Stay sutures were placed at the edges of the PA walls to allow the perfect alignment of the suture, which was carried out from the annulus to the transected margin of the vessel. Once the flap resection extended down to the valve annulus, meticulous care was taken to avoid distortion of the valve leaflets, keeping the same height of commissures.

## Echocardiographic examination

All echocardiographic examinations were performed by the same examiner using Philips HD11 ultrasound system with size appropriated phased-array transducers following the guidelines of the American Society of Echocardiography [7].

Aortic dimensions were measured in triplicate and averaged in the following sites: (i) neo-aortic annulus, (ii) maximum diameter of the sinus of Valsalva, (iii) sinotubular junction (transition between sinus of Valsalva and tubular portion of ascending Ao) and (iv) maximum diameter of proximal ascending Ao, using the

methods for measurements of the aortic root used in our service and previously described [5].

## Data collection and definitions

Medical records were reviewed for echocardiographic preoperative data and Z-score for PA, postoperative evaluations including transthoracic echocardiography and current functional status according to the New York Heart Association (NYHA) functional classification.

From October 2018 until December 2018, patients who underwent PA reduction were invited for clinical examination and detailed echocardiography with focus on neo-aortic root and neo-aortic valve function. Three patients could not attend this last call evaluation, and data of their last routine echocardiography from the years 2013 and 2014 were considered as the latest follow-up.

Angiotomography or angiography was obtained in 26 patients that needed further evaluation of the neo-aorta or to study coronary circulation.

Body surface area (BSA) was calculated using the Haycock formula [8]. Aortic measurements were indexed to BSA to calculate Z-score using the equations obtained by Pettersen *et al.* [9].

Neo-aortic root dilatation was defined as severe (Z-score  $>5$ ), moderate (Z-score 3–4.9) and mild (Z-score 1–3) at any site of the aortic root [10]. Neo-aortic valve regurgitation was assessed using colour Doppler and graded using a jet width/left ventricle outflow tract ratio as mild ( $R: <0.25$ ), moderate ( $R: 0.25-0.5$ ) and severe ( $R: >0.5$ ). Pulsed Doppler evidence of holodiastolic flow reversal in the abdominal Ao and the degree of left ventricular dilatation were also used to estimate moderate to important regurgitation [11].

## Statistics

Quantitative variables were described as mean  $\pm$  SD when normally distributed and verified by the Shapiro-Wilk test and median (first quartile–third quartile) when non-normally distributed. Categorical variables were described by absolute frequencies and percentages. Wilcoxon test was used to compare continuous variables (Z-score of PA and neo-aortic annulus) because these variables were non-normally distributed when verified by Shapiro-Wilk's test. The significance level was 0.05. The statistical analysis was performed using statistical software SPSS version 20.0.

## Ethics considerations

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

## RESULTS

### Operative mortality

In-hospital deaths occurred in 2 (5.88%) patients in the postoperative period. One patient had active bleeding that required haemostasis revision, delayed sternal closure and presented low cardiac output syndrome. The other patient developed

**Table 2:** Reinterventions

Variables	n = 31
Time after ASO (years), median (Q1–Q3)	2.0 (1.0–7.0)
Reintervention procedure, n (%)	
Angioplasty of recoarctation of the aorta	1 (6.7)
Balloon pulmonary valvuloplasty	2 (13.3)
Bilateral pulmonary branch stenting	1 (6.7)
Epicardial pacemaker implantation	1 (6.7)
Left pulmonary branch stenting	1 (6.7)
Mechanical aortic valve replacement	1 (6.7)
Mechanical pulmonary valve replacement + RVOT augmentation	1 (6.7)
Subaortic stenosis resection + sinus of Valsalva reduction plasty	1 (6.7)
Surgical correction of coarctation of the aorta	4 (26.7)
Surgical correction of pulmonary valve stenosis	1 (6.7)
Surgical correction of pulmonary valve stenosis + RVOT augmentation	1 (6.7)

ASO: arterial switch operation; RVOT: right ventricular outflow tract.

ventilator-associated pneumonia and severe sepsis. No patients died after hospital discharge.

## Reinterventions

Of 31 patients, 11 (35.48%) patients required one or more reinterventions during the follow-up period; these included 10 surgical operations and 5 percutaneous procedures without mortality. Detailed information about reintervention are available in the Supplementary Material (Table S2).

Only 2 (6.45%) patients had reoperations related to left ventricular outflow tract. One patient had aortic mechanical valve replacement (without neo-aortic root replacement) and subsequent epicardial pacemaker implantation. The other patient had resection of subaortic stenosis and sinus of Valsalva reduction plasty. In the last case, dilatation occurred on both coronary sinus but was absent on the non-coronary sinus of Valsalva where pulmonary reduction technique was done at the time of ASO.

The remainder of reinterventions were related to right ventricular outflow tract or coarctation of the Ao. All interventions are summarized in Table 2.

## Outcomes

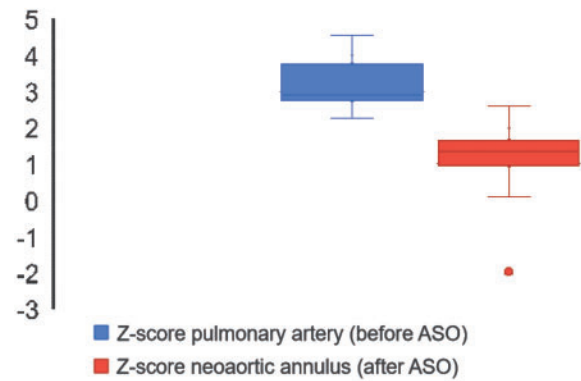
Follow-up time: the follow-up time was between 10 and 14 years in 11 patients (35.48%), 5 and 10 years in 9 patients (29.03%) and <5 years in 11 patients (35.48%). The median (Q1–Q3) follow-up time was 8 years (3–11).

Z-score comparison between PA and neo-aorta: before ASO, the median (Q1–Q3) Z-score of the PA annulus was 2.90 (2.75–3.75). At the latest follow-up, the median (Q1–Q3) Z-score of the neo-aortic annulus was 1.34 (0.95–1.66). The mean difference between the Z-scores of PA annulus and neo-aortic annulus was 1.56 ( $P < 0.0001$ ) (Fig. 2). Detailed information about Z-scores are available in the Supplementary Material (Table S3).

A total of 22 (71%) patients presented mild dilatation, and 1 patient showed a Z-score of -1.96 of the neo-aortic annulus.

Z-score for neo-aortic root: the mean  $\pm$  SD value Z-score of the sinus of Valsalva was  $+0.29 \pm 1$  and that of sinotubular junction

Z-score before and after ASO with PA reduction



**Figure 2:** Box-plot Z-scores of PA annulus and Z-scores of neo-aortic annulus. ASO: arterial switch operation; PA: pulmonary artery.

**Table 3:** Z-score values for PA and neo-aortic root and neo-aortic valve regurgitation

Variables	n = 31
PA Z-score, median (Q1–Q3)	2.9 (2.75–3.75)
Neo-aortic annulus Z-score, median (Q1–Q3)	1.34 (0.95–1.66)
Sinus of Valsalva Z-score, mean $\pm$ SD	$0.29 \pm 1.04$
Sinotubular junction Z-score, mean $\pm$ SD	$0.72 \pm 0.64$
Ascending aorta Z-score, mean $\pm$ SD	$1.10 \pm 0.74$
Neo-aortic valve regurgitation, n (%)	
None	14 (41.9)
Mild	16 (51.6)
Moderate	2 (6.5)

PA: pulmonary artery; SD: standard deviation.

was  $+0.71 \pm 0.6$ . A total of 16 (51%) patients presented mild dilatation of neo-aorta in at least one of these sites. One patient showed a Z-score of -2.19 of the sinus of Valsalva.

Z-score for ascending Ao: the mean  $\pm$  SD value was  $+1.09 \pm 0.7$ . A total of 17 (55%) patients presented mild dilatation and 1 patient presented a Z-score of -1.13 of the ascending Ao.

There was no severe dilatation of the neo-aortic root or ascending Ao during follow-up. One patient presented moderate dilatation of sinus of Valsalva during the follow-up period and was submitted to reduction plasty.

Neo-aortic valve regurgitation: regurgitation was none or mild in 29 (93%) patients. Two (6.45%) patients had moderate neo-aortic valve regurgitation. One patient was submitted to residual VSD correction and neo-aortic valve replacement during the follow-up period, and another one is on watchful observation. There was no severe neo-aortic valve regurgitation at the latest follow-up.

Functional status: all 31 patients were in functional class I or II of NYHA at the latest follow-up.

Data are summarized in Table 3.

## DISCUSSION

Progressive neo-aortic root dilatation and neo-aortic valve regurgitation is a recognized time-dependent phenomenon and a long-term complication of ASO [12–14]. It has become the major



cause of concern for late reoperations in these patients [15]. Several risk factors for dilatation and regurgitation have been reported, such as presence of VSD, coarctation of the Ao, aortic arch anomalies, prior PA banding, method for the reimplantation of coronary arteries and size discrepancy of the great arteries [10, 12, 16, 17]. The pathophysiological mechanisms for the neo-aortic root dilatation and development of moderate-to-severe neo-aortic regurgitation are poorly understood and probably multifactorial. Hypotheses have been made about histomorphological differences between the great vessels in TGA, position of the pulmonary valve in systemic circulation, surgical injury to the vasa-vasorum and ischaemic lesions to the arterial wall and geometrical factors of arterial root anastomosis and leaflet coaptation, as well as primary root dilatation followed by somatic growth [18–23].

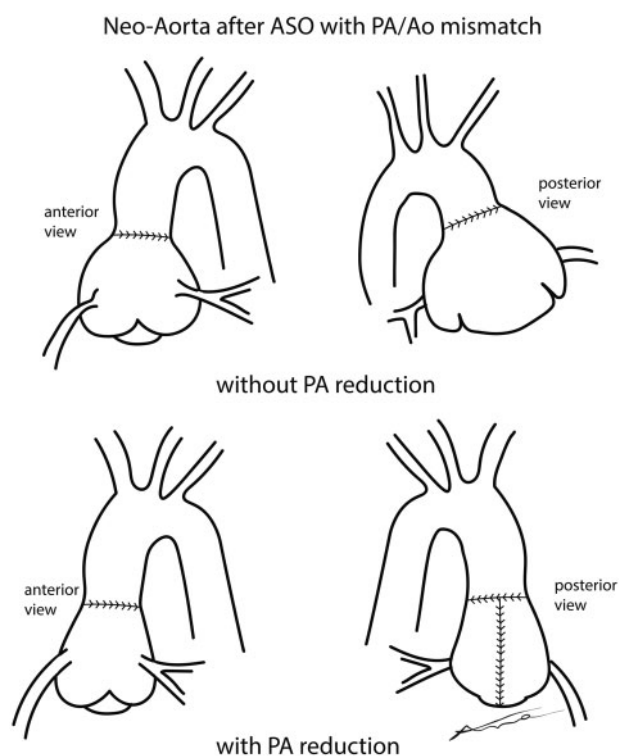
In our experience in the mid- and long-term follow-up, a common finding in patients who developed moderate to important neo-aortic root dilatation and neo-aortic valve regurgitation was the presence of size discrepancy between the great vessels observed before ASO, especially in patients with complex variants of TGA [5]. Our first series of ASO started in January 1998; since then, 425 patients were operated until December 2018. Initially, anastomosis of the great vessels was accomplished by adjusting the larger diameter of the PA to a much smaller ascending Ao, often requiring trimming of the suture or augmentation of the ascending Ao. This commonly resulted in an initially dilated neo-aortic root after ASO.

Pulmonary plasty techniques have been described for the purpose of achieving a better arterial root anastomosis, with good initial results, but lack of long-term period of observation [24–26]. In 2004, we started performing PA reduction by resecting a rectangular flap of the pulmonary arterial wall, reducing the entire pulmonary root including downsizing the valve annulus, achieving a symmetrical total reduction of the neo-aortic root and more harmonic anastomosis with the ascending Ao (Fig. 3). Since then, PA reduction was done in 34 patients using essentially the same technique. Only patients with severe PA/Ao mismatch (ratio >2:1) were selected for PA reduction.

Aside from achieving a satisfactory immediate result obtaining a symmetric anastomosis in all patients, observation at mid- and long-term follow-up showed a tendency towards stabilization of the neo-aortic dimension as well as a lower incidence of significant neo-aortic regurgitation. These results were demonstrated by serial echocardiographic examination in all patients during follow-up and corroborated by angiotomographic or angiographic studies obtained in 26 patients during the same period (Figs 4 and 5).

These observations became more evident when we compared these patients with the group of patients operated before PA reduction was introduced, in 2004. Although there is a difference in follow-up time between the 2 groups of patients, and a reliable and complete database was not available for statistical analysis, the evolution we observed is markedly different. In the first group of patients, there are 3 patients who were submitted to a Bentall procedure.

We believe that PA/Ao size discrepancy plays an important role in the mechanism of neo-aortic root dilatation and related valve regurgitation by altering the geometry of the great vessel root and affecting fluid dynamics in this structure, which may lead to changes in the wall shear stress, promoting vascular remodelling and susceptibility to dilatation [27, 28]. Hydraulic *in vitro* studies have shown the occurrence of vortices in dilated



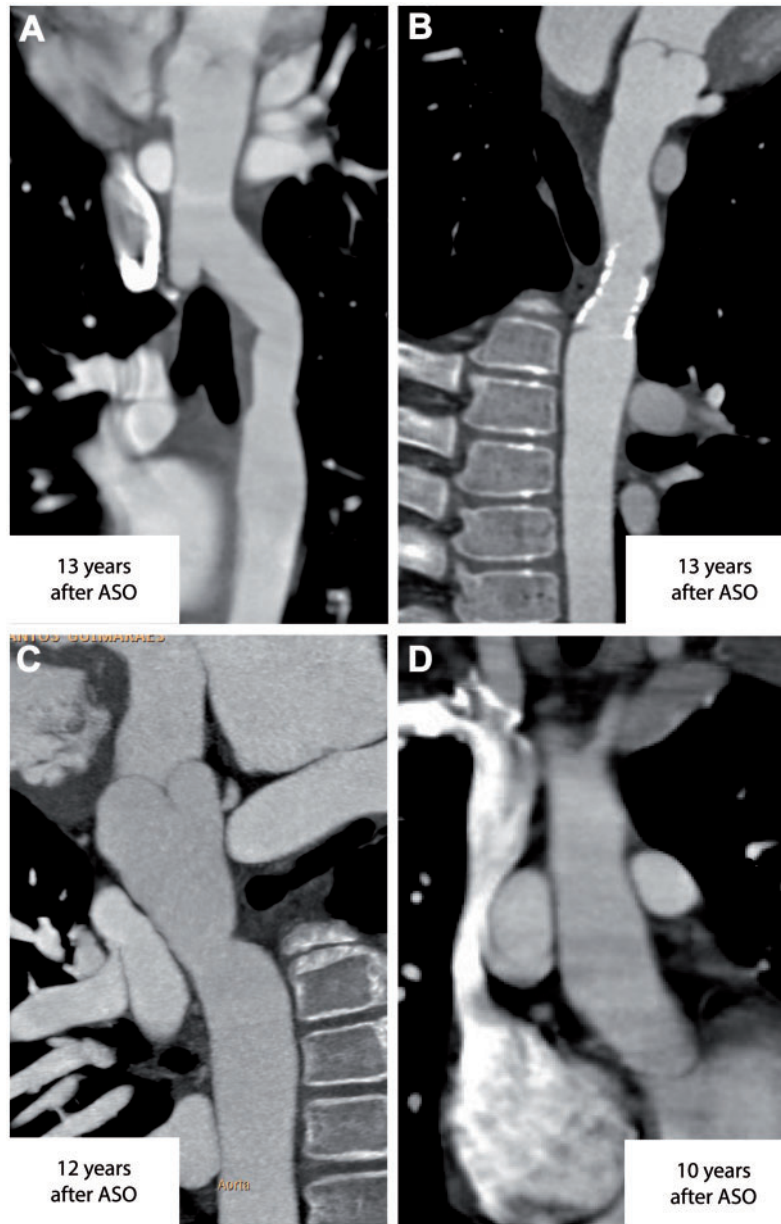
**Figure 3:** Schematic illustration of the neo-aorta after ASO in the presence of preoperative PA/Ao mismatch. Top image shows neo-aorta in patients who were not submitted to PA reduction, showing size discrepancy in anastomosis between neo-aortic root and ascending aorta. Bottom image shows neo-aorta in patients submitted to PA reduction, showing geometric concordance of the anastomosis. Ao: aorta; ASO: arterial switch operation; PA: pulmonary artery.

aortic sinuses that may result in aortic wall thinning and damaging in the regions of haemodynamic jet impact [29].

Preservation of the aortic diameter and valve function with the PA reduction may be explained by (i) reduction of the initial size of the neo-aorta that will be followed by an immediate postoperative dilating phase and final normal growth of the vessel with a more uniform development [30] and (ii) geometric concordance between the neo-aortic root and ascending Ao anastomosis, avoiding the distortion generated by suture trimming and resulting in a better hydraulic flow pattern, reducing the impact on the arterial wall. This diameter stabilization of the neo-aortic root, combined with a wider area of leaflets coaptation obtained with the PA resection, may be the reason for reduced incidence of neo-aortic valve regurgitation observed in this patient's evolution.

Even though the results obtained with PA reduction are encouraging, we have to consider some drawbacks in our technique: (i) suture malalignment of the valve leaflets during PA closure may result in neo-aortic valve regurgitation; (ii) neo-aortic valve configuration after PA resection with redundancy of posterior valve leaflet may affect its performance in a longer-term; (iii) the PA reduction adds more suture lines to the surgical technique and special attention to haemostasis should be paid; and (iv) indication to resect and the amount of resection are a surgeon's on-the-spot decision. Although we did not have complications related to neo-aortic stenosis, we have recorded neo-aortic root Z-scores below -1, which may indicate excessive resection of PA.

The main points that should be observed when performing the technique are (i) patient selection (severe mismatch between the great vessels, ratio > 2:1); (ii) site of resection (always on the non-



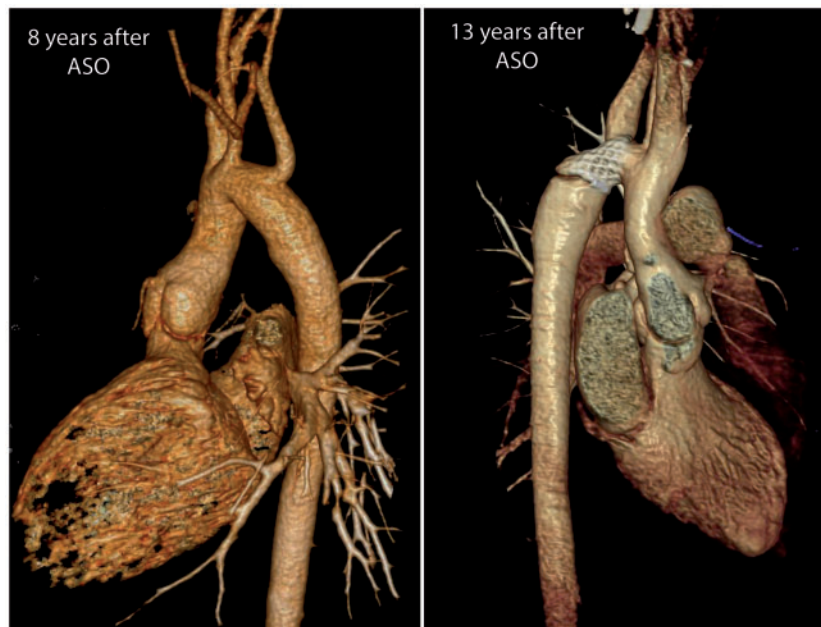
**Figure 4:** Angiotomographic images of neoaorta of 4 different patients (**A**, **B**, **C** and **D**) submitted to pulmonary artery reduction in the long-term follow-up after ASO. Patient B had angioplasty correction of reocclusion of the aorta. Patient C had interruption of aortic arch associated with the transposition of the great arteries before ASO. ASO: arterial switch operation.

coronary sinus of Valsalva, regardless of coronary anatomy); (iii) resection of a 3- to 4-mm fragment of PA (about one-third of the sinus diameter); and (iv) alignment of the suture (it is essential to use 1 stay suture on the superior edges of transected PA to align the flaps and start the suture from the root to the top of PA to avoid leaflet malalignment).

We also believe that PA reduction will not be effective in all patients with PA/Ao mismatch. Patients who show extreme dilatation of pulmonary sinuses of Valsalva before ASO will probably maintain the progressive dilatation in spite of the reduction, as we observed in one of our patients. Since more important neo-aortic root dilatation and need for replacement have been described occurring after 15–20 years of follow-up, our present findings may change as our observation period continues.

## Limitations

This study has several limitations, including its single institution, retrospective nature and the wide range of follow-up time. The morphometric study may have been influenced by non-blinded measurements. Lack of available normalized aortic root diameter in Brazilian paediatric population may have affected our findings. Other interesting variables were not included in this study for insufficient reliable statistical information. Comparison with the first group of patients, not submitted to pulmonary reduction, would be significant for the evaluation of our technique. Mechanisms for neo-aortic root enlargement and neo-aortic valve regurgitation and the effects of the technique described are speculative and require further investigation.



**Figure 5:** Three-dimensional angiotomography reconstruction of neo-aorta in different patients submitted to pulmonary artery reduction after ASO. Patient on the right had angioplasty correction of recoarctation of the aorta. ASO: arterial switch operation.

## CONCLUSION

In conclusion, PA reduction during ASO proved to be a feasible, reproducible and low-risk procedure to approach PA/Ao mismatch. Mid- and long-term follow-up showed a consistent tendency towards stabilization of the neo-aortic root dilatation and satisfactory neo-aortic valve performance after the procedure. Nevertheless, further investigation is required with a larger population, control group and longer-term follow-up.

## SUPPLEMENTARY MATERIAL

[Supplementary material](#) is available at *ICVTS* online.

**Conflict of interest:** none declared.

## Author contributions

**Fernanda Lübe Antunes Pereira:** Conceptualization; Data curation; Formal analysis; Project administration; Resources; Visualization; Writing—original draft; Writing—review & editing. **Cristiane Nunes Martins:** Investigation; Methodology; Supervision; Validation; Visualization. **Roberto Max Lopes:** Formal analysis; Validation; Visualization. **Matheus Ferber Drummond:** Formal analysis; Supervision; Validation; Visualization. **Fernando Antonio Fantini:** Formal analysis; Supervision; Validation; Visualization. **Erika Correa Vrandecic:** Methodology; Supervision; Validation; Visualization. **Mario Oswaldo Vrandecic Peredo:** Supervision; Visualization. **Bayard Gontijo Filho:** Conceptualization; Formal analysis; Investigation; Project administration; Supervision; Validation; Visualization; Writing—original draft; Writing—review & editing.

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