

### **CONGENITAL HEART SURGERY:**

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# Left-Sided Reoperations After Arterial Switch Operation: A European Multicenter Study



Vladimiro L. Vida, MD, PhD, Lorenza Zanotto, MD, Lucia Zanotto, PhD, and Giovanni Stellin, MD, and the European Congenital Heart Surgeons Association (ECHSA) Study Group\*

Pediatric and Congenital Cardiac Surgery Unit, Department of Cardiac, Thoracic, and Vascular Sciences, and Department of Statistical Sciences, University of Padua, Padua, Italy

Background. We sought to report the frequency, types, and outcomes of left-sided reoperations (LSRs) after an arterial switch operation (ASO) for patients with D-transposition of the great arteries (D-TGA) and double-outlet right ventricle (DORV) TGA-type.

Methods. Seventeen centers belonging to the European Congenital Heart Surgeons Association (ECHSA) contributed to data collection. We included 111 patients who underwent LSRs after 7,951 ASOs (1.4%) between January 1975 and December 2010. Original diagnoses included D-TGA (n = 99) and DORV TGA-type (n = 12). Main indications for LSR were neoaortic valve insufficiency (n = 52 [47%]) and coronary artery problems (CAPs) (n = 21 [19%]).

Results. Median age at reoperation was 8.2 years (interquartile range [IQR], 2.9–14 years). Seven patients died early after LSRs (6.3%); 4 patients with D-TGA (5.9%) and 3 patients with DORV TGA-type (25%) (p = 0.02).

Median age at last follow-up was 16.1 years (IQR, 9.9–21.8 years). Seventeen patients (16%) required another reoperation, which was more frequent in patients with DORV-TGA type (4 of 9 [45%]) than in patients with D-TGA (13 of 95 [14%]). Late death occurred in 4 patients (4 of 104 [3.8%]). The majority of survivors were asymptomatic at last clinical examination (84 of 100 [84%]).

Conclusions. Reoperations for residual LSRs are infrequent but may become necessary late after an ASO, predominantly for neoaortic valve insufficiency and CAPs. Risk at reoperation is not negligible, and DORV TGA-type anatomy, as well as procedures on the coronary arteries, were significantly associated with a higher morbidity and a lower overall survival. Recurrent reoperations after LSRs may be required.

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The arterial switch operation (ASO) is the standard surgical procedure for correction in patients with D-transposition of the great arteries (D-TGA) and double-outlet right ventricle TGA-type (DORV TGA-type) [1]. Despite excellent early- and long-term survival after an ASO [2–7], it is now evident that a percentage of these patients may require additional surgical or hemodynamic

maneuvers, which in the majority of cases are for neopulmonary stenosis [2, 5, 8, 9]. Less is known about the frequency, types, and outcomes of reoperations after ASO on the left side of the heart [9–16]. With the aim of obtaining more consistent data on this topic, we embarked on a multicenter study within the European Congenital Heart Surgeons Association (ECHSA).

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\*Additional members of the European Congenital Heart Surgeons Association (ECHSA) study group appear at the end of this article.

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Address correspondence to Dr Stellin, Pediatric and Congenital Cardiac Surgery Unit, Department of Cardiac, Thoracic, and Vascular Sciences, University of Padua, Via Giustiniani 2, 35128 Padua, Italy; email: giovanni. stellin@unipd.it.

#### **Patients and Methods**

The Clinical Investigation Committee of the University Hospital of Padua, the coordinating center, approved the retrospective review of medical records in accordance with the protection of patient confidentiality and consented to use data for publication; patients were not identified and individual consent was not obtained.

#### Abbreviations and Acronyms

ASO = arterial switch operation CABG = coronary artery bypass grafting CAP = coronary artery problems CHD = congenital heart disease DORV = double-outlet right ventricle D-TGA = D-transposition of the great arteries ECHSA = European Congenital Heart Surgeons Association **IQR** = interquartile range LSRs = left-sided reoperations LVAD = left ventricular assist device

obstruction

MVR = mitral valve replacement NYHA = New York Heart Association

LVOTO = left ventricular outflow tract

PA = pulmonary artery

RVOTO = right ventricular outflow tract

obstruction

RV-PA = right ventricle to pulmonary artery

This study is a retrospective evaluation and was conducted on behalf of the ECHSA. We included data relative to the follow-up course and outcome of any patient who required left-sided reoperation (LSR) after ASO for D-TGA and DORV TGA-type between January 1975 and December 2010.

We arbitrarily defined an LSR as any surgical procedure that is necessary for residual or new anatomic/functional problems after a previous ASO on the neo-aortic valve, the aortic root, the coronary arteries, and the left ventricular outflow tract (LVOT) (sites of the previous ASO). We excluded (1) patients who underwent reoperation after ASO for isolated right-sided lesions, (2) patients who underwent isolated left-sided procedures on the aortic isthmus and mitral valve, and (3) patients

with forms of DORV TGA-type who underwent other types of repair.

Variables analyzed in this study are summarized in Tables 1 to 4. We divided patients with D-TGA into simple forms (with intact ventricular septum) and complex forms (with associated congenital heart disease [CHD]).

The aim of this study was to investigate the frequency, types, and outcomes of LSRs after ASO for D-TGA and DORV TGA-type. Outcomes included postoperative morbidity after LSR, patient survival, need for further reoperation, and clinical status at the last clinical examination. Early mortality was defined as any death occurring within the first 30 days after operation or during hospitalization for a LSR. Any other death after hospital discharge was defined as late mortality.

## Statistical Analysis

Continuous variables are expressed as medians, with interquartile range (IQR) as a measure of variability. Comparison between groups was made using the Wilcoxon rank sum or Fisher's exact test if the variables were continuous or dichotomous, respectively. We compared the results of LSRs in patients with D-TGA and DORV TGA-type. A Kaplan-Meier survival analysis stratified by fundamental diagnosis (D-TGA and DORV TGA-type) and by the main diagnosis leading to LSR was performed. The comparison of survival probability among subgroups was performed by means of the log-rank test. The statistical significance was set at a familywise error rate of *p* less than 0.05. The R statistical package and Harrell's rms libraries were used for analysis.

## Results

## **Patients**

Seventeen of the 42 (41%) ECHSA centers initially contacted contributed to data collection. We included in this

Table 1. Demographics and Characteristics Patients Undergoing LSR at ASO

Variable		D-TGA n = 99	DORV TGA-Type $n = 12$	p Value
Male sex <sup>a</sup>	89 (80%)	79 (80%)	10 (83%)	1
Prenatal diagnosis <sup>a</sup>	10 (9%)	9 (9%)	1 (8.3%)	1
Bicuspid neoaortic valve <sup>a</sup>	8 (7%)	8 (8%)		0.6
Rashkind procedure <sup>a</sup>	61 (55%)	58 (59%)	3 (25%)	0.03
PGE-1 infusion <sup>a</sup>	61 (55%)	56 (57%)	5 (42%)	0.3
LVOT surgery at ASO <sup>a</sup>	11 (10%)	9 (9%)	2 (17%)	0.3
Age at ASO, d <sup>b</sup>	12 (6.5–83)	10 (6–76)	41 (8–90)	0.3
Weight at ASO, kg <sup>b</sup>	3.7 (3.2-4.2)	3.7 (3.2-4.3)	3.8 (3.4–3.9)	1
CPB time at ASO, min <sup>b</sup>	187 (149-241)	179 (141–217)	281 (248–300)	0.0003
Cross-clamp time at ASO, min <sup>b</sup>	110 (87–136)	105 (83–131)	169 (139–198)	0.00001
Trapdoor technique <sup>b</sup>	50 (45%)	43 (43%)	7 (58%)	0.4
LeCompte maneuver <sup>b</sup>	97 (87%)	88 (89%)	9 (75%)	0.1

<sup>&</sup>lt;sup>a</sup> Number of patients and percentage. <sup>b</sup> Median and interquartile range.

Table 2. Clinical and Instrumental Variables of Patients Who Underwent LSR and Outcomes

Variable	$\begin{array}{c} \text{Total} \\ N = 111 \end{array}$	D-TGA n = 99	DORV TGA-Type $n = 12$	p Value
Age at LSR, y <sup>a</sup>	8.2 (2.9–14)	8.8 (3–14.2)	4.7 (0.7–13.1)	0.3
Symptoms before LSR <sup>b</sup>	41 (37%)	36 (36%)	5 (42%)	0.7
Arrhythmias/ST-segment depression at electrocardiography <sup>b</sup>	17 (15%)	14 (14%)	3 (25%)	0.4
Neoaortic valve insufficiency <sup>b</sup>	86 (77%)	79 (80%)	7 (58%)	0.1
Mild/mild to moderate neoaortic valve insufficiency <sup>b</sup>	32 (29%)	27 (27%)	5 (42%)	0.3
Moderate/severe neoaortic valve insufficiency <sup>b</sup>	54 (49%)	52 (52%)	2 (17%)	0.02
Aortic annulus, mm <sup>a,c</sup>	29.6 (27-34.6)	30 (27–35)	28 (27–29)	0.6
Aortic annulus, z score <sup>a,c</sup>	3.9 (2.7-4.8)	4.1 (2.5–5)	3.9 (3.7-4)	0.09
Aortic sinuses, mm <sup>a,c</sup>	46 (42–48)	46 (42–48)	50 (48–51)	0.07
Aortic sinuses z score <sup>a,c</sup>	6.6 (5.5-7.4)	6.2 (5.2-7.1)	7.8 (7.6–8.1)	0.06
Complications after LSR <sup>b</sup>	21 (19%)	16 (16%)	5 (42%)	0.009
Mortality at LSR <sup>b</sup>	7 (6.3%)	4 (4.1%)	3 (25%)	0.03
Late mortality after LSR <sup>b</sup>	4 (3.8%)	4 (4.1%)		1

<sup>&</sup>lt;sup>a</sup> Median and interquartile range.

DORV = double-outlet right ventricle;

D-TGA = D-transposition of the great arteries;

LSR = left- sided reoperation.

study 111 patients who underwent LSRs after 7,951 ASOs (1.4%). Original diagnoses included D-TGA (n = 99)(composed of simple D-TGA with intact ventricular septum [n = 31] and more complex forms of D-TGA [n = 68]) and DORV TGA-type (n = 12). Associated CHDs included ventricular septal defect (n = 57), coarctation/ interruption of the aortic arch (n = 22), left ventricular outflow tract obstruction (LVOTO) (n = 11), right ventricular outflow tract obstruction (RVOTO) (n = 4), and other less common CHDs (n = 6). Thirty-seven (33%) patients had an abnormal coronary artery pattern, mainly with the circumflex coronary artery coming from the right coronary artery (19 of 37 patients [51%]). Patient characteristics at the time of ASO are listed in Table 1.

## LSRs After ASO

The median age at LSR was 8.2 years (IQR, 2.9–14 years). Forty-one (37%) patients were symptomatic with reduced exercise tolerance (n=29) and congestive heart failure (n=8). Other less common symptoms included chest

pain (n = 5), palpitations (n = 3), and recurrent respiratory infections (n = 1). Two patients were resuscitated after a cardiac arrest for ventricular fibrillation. Seventeen (15%) patients presented with arrhythmias/electrocardiographic changes: third-degree atrioventricular block (n = 3), supraventricular tachycardia (n = 2), ventricular fibrillation (n = 2), ventricular tachycardia (n = 2), transitional atrioventricular block (n = 2), junctional ectopic tachycardia (n = 2), second-degree atrioventricular block (n = 1), and ST-segment depression at electrocardiography (n = 5). Clinical/instrumental variables before LSR are listed in Table 2.

The main indication for LSR was neoaortic insufficiency (n = 52 of 111 LSRs [47%]; 52 of 7,951 ASOs [0.65%]) followed by coronary artery problems (CAPs) (n = 21 of 111 LSRs [19%]); 21 of 7,951 ASOs [0.26%]) and LVOTO (n = 17 of 111 LSRs [15%]; 7 of 7,951 ASOs [0.21%]) (Table 3).

CAP requiring surgical procedures included stenosis/ occlusion of the left main coronary artery (ostial/

Table 3. Main Diagnoses Leading to LSRs

Diagnosis	Total N = 111	D-TGA n = 99	DORV TGA-Type n = 12
Neoaortic valve insufficiency <sup>a</sup>	52 (47%)	49 (49%)	3 (25%)
Coronary artery problems <sup>a</sup>	21 (19%)	19 (19%)	2 (17%)
LVOTO <sup>a</sup>	17 (15%)	15 (15%)	2 (17%)
Aortic root dilatation + neoaortic valve insufficiency <sup>a</sup>	14 (12%)	12 (11%)	2 (17%)
Supravalvar aortic stenosis <sup>a</sup>	10 (9%)	7 (7.1%)	3 (25%)
Aortic root dilatation <sup>a</sup>	8 (7.2%)	6 (6.1%)	2 (17%)
Aortic valve stenosis <sup>a</sup>	1 (0.9%)	• • •	1 (8.3%)

<sup>&</sup>lt;sup>a</sup> Number of patients and percentage.

<sup>&</sup>lt;sup>b</sup> Number of patients and percentage.

<sup>&</sup>lt;sup>c</sup> In patients with aortic root dilatation.

Table 4. Types of LSRs and Associated Surgical Procedures

LSRs (126 Procedures in 111 Patients)	Total N = 111	D-TGA n = 99	$\begin{array}{c} DORV \\ TGA-Type \\ n=12 \end{array}$
Aortic valve replacement <sup>a,b</sup>	38 (34%)	36 (36%)	2 (17%)
LVOTO relief <sup>a,c</sup>	17 (15%)	15 (15%)	2 (17%)
Aortic valve plasty <sup>a,d</sup>	14 (13%)	12 (12%)	2 (17%)
Coronary ostium relocation <sup>a</sup>	11 (10%)	10 (10%)	1 (8.3%)
CABG <sup>a</sup>	11 (10%)	10 (10%)	1 (8.3%)
Bentall's procedure <sup>a,b</sup>	11 (10%)	9 (9%)	2 (17%)
Supravalvar aortic enlargement <sup>a</sup>	10 (9%)	7 (7.1%)	3 (25%)
Supravalvar aortic plasty (reduction) <sup>a</sup>	10 (9%)	8 (8.1%)	2 (17%)
Switchback operation <sup>a</sup>	4 (3.6%)	4 (4%)	
Ascending aorta replacement <sup>a</sup>	1 (0.9%)	1 (1%)	
Orthotopic heart transplantation <sup>a,e</sup>	1 (0.9%)	1 (1%)	
Other Associated Procedures (25 Procedures in 12	7 Patients)		
Pulmonary artery branch patch plasty <sup>a</sup>	6 (5.4%)	4 (4%)	2 (17%)
RVOTO resection/relief <sup>a</sup>	5 (4.5%)	2 (2%)	3 (25%)
Aortic arch reconstruction with patch <sup>a</sup>	5 (4.5%)	2 (2%)	3 (25%)
Mitral valve plasty <sup>a</sup>	2 (1.8%)	2 (2%)	
Extracorporeal membrane oxygenation <sup>a</sup>	2 (1.8%)	2 (2%)	
Mitral valve replacement <sup>a</sup>	1 (0.9%)	1 (1%)	
Left ventricle aneurysm resection <sup>a</sup>	1 (0.9%)	1 (1%)	
Left ventricular assist device <sup>a</sup>	1 (0.9%)	1 (1%)	
Tricuspid valve plasty <sup>a</sup>	1 (0.9%)	1 (1%)	

a Number of patients and percentage. b Aortic valve prostheses included mechanical valves (n = 46) and biological valves (n = 3). c LVOTO relief included LVOTO fibrotic/muscular resection (n = 15), modified Konno operation (n = 1), and baffle extension (n = 1). d Aortic valve plasty maneuvers (n = 23 in 14 patients) included annuloplasty (n = 10), leaflet plication (n = 3), annulus downsizing (n = 2), commissuroplasty (n = 2), commissural resuspension (n = 2), leaflet shaving (n = 2), leaflet patch enlargement (n = 1), and leaflet perforation patch repair (n = 1). e Patient with occlusion of left anterior descending coronary artery.

 $CABG = coronary \ artery \ bypass \ grafting; \qquad DORV = double-outlet \ right \ ventricle; \qquad D-TGA = D-transposition \ of the \ great \ arteries; \qquad LSRs = left \ sided \ reoperations; \qquad LVOTO = left \ ventricular \ outflow \ tract \ obstruction; \qquad RVOTO = right \ ventricular \ outflow \ tract \ obstruction.$ 

proximal)(n = 13) and stenosis/occlusion of the right coronary artery (ostial/proximal)(n = 5). Two patients had both left main and right coronary artery ostial stenosis, and 1 patient had left coronary sinus dilatation.

LSRs after ASO are listed in Table 4. Ten of the 17 (59%) patients who underwent procedures for LVOTO relief at the time of LSR had a LVOT operation at the time of the ASO. One patient with simple D-TGA and occlusion of the left main coronary artery underwent orthotopic heart transplantation. Other associated surgical maneuvers at the time of LSR are listed in Table 4.

Twenty-one (19%) patients had postoperative complications after LSRs (Table 5), which were more frequent in patients with DORV TGA-type (5 of 12 [42%]) than in patients with D-TGA (16 of 99 [16%]; p = 0.009).

Seven patients died early after LSRs (6.3%), including 4 patients with D-TGA (4 of 68 [5.9%]) and 3 patients with DORV TGA-type (3 of 12 [25%]; p = 0.02) (Table 2). Four patients who died early (57%) had CAP. Causes of hospital mortality are listed in Table 6.

# Follow-Up

Follow-up was completed in all patients who had undergone LSRs. Median follow-up time after ASO was 16.1

years (IQR, 9.9–21.8 years), and the median follow-up time after LSRs was 5.1 years (IQR, 1.2–10 years).

Seventeen patients (17 of 104 [16%]) (17 of the initial 7,951 patients who underwent ASO [0.2%]) required

Table 5. Complications After LSRs (27 Complications in 21 Patients)

Complication	Total N = 111	D-TGA n = 99	DORV TGA-Type n = 12
Low-output syndrome <sup>a,b</sup>	9 (8.1%)	6 (6%)	3 (25%)
Arrhythmias <sup>a</sup>	6 (5.4%)	5 (5%)	1 (8.3%)
Acute renal failure <sup>a</sup>	3 (2.7%)	2 (2%)	1 (8.3%)
Postoperative bleeding <sup>a</sup>	3 (2.7%)	3 (3%)	
Respiratory complications <sup>a</sup>	2 (2.7%)	2 (2%)	
Vocal cord paralysis <sup>a</sup>	2 (2.7%)	1 (1%)	1 (8.3%)
Neurologic complications <sup>a</sup>	1 (0.9%)	1 (1%)	
Pulmonary embolism <sup>a</sup>	1 (0.9%)	1 (1%)	•••

<sup>&</sup>lt;sup>a</sup> Number of patients and percentage. <sup>b</sup> 2 patients required postoperative extracorporeal membrane oxygenation support, and 1 patient required a left ventricular assist device.

DORV = double-outlet right ventricle; D-TGA = D-transposition of the great arteries; LSRs = left sided reoperations.

Table 6. Characteristics of Patients Who Died After LSRs

Patient	Diagnosis	Mortality	Procedure	Cause of Mortality
1	Complex D-TGA	Early	Aortic valve replacement	Low-output syndrome, neurologic injury
2	Complex D-TGA	Early	Aortic valve plasty + coronary ostium relocation	Pulmonary embolism
3	Complex D-TGA	Early	Coronary ostium relocation, ECMO	Low-output syndrome
4	Complex D-TGA	Early	Aortic valve replacement	Low-output syndrome
5	DORV TGA-type	Early	CABG	Low-output syndrome
6	DORV TGA-type	Early	Bentall's procedure	Low-output syndrome
7	DORV TGA-type	Early	Supravalvar aortic plasty (reduction) $+$ coronary ostium relocation	Low-output syndrome
8	Simple D-TGA	Late	Supravalvar aortic plasty (reduction) + CABG	Low-output syndrome
9	Complex D-TGA	Late	CABG	Sudden death
10	Complex D-TGA	Late	Supravalvar aortic enlargement	Congestive heart failure
11	Complex D-TGA	Late	Supravalvar aortic enlargement $+$ PA branch patch plasty	Low-output syndrome

CABG = coronary artery bypass grafting; extracorporeal membrane oxygenation;

 $\begin{aligned} DORV &= \text{double-outlet right ventricle;} & D-TGA &= D\text{-transposition of the great arteries;} \\ LSRs &= \text{left-sided reoperations;} & PA &= \text{pulmonary artery.} \end{aligned}$ 

ECMO =

another reoperation after the LSR (Table 7). Two patients underwent orthotopic heart transplantation. Recurrent operations were more frequent in patients with DORV TGA-type (4 of 9 [45%]) than in patients with D-TGA (13 of 95 [14%]).

There were 4 late deaths (4 of 104 [3.8%]), all in patients with D-TGA (4 of 95 [4.2%]). Two (1.9%) patients died after the second LSR, both of low-output syndrome (Table 6). The survival at 15 years after an LSR was 90%, and it was

higher for patients with D-TGA than for patients with DORV TGA-type (89% versus 75%; p = 0.04) (Figs 1, 2).

The majority of the 100 survivors were asymptomatic (New York Heart Association [NYHA] class I) at the last clinical examination (84/100 [84%]). The remaining patients were in NYHA class II (13 of 100 [13%]) and NYHA class III (3 of 100 [3%]). Symptoms at follow-up included fatigue/exercise intolerance (n=15), palpitations (n=1 [ventricular tachycardia]). One patient had renal failure (n=1).

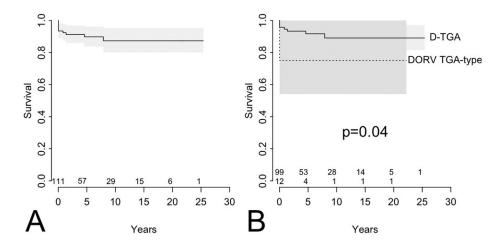
Table 7. Other Procedures After LSRs (23 Procedures in 17 Patients)

Patient	Diagnosis Surgical Procedures at LSF		Surgical Procedures After LSR
1	Simple D-TGA	CABG + supravalvar aortic plasty (reduction)	Aortic valve replacement <sup>a</sup>
2	Simple D-TGA	AVP	Bentall's procedure
3	Simple D-TGA	Switchback operation	Aortic valve replacement
4	Simple D-TGA	Switch back operation	Aortic valve replacement
5	Complex D-TGA	LVOTO + RVOTO relief	LVOTO resection + PA patch augmentation
6	Complex D-TGA	CABG	Orthotopic heart transplantation
7	Complex D-TGA	Aortic valve replacement	Bentall's procedure + MVR
8	Complex D-TGA	AVP + MVR	Aortic valve replacement + pacemaker
9	Complex D-TGA	Aortic valve replacement	Aortic valve replacement
10	Complex D-TGA	Supravalvar aortic enlargement $+$ PA branch patch plasty	Aortic valve replacement <sup>a</sup>
11	Complex D-TGA	AVP + LVOTO relief	Aortic valve replacement + RV-PA conduit
12	Complex D-TGA	Relocation coronary ostium + LVOTO relief	LVOTO resection
13	Complex D-TGA	Aortic valve replacement + LVAD	Orthotopic heart transplantation
14	DORV TGA-type	AVP + LVOTO relief + RVOTO relief	Aortic valve replacement
15	DORV TGA-type	Bentall's procedure	Bentall's procedure (for endocarditis)
16	DORV TGA-type	Supravalvar aortic enlargement + pulmonary artery branch patch plasty	Bentall's procedure
17	DORV TGA-type	AVP + aortic arch repair + RVOTO relief	Left main coronary enlargement + AVP + aortic arch repair

<sup>&</sup>lt;sup>a</sup> Both patients died after a second reoperation.

 $AVP = a ortic valve \ plasty; \qquad CABG = coronary \ artery \ bypass \ grafting; \qquad DORV = double-outlet \ right \ ventricle; \qquad D-TGA = D-transposition \ of the great \ arteries; \qquad LSRs = left-sided \ reoperations; \qquad LVAD = left \ ventricular \ assist \ device; \qquad LVOTO = left \ ventricular \ outflow \ tract \ obstruction; \\ MVR = mitral \ valve \ replacement; \qquad PA = pulmonary \ artery; \qquad RVOTO = right \ ventricular \ outflow \ tract \ obstruction; \qquad RV-PA = right \ ventricle \ to \ pulmonary \ artery.$ 

Fig 1. Kaplan-Meier survival estimates (with 95% confidence bands): (A) overall and (B) stratified by D-transposition of the great arteries (D-TGA) versus double-outlet right ventricle (DORV) TGA-type.



## Comment

The ASO for treating patients with D-TGA and DORV TGA-type is associated with excellent early- and long-term survival and a good quality of life in the vast majority of patients [1–7, 17].

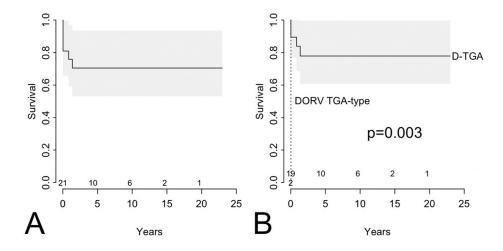
After more than 40 years from the first ASO, we now have the chance to observe the long-term results on right-sided and left-sided heart structures that are involved in this correction. It is now clear that a certain percentage of patients will need further reintervention/reoperation [10, 15, 17–19], which in the majority of patients is on the right side of the heart, for neopulmonary stenosis either at the anastomosis site or at the pulmonary artery bifurcation (after the LeCompte maneuver) [7, 9, 10]. Less commonly, reoperations involve the left side of the heart, such as the neoaortic valve, the aortic root, the subaortic area, and the coronary arteries [4, 5, 9].

The onset of neoaortic valve insufficiency after ASO seems to be a multifactorial process resulting in progressive aortic root dilatation and consequent further progressive neoaortic valve insufficiency [11, 12, 14]. The

presence of aortic root dilatation has been demonstrated in up to 60% to 70% of patients after ASO; nonetheless, it does not tend to be progressive during late follow-up. Conversely, the progression of the degree of neoaortic valve insufficiency rarely occurs during the first 10 to 15 years after ASO, but it was found that it increases significantly later, and this is associated with the degree of postoperative neoaortic valve insufficiency at discharge soon after ASO [14, 20, 21]. Anatomic causes identified to be responsible for aortic root dilatation and neoaortic valve insufficiency included the presence of a ventricular septal defect and aortic/pulmonary mismatch and the postoperative geometry of the aortic root [19]. In addition, previous pulmonary artery banding and coronary reimplantation techniques (ie, the trapdoor technique) were also previously identified as significant risks for aortic root dilatation and neoaortic valve insufficiency [14, 12].

Regarding the coronary arteries, despite good results after their translocation [22, 23], the risk of a clinically silent late coronary artery obstruction is present, as is the need for coronary reintervention procedures [24]. Some

Fig 2. Kaplan-Meier survival estimates (with 95% confidence bands) according to coronary procedures: (A) overall and (B) stratified by D-transposition of the great arteries (D-TGA) versus double-outlet right ventricle (DORV) TGA-type.



authors identified the presence of complex native coronary anatomy as a predictor for coronary reinterventions [7, 24, 25].

The aim of this study was to provide more consistent data about the frequency and types of reoperations of left-sided heart structures (focusing on the neoaortic valve, aortic root, coronary arteries, and subaortic area) and outcomes after ASO for D-TGA and DORV TGA-type.

We were able to collect complete data on 111 patients who underwent LSRs over a total of 7,951 ASOs. It means that LSRs after ASO are rare (overall incidence of 1.4%) and are required mainly for neoaortic valve insufficiency (0.68%)(similar to other single-center reports in which the frequency ranged from 0.6%–1.3%) [14, 15, 26] and for coronary artery malperfusion/ischemia (0.26%) (which was lower than in other single-center reports in which it was up to 2% [5, 24]. Patients with CAP were treated by means of coronary revascularization or more conservatively by relocating the coronary artery ostium, when indicated, to treat late kinking or distortion of the proximal coronary course.

As expected, we also found a certain recurrence of LVOT operations (59%) in patients who underwent LVOTO relief at the time of ASO (all with a ventricular septal defect); we believe this was related more to an anatomic problem than to a technical issue.

We found that the risk of LSRs was not negligible, with a mortality rate of 6.3%, mainly for postoperative low-output syndrome. Patients with DORV TGA-type and patients with CAP presented a higher morbidity and mortality.

At midterm follow-up after LSRs, the majority of patients were asymptomatic and doing well. Nonetheless, recurrent reoperations after LSRs may be required (16% of patients who had LSRs; 16 of 7,951 ASOs [0.2%]). These reoperations were more common in patients with DORV TGA-type and were mainly on the aortic valve and the aortic root. Late mortality after LSRs was fairly low (4 of 104 [3.8%]), and in 2 patients it was related to the second reoperation.

Finally, we would like to comment on the fact that LSRs may be particularly difficult from a technical point of view. In fact, access to the aortic root is particularly challenging after the LeCompte maneuver; the pulmonary trunk and branches are stretched over the aortic root and the vascular tissues of the aortic and pulmonary arteries are usually compressed and very thin and fragile. In addition, a complex coronary pattern and previous operations or hemodynamic procedures on the right side of the heart can further increase the technical challenge in these patients. Preoperative imaging of the aortic root and coronary arteries is mandatory in the case of an LSR.

Our study has several limitations. First, this is a retrospective data examination, and certain intercenter and intracenter variability in surgical treatment is expected. Second, we do not have any information about the characteristics of the overall population of patients who

underwent ASOs; as a consequence we cannot speculate about the impact of anatomic variables or different surgical techniques (ie, trapdoor technique) on the incidence of LSRs. Third, the rate of LSRs is calculated based on the denominator of 7,951 patients who underwent ASO. Because we do not have data about the completeness of follow-up for each participating center, some of the ASO survivors potentially lost to follow-up could have undergone LSRs that were not accounted for, and this would have potentially decreased the observed rate of LSRs. Finally, the follow-up is relatively short to reach definitive conclusions.

Nonetheless, we were able to collect, to our knowledge, the largest series of patients who underwent LSRs after ASO. We concluded that reoperations for residual left-sided lesions are infrequent but may become necessary late after ASO, neoaortic valve insufficiency and CAP being the most frequent indications. Risk at reoperation is not negligible and DORV TGA-type anatomy, as well as the procedures on the coronary arteries, were significantly associated with a higher hospital complication rate and lower overall survival. Recurrent reoperations after LSR may be required, and lifetime follow-up in these patients is necessary.

European Congenital Heart Surgeons Association (ECHSA) Study Group: Massimo Padalino, MD¹; Georges Sarris, MD³; Eleftherios Protopapas, MD³; Carol Prospero, MD⁴; Christian Pizarro, MD⁴; Edward Woodford, MD⁴; Thomas Tlaskal, MD⁵; Hakan Berggren, MD⁶; Martin Kostolny, MDづ; Ikenna Omeje, MDづ; Boulos Asfour, MD8; Alexander Kadner, MD9; Thierry Carrel, MD9; Paul H. Schoof, MD¹¹0; Matej Nosal, MD¹¹1; Josè Fragata, MD¹²; Michał Kozłowski, MD¹³; Bohdan Maruszewski, MD¹³; Luca A. Vricella, MD¹⁴; Duke E. Cameron, MD¹⁴; Vladimir Sojak, MD¹⁵; Mark Hazekamp, MD¹⁵; Jukka Salminen, MD¹⁶; Ilkka P. Mattila, MD¹⁶; Julie Cleuziou, MD¹¹; Patrick O. Myers, MD¹², Viktor Hraska, MD¹9

<sup>1</sup>Pediatric and Congenital Cardiac Surgery Unit, Department of Cardiac, Thoracic and Vascular Sciences, University of Padua, Padua, Italy; <sup>3</sup>Athens Heart Surgery Institute and Department of Pediatric and Congenital Cardiac Surgery, Iaso Children's Hospital, Athens, Greece; <sup>4</sup>Nemours Cardiac Center, Alfred I. duPont Hospital for Children, Wilmington, Delaware, USA; 5Children's Heart Centre, University Hospital Motol, Prague, Czech Republic; <sup>6</sup>Department of Molecular and Clinical Medicine, Children's Heart Center, The Queen Silvia's Children's Hospital, Göteborg, Sweden; <sup>7</sup>Great Ormond Street Hospital, Cardiothoracic Unit, London, UK; 8Herma Heart Center, Medical College of Wisconsin, Wisconsin, USA; <sup>9</sup>Department for Cardiovascular Surgery, University of Bern, Bern, Switzerland; <sup>10</sup>University Medical Center Utrecht, Utrecht, Netherlands; <sup>11</sup>Childrens Heart Centre Slovak Republic, Bratislava, Slovakia; <sup>12</sup>Department of Cardiothoracic Surgery, Hospital de Santa Marta and Nova Medical School, Lisbon, Portugal; <sup>13</sup>Children's Memorial Health Institute Varsavia, Poland; 14Division of Cardiac Surgery, Johns Hopkins University, Baltimore, USA; <sup>15</sup>Department of Cardiothoracic Surgery, Leiden University Medical Center, Leiden, Netherlands; 16 Division of Pediatric Surgery, Department of Children and Adolescents, Helsinki University Hospital, Helsinki, Finland; <sup>17</sup>Department of Cardiovascular Surgery, German Heart Center Munich Technische Universität München, Munich, Germany; 18 Divison of cardiovascular Surgery, Geneva University Hospitals, Geneva, Switzerland; 19Herma Heart Center, Medical College of Wisconsin, Milwaukee, WI, USA.

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#### References

- 1. Walters HL, 3rd, Mavroudis C, Tchervenkov CI, Jacobs JP, Lacour-Gayet F, Jacobs ML. congenital heart surgery nomenclature and database project: double outlet right ventricle. Ann Thorac Surg 2000;69(4 Suppl):S249–63.
- 2. Lalezari S, Bruggemans EF, Blom NA, Hazekamp MG. Thirty-year experience with the arterial switch operation. Ann Thorac Surg 2011;92:973–9.
- 3. Konstantinov IE, Alexi-Meskishvili VV, Williams WG, Freedom RM, Van Praagh R. Atrial switch operation: past, present, and future. Ann Thorac Surg 2004;77: 2250–8.
- Lim HG, Kim WH, Lee JR, Kim YJ. Long-term results of the arterial switch operation for ventriculo-arterial discordance. Eur J Cardiothorac Surg 2013;43:325–34.
- 5. Rudra HS, Mavroudis C, Backer CL, et al. The arterial switch operation: 25-year experience with 258 patients. Ann Thorac Surg 2011;92:1742–6.
- Rodefeld MD, Ruzmetov M, Vijay P, Fiore AC, Turrentine MW, Brown JW. Surgical results of arterial switch operation for Taussig-Bing anomaly: is position of the great arteries a risk factor? Ann Thorac Surg 2007;83: 1451-7.
- Feng B, Liu Y, Hu S, et al. Arterial switch for transposition of the great vessels and Taussig-Bing anomaly after six months of age. Ann Thorac Surg 2009;88:1948–51.
- 8. Moll JJ, Michalak KW, Młudzik K, et al. Long-term outcome of direct neopulmonary artery reconstruction during the arterial switch procedure. Ann Thorac Surg 2012;93:177–84.
- 9. Raju V, Burkhart HM, Durham LA, 3rd, et al. Reoperation after arterial switch: a 27-year experience. Ann Thorac Surg 2013;95:2105–12; discussion 2112–3.
- **10.** Koshiyama H, Nagashima M, Matsumura G, Hiramatsu T, Nakanishi T. Yamazaki K. Arterial switch operation with and without coronary relocation for intramural coronary arteries. Ann Thorac Surg 2016;102:1353–9.
- 11. Fricke TA, d'Udekem Y, Richardson M, et al. Outcomes of the arterial switch operation for transposition of the great

- arteries: 25 years of experience. Ann Thorac Surg 2012;94: 139-45.
- **12.** Co-Vu JG, Ginde S, Bartz PJ, Frommelt PC, Tweddell JS, Earing MG. Long-term outcomes of the neoaorta after arterial switch operation for transposition of the great arteries. Ann Thorac Surg 2013;95:1654–9.
- **13.** Ma K, Li S, Hu S, Hua Z, et al. Neoaortic valve regurgitation after arterial switch: ten years outcomes from a single center. Ann Thorac Surg 2016;102:636–42.
- Angeli E, Gerelli S, Beyler C, et al. Bicuspid pulmonary valve in transposition of the great arteries: impact on outcome. Eur J Cardiothorac Surg 2012;41:248–55.
- 15. Lo Rito M, Fittipaldi M, Haththotuwa R, et al. Long-term fate of the aortic valve after an arterial switch operation. J Thorac Cardiovasc Surg 2015;149:1089–94.
- **16.** Kalfa DM, Lambert V, Baruteau AE, et al. Arterial switch for transposition with left outflow tract obstruction: outcomes and risk analysis. Ann Thorac Surg 2013;95: 2097–103.
- 17. Tsuda E, Imakita M, Yagihara T, et al. Late death after arterial switch operation for transposition of the great arteries. Am Heart J 1992;124:1551–7.
- **18.** Prifti E, Crucean A, Bonacchi M, et al. Early and long term outcome of the arterial switch operation for transposition of the great arteries: predictors and functional evaluation. Eur J Cardiothorac Surg 2002;22:864–73.
- 19. Schwartz ML, Gauvreau K, del Nido P, Mayer JE, Colan SD. Long-term predictors of aortic root dilation and aortic regurgitation after arterial switch operation. Circulation 2004;110(11 Suppl 1):II128–32.
- Lange R, Cleuziou J, Hörer J, et al. Risk factors for aortic insufficiency and aortic valve replacement after the arterial switch operation. Eur J Cardiothorac Surg 2008;34: 711–7
- Koolbergen DR, Manshanden JS, Yazdanbakhsh AP, et al. Reoperation for neoaortic root pathology after the arterial switch operation. Eur J Cardiothorac Surg 2014;46:474–9; discussion 479.
- 22. Fricke TA, Bulstra AE, Naimo PS, et al. Excellent long-term outcomes of the arterial switch operation in patients with intramural coronary arteries. Ann Thorac Surg 2016;101: 725–9.
- Thrupp SF, Gentles TL, Kerr AR, Finucane K. Arterial switch operation: early and late outcome for intramural coronary arteries. Ann Thorac Surg 2012;94:2084–90.
- **24.** Angeli E, Formigari R, Pace Napoleone C, et al. Long-term coronary artery outcome after arterial switch operation for transposition of the great arteries. Eur J Cardiothorac Surg 2010;38:714–20.
- Vida VL, Torregrossa G, De Franceschi M, et al. Pediatric coronary artery revascularization: a European multicenter study. Ann Thorac Surg 2013;96:898–903.
- **26.** Delmo Walter EM, Huebler M, Alexi-Meshkishvili V, Sill B, Berger F, Hetzer R. Fate of the aortic valve following the arterial switch operation. J Card Surg 2010;25:730–6.