

## Cardiovascular Magnetic Resonance Findings Late After the Arterial Switch Operation

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**Background**—Despite its robust diagnostic capabilities in adolescents and adult patients after the arterial switch operation, little information is available on the cardiovascular magnetic resonance findings in this population.

**Methods and Results**—The cardiovascular magnetic resonance findings of 220 consecutive patients evaluated in our center were retrospectively reviewed (median age at cardiovascular magnetic resonance, 15.4 years; 66.8% male sex). Compared with published normal values, left and right ventricular end-diastolic volume  $z$  scores were mildly enlarged ( $0.48 \pm 1.76$  and  $0.33 \pm 1.5$ ;  $P=0.0003$  and  $0.0038$ , respectively), with 26% of patients having left ventricular dilatation and 20% having right ventricular dilatation. Left ventricular dysfunction was present in 21.5% of patients (mild in most), and only 5.1% of patients had mild right ventricular dysfunction. Myocardial scar was found in 1.8% of patients. Dilatation of the neo-aortic root was common (76%), and root  $z$  score increased at an average rate of 0.03 points per year. By multivariable analysis, neo-aortic root dilatation was associated with worse neo-aortic valve regurgitation (OR, 5.29;  $P=0.0016$ ). The diameters of the thoracic aorta distal to the root were near-normal in most patients, whereas the neomain pulmonary artery was typically oval shaped with decreased anteroposterior and normal lateral diameters.

**Conclusions**—Although the majority of arterial switch operation patients have normal ventricular size and function and myocardial scar is rare, an important minority exhibits ventricular enlargement or dysfunction. Neo-aortic root dilatation, which is present in most patients and progresses over time, is strongly associated with significant neo-aortic valve regurgitation. The findings of this study provide reference values against which arterial switch operation patients can be compared with their peers. (*Circ Cardiovasc Imaging*. 2016;9:e004618. DOI: 10.1161/CIRCIMAGING.116.004618.)

**Key Words:** arterial switch operation ■ magnetic resonance imaging ■ regurgitation aortic valve ■ transposition of great vessels ■ valvular heart disease, congenital ■ ventricular function

Because the arterial switch operation (ASO) became the standard treatment for infants and children with D-loop transposition of the great arteries (TGA) in the early-to-mid 1980s, survival has improved with the majority of patients now reaching adulthood.<sup>1</sup> Although late mortality is rare, complications involving the implanted coronary arteries, pulmonary arteries, and neo-aortic valve and root are increasingly recognized as sources of morbidity.<sup>2,3</sup> Although echocardiography is capable of providing much of the clinically relevant information for noninvasive assessment of most ASO patients during infancy and childhood, its ability to adequately assess the key anatomic and functional elements in older patients is hindered by deteriorating acoustic windows.<sup>4</sup> Cardiovascular magnetic resonance (CMR) has been shown to be a robust imaging modality in adolescents and adult patients with a wide variety of congenital heart disease, including those after the ASO.<sup>5,6</sup> Specifically, unlike echocardiography, CMR is not hindered by body size and is considered a reliable technique

for assessment of the great vessels, biventricular size and function, myocardial viability, and valve regurgitation.<sup>7</sup>

### See Editorial by de Roos See Clinical Perspective

Although CMR can provide comprehensive anatomic and functional assessment in ASO patients, relatively sparse information has been published to date, and the ranges of ventricular and arterial dimensions and functional parameters have not been characterized. The goal of the present study, therefore, was to describe the range of biventricular size and function, frequency and location of focal myocardial fibrosis evaluated by late gadolinium enhancement (LGE) imaging, spectrum of great vessel dimensions, and frequency and severity of neo-aortic valve regurgitation (neo-AR) in a large cohort of ASO patients evaluated at our center. In addition, we sought to explore factors associated with left ventricular (LV) enlargement and dysfunction, as well as neo-AR.

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## Methods

### Patients

A retrospective search of the Boston Children's Heart Center database identified all patients who fulfilled the following criteria: (1) underwent an ASO at our institution during the first year of life; (2) had at least 1 CMR examination at our laboratory from January 1998 through December 2014; and (3) had an anatomic diagnosis of normal visceral-atrial situs and ventricular D-loop. Patients with inadequate image data for measurements of at least 1 of the following key structures were excluded: (1) great vessel dimension imaged either by a contrast-enhanced 3D magnetic resonance angiography or a noncontrast electrocardiographically gated isotropic 3D steady-state free precession (SSFP) sequence, or (2) ventricular size and function assessed by cine SSFP.

Demographic, clinical, and procedural data were abstracted from the medical record. Cardiac anatomy was determined based on all available diagnostic data and intraoperative observation. The anatomy of the coronary arteries was determined by intraoperative inspection as documented in the operative report and described according to Blume et al.<sup>8</sup> The presence of symptoms was ascertained from the medical records and was classified as none (asymptomatic) or having 1 or more of the following: (1) palpitations, (2) chest pain, or (3) exercise intolerance. The Boston Children's Hospital Committee on Clinical Investigation approved the study protocol and waived requirement for informed consent.

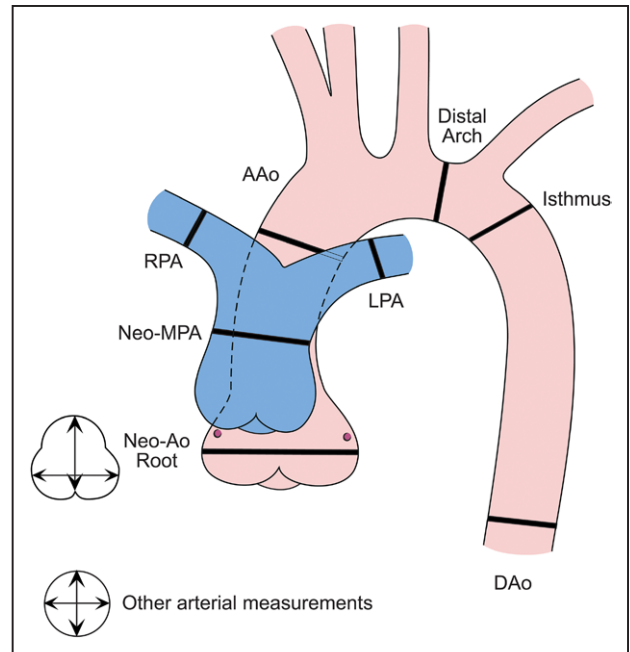
### CMR Imaging

CMR examinations were performed on a 1.5T scanner (Signa Horizon LX or TwinSpeed, GE Medical Systems, Milwaukee, WI, from 1998 through June 2004; and Philips Achieva, Philips Healthcare, Best, the Netherlands, since July 2005). Young patients who were unable to cooperate with the examination were imaged under general anesthesia as previously described.<sup>9</sup> The standardized imaging protocol for ASO patients described by Fratz et al<sup>10</sup> was utilized. Briefly, the following sequences were acquired: (1) nongated localizing images; (2) electrocardiographically gated cine SSFP in ventricular long- and short-axis planes, long-axis planes of the LV and right ventricular (RV) outflow tracts, and oblique planes to visualize the branch pulmonary arteries; (3) contrast-enhanced (Gadopentetate dimeglumine; Bayer HealthCare Pharmaceuticals, Wayne, NJ) or noncontrast isotropic 3D SSFP magnetic resonance angiogram for assessment of the great vessels; (4) flow measurements in the ascending aorta (AAo), main pulmonary artery (MPA), and branch pulmonary arteries; and (5) LGE imaging in ventricular long- and short-axis planes 10 to 15 minutes after contrast administration.

### CMR Measurements

LV and RV end-diastolic and end-systolic volumes, stroke volumes, ejection fractions (EFs), and mass were measured from a stack of cine SSFP short-axis images as described by Alfakih et al.<sup>11</sup> Flow measurements were performed in a standard fashion as previously described.<sup>12</sup> Ventricular volumes and flow measurements were performed using commercial software (QMass version 6.2.3 and QFlow version 4.1.7; Medis, Leiden, the Netherlands).

Measurements of the neo-aorta, neo-MPA, and branch pulmonary arteries were performed on a commercial computer workstation (Extended MR Workspace version 2.6; Philips Medical Systems, Best, the Netherlands). Diameters were evaluated by constructing user-defined subvolume maximum intensity projections and multiplanar reformatted images as previously described.<sup>13</sup> Aortic measurements were obtained at the following 5 levels (Figure 1): neo-aortic root, mid-AAo, distal transverse arch, isthmus, and descending aorta at the level of the diaphragm. Each aortic segment was reformatted in a double oblique plane, and 2 orthogonal measurements were recorded at each level as described by Kaiser et al.<sup>14</sup> The aortic root was measured from sinus-to-commissure in one dimension (labeled as anteroposterior [AP]) and cusp-to-cusp in the other (labeled as lateral dimension) according to the method of Burman et al.<sup>15</sup> The



**Figure 1.** Diagram showing arterial measurements by magnetic resonance angiography. AAO indicates ascending aorta; DAo, descending aorta; LPA, left pulmonary artery; MPA, main pulmonary artery; and RPA, right pulmonary artery.

pulmonary arteries were similarly measured as described by Knobel et al.<sup>16</sup> Body surface area (BSA) at the time of CMR was calculated from the patient height and weight using the method of Haycock et al.<sup>17</sup> Volumetric measurements were adjusted to BSA<sup>1,3</sup>, and linear measurements were indexed to BSA<sup>0.5</sup>.<sup>18-20</sup> *z* scores were calculated from published normal values.<sup>11,14,16</sup>

### Statistical Analysis

Data were summarized as number and percentage for categorical variables, mean±standard deviation for normally distributed continuous variables, and median (25th, 75th percentiles) and range for continuous data with a skewed distribution. For descriptive analyses of CMR data, the most recent CMR was summarized. For ventricular and great vessel size, *z* scores >−2.00 and <+2.00 were considered within normal limit. Mild dilatation was defined as *z* scores ≥+2.00 and <+4.00, and mild hypoplasia was defined as *z* scores ≤−2.00 and >−4.00. Moderate dilatation was defined as *z* scores ≥+4.00 and <+6.00, and moderate hypoplasia was defined as *z* scores ≤−4.00 and >−6.00. Severe dilatation was defined as *z* scores ≥+6.00, and severe hypoplasia was defined as *z* scores ≤−6.00.

For analyses of the relations between great vessel dimensions and time from ASO, CMR measurements were grouped across 5 predefined time periods (0–<10, 10–<15, 15–<20, 20–<25, and ≥25 years post-ASO); for subjects with >1 CMR, the most recent study was used for analysis. Of the 220 subjects, 154 (70%) had 1 CMR and 66 (30%) had 2 CMR studies. For those with 2 or more examinations, these additional studies were utilized to analyze aortic growth over time. Generalized estimating equation models with an exchangeable working correlation matrix were used to evaluate the association between binary outcomes (LV dysfunction defined as EF <55%, LV dilation defined as *z* score >2, and moderate or greater aortic regurgitation defined as regurgitation fraction >20%) and study variables (demographic and clinical characteristics and CMR parameters). For each outcome, study variables with a univariate *P*<0.2 were included in a forward-selection model building procedure to identify the most parsimonious model. The multivariable models include time since ASO to account for varying follow-up times among the patients.

Generalized estimating equation models were also used to evaluate the association between the great vessel dimensions (neo-aortic

root, neo-MPA, and branch pulmonary arteries diameter  $z$  scores) and the study variables, accounting for time since ASO. In addition to time since ASO, the models considered sex and the time by sex interaction as covariates. However, because these terms were not significant for any model, they were not included in further analyses. Finally, generalized estimating equation models were used to evaluate bivariate associations between aortic regurgitation fraction and LV size, neo-aortic root size, and heart rate (HR) at CMR.

Statistical analysis was performed using SAS version 9.3 (SAS Institute, Cary NC). All tests were 2-sided, and statistical significance was set at 0.05.

## Results

### Patients

The demographic and anatomic characteristics of the 220 study patients are summarized in Table 1. Most patients (93%)

**Table 1. Demographic and Anatomic Characteristics (n=220)**

	Median (range) or n (%)
Male sex	147 (66.8)
Age at ASO, d	5 (1–334)
Age at CMR, y	15.4 (0.1–29)
Interval between ASO and CMR, y	15.3 (0.1–29)
Height, cm	156.8 (60–193)
Weight, kg	52.2 (5.9–137.3)
Body surface area, m <sup>2</sup>	1.55 (0.23–2.72)
BMI, kg/m <sup>2</sup>	22.3 (12–45)
Underweight (BMI <18.5 kg/m <sup>2</sup> )	56 (25.4)
Normal (BMI ≥18.5 but <25 kg/m <sup>2</sup> )	107 (48.6)
Overweight (BMI ≥25 but <30 kg/m <sup>2</sup> )	36 (16.4)
Obese (BMI ≥30 kg/m <sup>2</sup> )	21 (9.6)
Heart rate at CMR	78 (45–160)
<b>Anatomic diagnoses*</b>	
D-loop TGA	205 (93.2)
VSD	94 (42.7)
Subvalvar or valvar PS	23 (10.5)
Subvalvar or valvar AS	19 (8.7)
Coarctation	25 (11.4)
Double-outlet right ventricle	15 (6.8)
<b>Coronary artery anatomy, n=203</b>	
Usual for D-loop TGA	139 (68.5)
Left circumflex from right sinus	28 (13.8)
Inverted left circumflex and RCA	11 (5.4)
Single RCA	10 (4.9)
Single LCA	5 (2.5)
Intramural LCA	2 (0.9)
Other	8 (3.9)

AS indicates aortic stenosis; ASO, arterial switch operation; BMI, body mass index; CMR, cardiovascular magnetic resonance; LCA, left coronary artery; PS, pulmonary stenosis; RCA, right coronary artery; TGA, transposition of the great arteries; and VSD, ventricular septal defect.

\*Some patients had multiple associated anomalies.

had D-loop TGA, and the remaining had double-outlet RV with a subpulmonary ventricular septal defect (Taussig–Bing anomaly). Approximately half the patients had TGA with intact ventricular septum and no associated anomalies except for an atrial communication or a patent ductus arteriosus (so-called simple TGA). The other half had a ventricular septal defect or additional associated anomalies. Notably, only 49% of the patients had a body mass index within normal limits at the time of CMR; 25% had subnormal values and 26% were either overweight or obese.

The operative and interventional catheterization procedures of the study patients are detailed in Table 2. Surgical and transcatheter interventions to relieve pulmonary arterial obstruction were the most prevalent procedures after the ASO. Of the 220 patients, 8 (3.6%) underwent reoperation for coronary obstruction.

### Ventricular Size, Function, and Viability

LV and RV volumes, EFs, mass, and mass-to-volume ratio are summarized in Table 3. On average, the left and right ventricles were mildly enlarged compared with published normal controls (LV end-diastolic volume [EDV]  $z$  score  $0.48 \pm 1.76$  and RVEDV  $z$  score  $0.33 \pm 1.5$  versus  $0.0 \pm 2.0$ ;  $P=0.0003$  and  $0.0038$ , respectively). Of the 214 patients with measurable ventricular volumes, 136 (74%) had normal LVEDV, 29 (16%)

**Table 2. Surgical Procedures and Interventional Catheterizations (n=220)**

	n (%)
<b>Operations before ASO</b>	
Aortopulmonary shunt	9 (4.1)
Pulmonary artery band	9 (4.1)
Aortic arch repair	3 (1.4)
<b>Operations concomitant with ASO</b>	
VSD closure	76 (34.5)
Aortic arch repair	17 (7.7)
Neopulmonary artery augmentation	8 (3.6)
Atrioventricular valve repair	3 (1.4)
Other	13 (5.9)
<b>Operations after ASO</b>	
Neopulmonary valve/artery repair or replacement	25 (11.4)
Branch pulmonary artery augmentation	20 (9.1)
Neo-aortic valve/root repair or replacement	18 (8.2)
Coronary artery intervention	8 (3.6)
Aortic arch repair	5 (2.3)
<b>Catheter interventions after ASO</b>	
Branch pulmonary artery dilation/stent	34 (15.5)
Main pulmonary artery dilation/stent	28 (12.7)
Aortic arch dilation/stent	8 (3.6)
Other	10 (4.5)

All procedures were before cardiovascular magnetic resonance. ASO indicates arterial switch operation; and VSD, ventricular septal defect.

**Table 3. Range of Ventricular Dimensions and Function in 214 Patients After ASO**

	Mean	SD	Median	25th, 75th, %	Minimum to Maximum
<b>Left ventricle</b>					
EDVi (mL/BSA)	99.4	23.2	95.5	85.2, 108.9	59.5 to 220.6
EDVi (mL/BSA <sup>1.3</sup> )	88.6	23.3	84.7	76.2, 97.4	52 to 246.2
EDV z score	0.48	1.76	0.42	-0.70, 1.50	-2.48 to 8.06
ESVi (mL/BSA)	40.6	12.9	37.9	32.7, 45.6	15.6 to 109.5
ESVi (mL/BSA <sup>1.3</sup> )	36.4	12.2	34.2	29.7, 40.5	14.6 to 102.2
LVSv index (mL/m <sup>2</sup> )	58.5	13.9	57.2	50.2, 64.6	19.0 to 145.9
LVEF (%)	59.2	6.5	59.4	55.4, 63.0	29.1 to 73.7
Mass index (g/BSA)	56.7	13.0	54.3	47.1, 64.3	33.7 to 111.9
Mass index (g/BSA <sup>1.3</sup> )	50.4	12.4	48.3	42.1, 56.2	31.3 to 124.9
Mass z score	-1.04	1.45	-1.13	-2.07, -0.09	-3.95 to 3.01
Mass/volume ratio	0.59	0.14	0.58	0.51, 0.63	0.33 to 1.53
<b>Right ventricle</b>					
EDVi (mL/BSA)	98.5	22.5	95.7	84.7, 110.4	33.4 to 193.9
EDVi (mL/BSA <sup>1.3</sup> )	87.5	20.8	85.1	74.4, 97.2	50.6 to 210.1
EDV z score	0.33	1.53	0.26	-0.82, 1.49	-2.79 to 4.76
ESVi (mL/BSA)	41.7	13.7	39.6	32.99, 47.4	12.4 to 106.2
ESVi (mL/BSA <sup>1.3</sup> )	37.1	12.0	34.7	28.9, 42.5	16.4 to 99.1
RVSv index (mL/m <sup>2</sup> )	56.5	11.9	55.6	49.3, 63.3	21.0 to 107.7
RVEF (%)	57.9	6.34	57.8	53.8, 62.0	37.5 to 76.4
Mass index (g/BSA)	23.3	7.3	22.2	19.1, 26.4	9.3 to 59.9
Mass index (g/BSA <sup>1.3</sup> )	20.7	6.5	19.0	16.7, 23.9	8.6 to 49.2
Mass/volume ratio	0.24	0.07	0.23	0.20, 0.27	0.11 to 0.55

ASO indicates arterial switch operation; BSA, body surface area; EDV, end-diastolic volume; EDVi, end-diastolic volume index; EF, ejection fraction; ESV, end-systolic volume; ESVi, end-systolic volume index; LV, left ventricle; RV, right ventricle; SD, standard deviation; and SV, stroke volume.

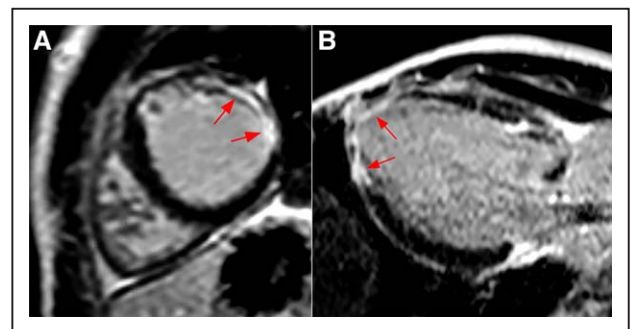
had mild dilatation, 3 (1.6%) had moderate dilatation, and 2 (1.1%) had severe dilatation. LVEDV index was inversely related to HR with a 1 beat/min decrease in HR associated with 0.32 mL/m<sup>2</sup> increase in LVEDV index (95% confidence interval [CI], 0.21–0.43;  $P < 0.0001$ ). RVEDV z score was normal in 148 patients (80%), mildly dilated in 25 (13.5%), and moderately dilated in 2 (1.1%). No patient had severe RV dilatation. Similar to the LV, RVEDV index was inversely related to HR with a 1 beat/min decrease in HR associated with 0.43 mL/m<sup>2</sup> increase in RVEDV index (95% CI, 0.31–0.54;  $P < 0.0001$ ).

The majority of patients (168, 78.5%) had normal global LV systolic function (EF  $\geq 55\%$ ). Of the remaining patients, 43 (21%) had mild dysfunction (EF 54–40%), 2 (0.9%) had moderate dysfunction (EF 39–30%), and 1 (0.5%) had severe dysfunction (EF  $< 30\%$ ). Similarly, most patients (204, 94.9%) had normal RVEF (EF  $\geq 48\%$ ). Of the remaining patients, 11 (5.1%) had mild dysfunction (EF 47–35%), and no subject had moderate or severe RV dysfunction.

A total of 173 patients (78.6%) demonstrated no pathological pattern of LGE on myocardial delayed enhancement imaging. In 43 patients (19.6%), there was LGE in either the inferior or the superior septal-free wall junction, or both. The remaining 4 patients (1.8%) exhibited LGE pattern consistent

with a myocardial ischemia (Figure 2): 2 in the inferior-septal segment, 2 in the anterolateral, and 1 each in the apical lateral and anterior-basal segments.

Univariate analysis identified several parameters to be associated with LV dilatation (defined as EDV z score  $> 2.0$ ), including older age at ASO, increased time since ASO, higher



**Figure 2.** Myocardial scar (arrows) in the lateral and apical left ventricular (LV) segments in a 20-year-old arterial switch operation (ASO) patient demonstrated by late gadolinium enhancement (LGE) imaging. The left coronary was compressed between the dilated neo-aortic root and the neo-main pulmonary artery. **A**, Short-axis. **B**, Long-axis.

aortic regurgitation fraction, and RV dilatation or dysfunction. Similarly, parameters associated with LV dysfunction (defined as EF <55%) included male sex, higher aortic regurgitation fraction, and RV dilatation or dysfunction. Multivariable analyses identified higher RVEDV *z* score (OR, 3.16 for each unit increase; 95% CI, 1.94–5.17; *P*<0.0001) and higher aortic root AP diameter *z* score (OR, 1.36 for each unit increase; 95% CI, 1.05–1.77; *P*=0.0207) to be associated with LV dilatation and male sex (OR, 4.27; 95% CI, 1.6–11.47; *P*=0.0039) and lower RV EF *z* score (OR, 0.49 for each unit increase; 95% CI, 0.35–0.7; *P*<0.0001) to be associated with LV dysfunction. Notably, the presence of LGE, including enhancement of the septal-free wall junctions, was not associated with LV dilatation or dysfunction.

### Arterial Dimensions

Table 4 summarizes aortic dimensions and Table 5 pulmonary arterial diameters in 206 patients with measurable images. In general, the neo-aortic root was dilated in the AP (sinus-to-commissure) dimension in 157 patients (76%) with a mean *z* score of 3.5±1.9. Of those, neo-aortic root dilatation was mild in 54%, moderate in 29%, and severe in 17%. Only 49 patients (24%) had an AP dimension within normal limit. The lateral diameter of the neo-aortic root (sinus-to-sinus) was slightly larger than the AP diameter (2.87±0.4 versus 2.68±0.39 cm/BSA<sup>0.5</sup>; *P*<0.0001). The ratio between

the AP and the lateral diameters of the neo-aortic root was 0.93±0.06, indicating that on average the dilatation was symmetrical. In contrast to the neo-aortic root, the AAO at the level of the right pulmonary artery measured within normal limit in 147 patients (71.4%), with only 19 patients (9.2%) exhibiting dilatation (mild in 13, moderate in 4, and severe in 2). Furthermore, the AAO was mildly hypoplastic in 40 patients (19.4%). The distal transverse aortic arch and isthmus were generally mildly enlarged compared with normal controls, whereas the descending aorta diameter at the diaphragm was normal in most patients.

Compared with published normal controls, the AP diameter of the neo-MPA was mildly hypoplastic (mean *z* score -3.3±1.8), whereas the lateral diameter was generally normal (mean *z* score -0.66±1.5). Right pulmonary artery diameters generally measured within normal limit, whereas left pulmonary artery diameters were mildly hypoplastic in both AP and superior-inferior dimensions (Table 5). The average branch PA flow distribution was 54.3±9.2% in the right pulmonary artery and 45.7±9.2% in the left pulmonary artery.

Generalized estimating equation models were constructed to evaluate the association between time since ASO and arterial dimensions. For each year after ASO, the AP diameter of the neo-aortic root *z* score increased 0.03 points (95% CI, 0.002–0.06; *P*=0.035; Figure 3). Other aortic dimensions were

**Table 4. Aortic Dimensions in 206 Patients After ASO**

Variable	Mean	SD	Median	25th, 75th, %	Minimum to Maximum
<b>Aortic root</b>					
A-P diameter (cm/BSA <sup>0.5</sup> )*	2.68	0.39	2.63	2.39, 2.90	1.81 to 4.07
A-P diameter <i>z</i> score	3.54	1.91	3.27	2.05, 4.89	-0.84 to 9.37
Lateral diameter (cm/BSA <sup>0.5</sup> )†	2.87	0.40	2.81	2.60, 3.14	1.99 to 4.36
<b>Ascending aorta</b>					
A-P diameter (cm/BSA <sup>0.5</sup> )	1.73	0.32	1.75	1.52, 1.86	1.11 to 2.96
A-P diameter <i>z</i> score	-0.26	1.91	-0.32	-1.56, 0.64	-5.13 to 7.41
Lateral diameter (cm/BSA <sup>0.5</sup> )	1.73	0.32	1.70	1.5, 1.85	1.00 to 3.20
<b>Distal transverse arch</b>					
R-L diameter (cm/BSA <sup>0.5</sup> )	1.63	0.24	1.60	1.47, 1.79	0.98 to 2.43
R-L <i>z</i> score	1.82	2.29	1.53	0.33, 3.30	-5.87 to 8.35
S-I (cm/BSA <sup>0.5</sup> )	1.64	0.24	1.62	1.48, 1.77	1.00 to 2.33
<b>Aortic isthmus</b>					
A-P diameter (cm/BSA <sup>0.5</sup> )	1.53	0.23	1.54	1.41, 1.67	0.72 to 2.07
A-P diameter <i>z</i> score	1.31	1.94	1.34	0.33, 2.45	-7.52 to 6.32
Lateral diameter (cm/BSA <sup>0.5</sup> )	1.52	0.23	1.53	1.41, 1.67	0.64 to 2.09
<b>Descending aorta</b>					
A-P diameter (cm/BSA <sup>0.5</sup> )	1.17	0.13	1.15	1.08, 1.25	0.84 to 2.01
A-P diameter <i>z</i> score	0.70	1.16	0.57	-0.08, 1.45	-2.33 to 4.74
Lateral diameter (cm/BSA <sup>0.5</sup> )	1.18	0.14	1.17	1.08, 1.26	0.88 to 2.15

A-P indicates antero-posterior; ASO, arterial switch operation; BSA, body surface area; R-L, right-left; SD, standard deviation; and S-I, superior-inferior.

\*Measurement from sinus to commissure.<sup>15</sup>

†Measurement from sinus to sinus.

**Table 5. Pulmonary Artery Dimensions and Flow Distribution in 206 Patients After ASO**

Variable	Mean	SD	Median	25th, 75th, %	Minimum to Maximum
<b>Main pulmonary artery</b>					
A-P diameter (mm/BSA <sup>0.5</sup> )	1.28	0.30	1.27	1.07, 1.47	0.60 to 2.86
A-P diameter z score	-3.27	1.78	-3.19	-4.42, -2.07	-8.57 to 1.90
Lateral diameter (mm/BSA <sup>0.5</sup> )	1.61	0.35	1.57	1.35, 1.80	0.86 to 2.84
Lateral diameter z score	-0.66	1.50	-0.70	-1.76, 0.13	-3.82 to 5.20
<b>RPA</b>					
A-P diameter (mm/BSA <sup>0.5</sup> )	1.00	0.32	0.98	0.81, 1.17	0.27 to 1.92
A-P diameter z score	-0.96	2.39	-1.13	-2.53, 0.26	-5.97 to 6.29
S-I diameter (mm/BSA <sup>0.5</sup> )	1.27	0.35	1.26	1.03, 1.49	0.39 to 2.33
S-I diameter z score	-0.68	2.50	-0.64	-2.33, 0.78	-7.08 to 7.08
<b>LPA</b>					
A-P diameter (mm/BSA <sup>0.5</sup> )	0.85	0.30	0.81	0.65, 1.04	0.28 to 1.89
A-P diameter z score	-3.82	2.78	-4.22	-5.74, -1.94	-9.95 to 6.59
S-I diameter (mm/BSA <sup>0.5</sup> )	1.04	0.32	1.04	0.80, 1.25	0.30 to 2.19
S-I diameter z score	-3.12	2.27	-3.03	-4.55, -1.82	-8.71 to 4.10
<b>Branch PA flow distribution</b>					
RPA (%)	54.3	9.2	53.7	48.5, 59.1	32.0 to 88.5
LPA (%)	45.7	9.2	46.3	40.9, 51.5	11.5 to 67.9

A-P indicates antero-posterior; ASO, arterial switch operation; BSA, body surface area; LPA, left pulmonary artery; RPA, right pulmonary artery; SD, standard deviation; and S-I, superior-inferior.

not significantly associated with time since ASO. On the pulmonary arterial side, the MPA diameter z score decreased 0.04 points for each year after ASO (95% CI, -0.073 to -0.004;  $P=0.031$ ) and the left pulmonary artery diameter z score decreased 0.07 points (95% CI, -0.117 to -0.026;  $P=0.002$ ). Right pulmonary artery diameter z score was not significantly associated with time since ASO.

### Semilunar Valve Function

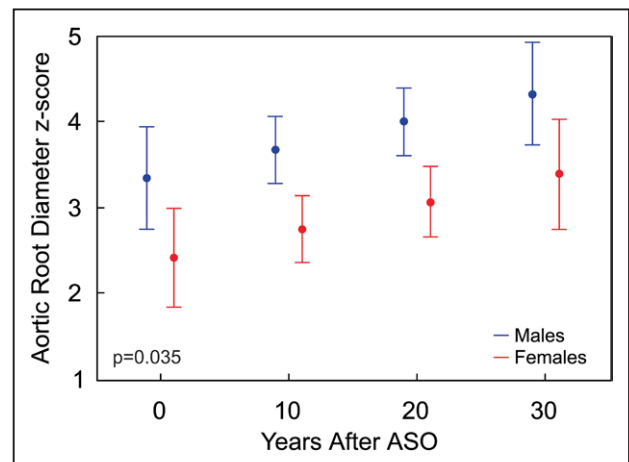
Flow measurements in the proximal neo-aorta ( $n=206$ ) and neo-MPA ( $n=178$ ) allowed measurements of semilunar valve regurgitation. The mean neo-aortic and neopulmonary valve regurgitation fractions were  $7.1\pm 9.1\%$  and  $6.5\pm 7.4\%$ , respectively (median 4% for both). Of the 206 patients with flow measurements in the proximal aorta, 118 (57.3%) had none or trivial neo-aortic regurgitation (regurgitation fraction  $<5\%$ ); 72 (35%) had mild (regurgitation fraction 5–20%), and 16 (7.7%) had moderate or greater neo-aortic regurgitation (regurgitation fraction  $>20\%$ ). Similarly on the pulmonary side, 105 (59%) had none or trivial regurgitation, 57 (32%) had mild, and 16 (9%) had moderate or greater neopulmonary regurgitation.

By univariate analysis, moderate or worse neo-aortic regurgitation was associated with a larger aortic root diameter (OR, 4.36 for 1 mm/BSA<sup>0.5</sup> increase; 95% CI, 1.66–11.5;  $P=0.0029$ ) and a larger diameter of the AAo (OR, 1.24 for 1 mm/BSA<sup>0.5</sup> increase; 95% CI, 1.03–1.49;  $P=0.021$ ). Age at ASO, time since ASO, diagnosis of double-outlet RV, and RV parameters were not associated with moderate or worse neo-aortic regurgitation. By multivariable analysis, a 1-mm increase in aortic

root lateral diameter indexed to BSA<sup>0.5</sup> was associated with a 5.29-fold increase in the odds of moderate or greater aortic regurgitation (95% CI, 1.88–14.9;  $P=0.0016$ ). There was no association between time since ASO and the odds of moderate or greater aortic regurgitation ( $P=0.99$ ).

### Symptoms and CMR Parameters

The majority (80.5%) of patients were asymptomatic. Of the 43 patients (19.5%) who reported symptoms, 16 (37%)



**Figure 3.** Neo-aortic root diameter z score by time since the arterial switch operation, stratified by sex. Data are mean estimates  $\pm 95\%$  confidence intervals.  $P$  value corresponds to the main effect of sex, generated from a generalized estimating equation model with an unstructured working correlation matrix and main effects for time since arterial switch operation (ASO) and sex.

had palpitations, 27 (63%) had chest pain, 4 (9%) had exercise intolerance, and 4 (9%) had 2 or more symptoms. Compared with asymptomatic patients, those with symptoms did not have a higher prevalence of LV dilatation, positive LGE, neo-AR, or higher frequency of post-ASO surgical or catheterization procedures. The prevalence of LV dysfunction tended to be higher in symptomatic patients (33% versus 19%;  $P=0.0573$ ).

### Discussion

With improved early and midterm survival of patients with D-loop TGA and related anomalies undergoing the ASO, attention has shifted from early mortality to the long-term sequelae of the procedure. Specifically, progressive neo-aortic root dilatation, neo-AR, LV enlargement or dysfunction, and coronary insufficiency are some of the abnormalities seen in adolescents and adults after the ASO.<sup>3</sup> Although transthoracic echocardiography is capable of providing most of the clinically relevant diagnostic information in infants and young children, its ability to quantitatively assess biventricular size and function, valve regurgitation, and great vessel dimensions and flow diminishes in older patients because of worsening acoustic windows.<sup>4</sup> Furthermore, the role of echocardiography in the assessment of coronary insufficiency is limited. These weaknesses are overcome by CMR, which assumes an important role in the routine evaluation of ASO patients as they transition from childhood to adolescence.<sup>7</sup> However, despite its established role in congenital cardiac practice, the literature on CMR after the ASO comprises only small case series.<sup>6,21,22</sup> The present study is the first to characterize the range of biventricular size and function, great vessel dimensions, semilunar valve function, and myocardial viability in a large cohort of mostly asymptomatic adolescents and young adult patients followed in a single center in which CMR has been used routinely in this patient group starting in the second decade of life.<sup>23</sup> The reference data presented here can be used to determine how individual patients compare with their peers.

Although enlargement of the neo-aortic root is ubiquitous after the ASO, it is unclear whether the dilatation stabilizes or worsens as patients reach adolescence or adulthood. Although several echocardiographic studies conducted predominantly in children have suggested that neo-aortic root growth rate is commensurate with somatic growth,<sup>24</sup> we found a significantly higher growth rate compared with control subjects. Our findings are in agreement with those of van der Bom et al<sup>25</sup> who applied a similar analytic technique in a study of 116 adult ASO patients. In addition, multivariable analysis in our cohort showed that neo-aortic root dilatation was associated with moderate or greater neo-AR with each millimeter/BSA<sup>0.5</sup> increase in root diameter associated with a 5.29-fold increase in the likelihood of greater than or equal to moderate AR. Overall, the frequency of at least mild AR in our cohort (43%) was slightly lower than the echocardiographic findings of Tobler et al<sup>26</sup> (52%), possibly reflecting differences between modalities. However, the prevalence of moderate or worse AR was low in both studies. Notably, dimensions of the aorta distal to the root in this study were mostly comparable with normal controls. On the pulmonary side, we found that

the neo-MPA has, on average, an oval shape with decreased AP diameter and normal lateral diameter. The calibers of the branch pulmonary arteries were smaller than in normal individuals, but the differential branch PA flow distribution was nearly normal.

Little information exists about ventricular size and function late after the ASO. This study found that majority of patients had normal LVEDVs and RVEDVs. However, 26% had LV dilation (severe in only 1.1%) and 20% had RV dilatation (none was severe). As expected, ventricular volumes were inversely related to HR. Hence, chronotropic incompetence is a likely contributor to ventricular enlargement in this cohort. Similarly, most patients had normal global LV and RV systolic function. However, 21.5% of patients had LV dysfunction (mostly mild), and only 5.1% had mildly depressed RV dysfunction. These observations are in accord with much smaller series that evaluated LV size and function by strain imaging echocardiography and by CMR. In a study of 22 patients at a mean age of 12 years, Pettersen et al<sup>27</sup> demonstrated that compared with controls, ASO patients had significantly reduced LV and RV global longitudinal strain, as well as LV torsion. Grotenhuis et al<sup>28</sup> in a study of 15 ASO patients by CMR found increased LVEDV and decreased LVEF compared with age-matched control subjects. Another study of 22 ASO patients identified increased flow velocities in the pulmonary arteries, RV hypertrophy, and abnormal RV relaxation parameters even in the absence of anatomic narrowing of the pulmonary arteries.<sup>29</sup>

Myocardial ischemia and infarction associated with coronary stenosis related to their transfer to the neo-aortic root during the ASO has been a focus of attention.<sup>3</sup> Although several small studies have reported on assessment of the coronary arteries and myocardial viability by echocardiography, computed tomography, nuclear scintigraphy, and CMR, little is known about the prevalence of coronary ischemia sufficient to cause myocardial fibrosis. In this cohort, LGE was noted in  $\approx 20\%$  of patients. However, most had a nonischemic pattern, with the majority having small focal enhancement in the septal-free wall junction. Only 4 patients (1.8%) had an LGE pattern consistent with myocardial ischemia. With such low prevalence, it is not surprising that previous small studies often did not identify evidence of myocardial ischemia.<sup>6,22,30</sup> Furthermore, we found no significant difference between those with and those without LGE with regard to symptoms.

### Limitations

Although the retrospective study design imposes some inherent limitations, the CMR imaging protocol applied to patients after the ASO in our institution has been consistent. We have not included information on morphological assessment of the origin and proximal course of the coronary arteries because this particular imaging technology has become robust only in recent years. Although it is conceivable that referral bias may have resulted in a cohort that does not represent all ASO patients, 2 observations suggest that if such bias exists it is minimal. First, CMR has been used for routine noninvasive surveillance of adolescent and young adult patients at our institution during the latter part of the study period when

the majority of patients were examined. Second, patient characteristics (eg, demographics, frequencies of associated anomalies and coronary anatomy, and rates and types of reinterventions) were similar to those reported in large series of ASO patients from our institution and elsewhere that have not required CMR for inclusion.<sup>2,8</sup>

### Conclusion

In this relatively large cohort of mostly asymptomatic adolescents and young adult ASO patients evaluated by CMR, most had normal biventricular size and function, only 1.8% had evidence of myocardial scar, and most had mild or less AR. However, an important minority exhibited LV dilatation and dysfunction and significant AR. The size of the neo-aortic root increased as a function of time after ASO and was strongly associated with the degree of AR. The findings of this study provide reference values against which ASO patients can be compared with their peers.

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### Disclosures

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### CLINICAL PERSPECTIVE

The excellent survival rate of the arterial switch operation for transposition of the great arteries and other conotruncal anomalies has resulted in a growing population of adolescents and young adult patients with anatomic palliation of their congenital heart disease. However, little information is available on the cardiovascular magnetic resonance findings in this population. This study analyzed the cardiovascular magnetic resonance characteristics of 220 consecutive patients who underwent the arterial switch operation at Boston Children’s Hospital at a median age of 5 days and had a cardiovascular magnetic resonance at a median age of 15.4 years (range, 0.1–29 years). Left or right ventricular enlargement was found in 26% and 20% of patients, respectively. Left ventricular systolic dysfunction was present in 21.5% of patients (mild in most) and right ventricular dysfunction in 5.1%. Myocardial scar was detected by late gadolinium enhancement imaging in 1.8% of patients. Dilatation of the neo-aortic root was common (76%), and root  $z$  score increased at an average rate of 0.03 points per year. Trivial neo-aortic valve regurgitation was common, 35% had mild regurgitation, and 8% had moderate or severe regurgitation. Multivariable analysis identified the maximum diameter of the neo-aortic root to be associated with worse neo-aortic regurgitation. The diameters of the thoracic aorta distal to the root were near-normal in most patients, whereas the neomain pulmonary artery was typically oval-shaped with decreased anteroposterior and normal lateral diameters. The findings of this study provide reference values against which arterial switch operation patients can be compared with their peers.

**Cardiovascular Magnetic Resonance Findings Late After the Arterial Switch Operation**  
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