Cardiovascular Outcomes After the Arterial Switch Operation for D-Transposition of the Great Arteries

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Background—Data regarding long-term outcomes after the arterial switch operation for D-transposition of the great arteries are scarce.

Methods and Results—A single-institution retrospective cohort study was conducted to assess cardiovascular outcomes after an arterial switch operation between 1983 and 1999. Patients without follow-up visits within 3 years were contacted and secondary sources of information obtained. Overall, 400 patients, 154 (38.3%) with a ventricular septal defect, 238 (59.5%) with an intact septum, and 9 (2.3%) with a Taussig-Bing anomaly, were followed for a median of 18.7 years. In perioperative survivors, overall and arrhythmia-free survival rates at 25 years were 96.7±1.8% and 96.6±0.1%, respectively. Late mortality was predominantly a result of sudden deaths and myocardial infarction. At 25 years, 75.5±2.5% remained free from surgical or catheter-based reintervention. Freedom from an adverse cardiovascular event was 92.9±1.9% at 25 years. Independent predictors were a single right coronary artery (hazard ratio, 4.58; 95% confidence interval, 1.32-15.90, \( P = 0.0166 \)) and postoperative heart failure (hazard ratio, 6.93; 95% confidence interval, 1.57-30.62; \( P = 0.0107 \)). At last follow-up, the left ventricular ejection fraction was 60.3±8.9%, 97.3% had class I symptoms, and 5.2% obstructive coronary artery disease. Peak oxygen uptake was 35.1±7.6 mL/kg/min (86.1±15.1% predicted), with a chronotropic index <80% in 34.2%. At least moderate neoaortic and pulmonary regurgitation were present in 3.4% and 6.6%, respectively, and more than mild neoaortic and pulmonary stenosis in 3.2% and 10.3%.

Conclusions—Long-term and arrhythmia-free survival is excellent after arterial switch operation. Although sequelae include chronotropic incompetence and neoaortic, pulmonary, and coronary artery complications, most patients maintain normal systolic function and exercise capacity. (Circulation. 2013;127:331–339.)

Key Words: mortality ▪ survival ▪ transposition of the great arteries

D-looped transposition of the great arteries (D-TGA) accounts for 5% to 7% of congenital heart defects.\(^1\) Intra-atrial baffle repair, as pioneered by Senning\(^2\) and Mustard,\(^3\) radically altered the otherwise grim associated prognosis, allowing most patients with D-TGA to thrive well into adulthood.\(^4\) However, recognized long-term complications include systemic right ventricular dysfunction, brady- and tachyarrhythmias, baffle obstructions and shunts, and sudden death.\(^4\)–\(^7\)

Clinical Perspective on p 339

In the mid 1970s, Jatene developed the arterial switch operation (ASO),\(^8\) which soon after supplanted atrial redirection as the preferred surgical option for D-TGA without pulmonary stenosis. It involves translocating the pulmonary artery and aorta above their sinuses and reimplanting the ostia of the coronary arteries in the neoaorta. The so-called Lecompte maneuver may be performed to place the main pulmonary artery bifurcation anterior to the ascending aorta.\(^9\) The ASO allows the morphological left ventricle to remain systemic and avoids multiple atrial incisions and suture lines that predispose to arrhythmias. Midterm results appear favorable, although identified complications include aortic insufficiency, pulmonary stenosis, and obstructive coronary disease.\(^10\)–\(^14\) Follow-up data beyond a median of 5 to 10 years remain scarce.\(^10\)–\(^17\) We therefore sought to characterize longer-term survival and cardiovascular outcomes in a single-center early cohort of patients with D-TGA and ASO.

Materials and Methods

Study Population

We included all patients with D-TGA or a Taussig-Bing anomaly who had an ASO at Boston Children’s Hospital between January 1983 and December 1999 and a last known permanent contact address in the New England area. Eligible candidates were identified by searching...

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institutional databases in the Departments of Cardiac Surgery and Cardiology. Patients without follow-up data within 3 years were contacted by mail and telephone, and questioned about their health status since last seen at our institution. For patients under 18 years of age, parents or guardians were contacted instead. When relevant, consent was obtained via mailed medical record release forms to supplement follow-up data with information from secondary sources (ie, from other physician and hospital encounters). The study was conducted in accordance with guidelines from the Committee on Clinical Investigation and approved by the institutional review board.

Primary anatomic subtypes were classified as D-TGA with an intact ventricular septum, D-TGA with ≥1 ventricular septal defects, or a Taussig-Bing anomaly.2 The aortic arch was considered abnormal in the presence of aortic coarctation, interruption, or hypoplasia. Atrioventricular valves were classified as abnormally attached if portions of the mitral or tricuspid valve were malaligned, or if they were associated with positional anomalies (ie, straddling or overriding). The coronary anatomy was categorized as usual; circumflex originating from the right coronary artery (RCA); single RCA; single left coronary artery (LCA), inverted coronary arteries, RCA originating from the left anterior descending (LAD) artery; intramural LCA; intramural LAD with circumflex from RCA; single LCA with intramural RCA; intramural RCA, circumflex, and RCA separate from LAD; and other.20 Any variant other than usual was considered a coronary anomaly.

Clinical Variables and Follow-Up

Data were retrospectively collected from a detailed review of medical records, preoperative echocardiographic and cardiac catheterization data, operative notes, and follow-up reports, including physical examination, interventions, functional status, long-term complications, and noninvasive tests (ie, echocardiography, cardiac MRI, cardiopulmonary exercise testing, and nuclear imaging). Data quality checks consisted of identifying and tracking missing, incomplete, or inconsistent information. Invalid formats and codes were flagged and data queries issued to clarify and resolve discrepancies on a per-patient basis.

Surgical intervention was defined as any cardiovascular surgery subsequent to the ASO, including aortic arch, caval thrombosis, and coronary bypass surgery. An arrhythmic event was defined as documented atrial flutter/intra-atrial reentrant tachycardia, atrial fibrillation, bradycardia requiring pacemaker implantation, sustained ventricular tachycardia or fibrillation, resuscitated cardiac arrest, or sudden death of presumed arrhythmic etiology. The combined adverse cardiovascular event outcome consisted of an arrhythmic event, acute coronary syndrome, heart failure-related hospitalization, cerebrovascular accident, or cardiovascular death. The diagnosis of coronary arterial obstruction required documented stenosis ≥50% in at least 1 coronary artery, an acute coronary syndrome, or objective evidence of myocardial ischemia by exercise or perfusion imaging studies. An acute coronary syndrome was defined by electrocardiographic changes (ie, transient ST segment elevation ≥1 mm, ST segment depression ≥1 mm, new T wave inversion ≥1 mm, pseudonormalization of previously inverted T waves, new Q-waves [1/3 the height of the R wave or ≥0.04 seconds], new R wave > S wave in lead V1 [posterior MI], new left bundle-branch block), with an increase in cardiac enzymes (positive troponin I or T or CK-MB more than twice upper limit of normal).19

Echocardiographic assessment included color, continuous wave, and pulse wave Doppler data for all valves according to established criteria.20 Peak Doppler gradients were presented for neoaoartic and pulmonary valves, with values ≥25 mm Hg and ≥36 mm Hg considered to indicate at least moderate stenosis, respectively.21 The level of neoaoartic and pulmonary valve obstruction was further classified as subvalvular, valvular, and supravalvular. Obstruction at the level of left and right pulmonary arteries was also assessed. Estimates of left ventricular ejection fractions were based on all available echocardiographic data, as per standard practice. Aortic dimensions were measured at the level of the annulus, root, sinotubular junction, and ascending aorta when at their maximum in the cardiac cycle. For parameters duplicated by cardiac magnetic resonance imaging (ie, left ventricular volumes and ejection fraction and aortic dimensions) within 1 year of echocardiography, cardiac magnetic resonance data were retained. In addition, right ventricular volumes and ejection fractions were assessed by cardiac magnetic resonance.

For cardiopulmonary exercise testing, peak oxygen consumption was defined as the highest value of oxygen uptake attained in the final 20 seconds of exercise when the respiratory exchange ratio was >1.09. Heart rate reserve was defined as peak heart rate – resting heart rate and chronotropic index as (peak heart rate – resting heart rate)/ (220 – age – resting heart rate).22 Chronotropic incompetence was defined as a failure to achieve a chronotropic index >80%.

Mode of Death

Mortality ascertainment was supplemented by linking to the National Death Index (www.cdc.gov/nchs/ndi.htm) and original source material was reviewed for all fatalities. Death was considered perioperative if it occurred within 30 days of surgery or before hospital discharge and was subclassified as early (ie, within 30 days) or late (ie, after 30 days but during the same hospitalization).23 Death was classified as secondary to heart failure if it complicated worsening heart failure, as defined by evidence of ≥1 of the following: orthopnea, nocturnal dyspnea, pulmonary edema, increasing peripheral edema, renal hypoperfusion (ie, worsening renal function), or radiological signs of congestive heart failure.24 Sudden death was defined as death occurring within 1 hour of acute symptoms.25 Death was considered secondary to myocardial infarction if it was preceded by a clinical presentation consistent with an acute coronary syndrome or if the diagnosis was confirmed by autopsy. Remaining deaths were classified as other.

Statistical Analysis

Continuous variables are summarized by mean±standard deviation or median and interquartile range (IQR; 25th, 75th percentile) depending on normality of distribution. Categorical variables are represented by frequencies and percentages. Baseline comparisons between patients with D-TGA and intact ventricular septum, ventricular septal defect, and Taussig-Bing anomaly were performed by 1-way analysis of variance (ANOVA), Kruskal-Wallis tests, or Fisher-Freeman-Halton tests, where appropriate.

Factors associated with perioperative mortality were explored in univariate and multivariate logistic regression analyses from which odds ratios (OR) and 95% confidence intervals (CI) were generated. For time-to-event analyses, time 0 was defined as time of ASO. Patient-time was accrued until the outcome of interest (ie, all-cause mortality, surgical or catheter-based reintervention, arrhythmic event, and adverse cardiovascular event), with censoring at the time of last follow-up. No patient underwent cardiac transplantation. Event-free survival was plotted using the Kaplan–Meier method, with comparisons by log-rank statistics. After verification of proportionality assumptions, univariate and stepwise multivariate Cox proportional hazards models were used to assess factors associated with the outcome of interest. Variables significant at the 0.2 level in univariate analyses were considered in the respective stepwise (P entry=0.05; P removal 0.10) multivariate logistic and Cox regression models. Correlations between normally distributed continuous variables were assessed using Pearson’s correlation coefficient. Two-tailed probability values <0.05 were considered statistically significant. Analyses were performed with SAS software Version 9.2 (SAS Institute, Cary, NC).

The authors had full access to and take full responsibility for the integrity of the data. All authors have read and agree to the manuscript as written.

Results

Baseline Characteristics

A total of 400 patients, 123 (30.8%) female, underwent ASO at a median age of 5 (IQR 3, 10) days. The ventricular septum was intact in 238 (59.5%) patients, 154 (38.3%) had ≥1 ventricular septal defect, and 9 (2.3%) had a Taussig-Bing anomaly. Twenty-six (6.5%) patients had aortic arch anomalies, 6 (1.5%) had a left ventricular outflow tract gradient ≥50 mm Hg, and 6 (1.5%) had abnormally attached atrioventricular valves. Coronary anomalies were present in
136 (34%) patients, the most common variant being a circumflex artery originating from the RCA (n=72). Baseline characteristics are summarized in Table 1.

**Perioperative Deaths**

Figure 1 provides an overview of vital status. Perioperative deaths occurred in 26 (6.5%) patients during a 17-year time-span. The perioperative mortality rate decreased significantly over time, from 15.1% (8 of 53) during the first 4 years (1983–1986) to 3.9% (4 of 103) during the final 4 years (1996–1999), \( P=0.0226 \). The only multivariate predictors of perioperative mortality were a Taussig-Bing anomaly (OR, 8.4; 95% CI, 2.0-35.6; \( P=0.0057 \)) and postoperative hemorrhage requiring surgical re-exploration (OR, 10.3; 95% CI, 1.9-56.6; \( P=0.0073 \)).

**Later Deaths**

During a median follow-up of 18.7 (IQR 14.7, 22.5) years, later deaths occurred in 6 of 374 (1.6%) perioperative survivors, yielding a survival rate of 99.2±0.5% at 10 years and 96.7±1.8% at 25 years. Three deaths in perioperative survivors were classified as sudden. A 15-year-old patient with suprasystemic pulmonary pressures and a circumflex artery originating from the RCA died suddenly at rest. A 24-year-old with a single RCA, postoperative complete heart block, severe left ventricular dysfunction, a biventricular implantable defibrillator, and recurrent episodes of ventricular tachycardia with appropriate shocks, was found in asystole. The third sudden death occurred in a 28-day-old infant 5 days after hospital discharge after ASO at 4 days of life, which was complicated by pulmonary hypertension.

Two deaths were attributable to myocardial infarction. The first occurred in a 6-week-old infant with inverted coronary arteries and a postoperative course complicated by severe left ventricular dysfunction and moderate right ventricular dysfunction. Autopsy revealed a recent biventricular myocardial infarction with occlusion of the ostial LCA and a <1-mm orifice of the RCA. The second death involved a child 2.5 months of age with a single RCA who presented with tachypnea, tachycardia, poor ventricular function, and ST depression over multiple electrocardiographic leads. Autopsy revealed a

### Table 1. Baseline Characteristics

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>All Patients n=400</th>
<th>TGA-IVS n=238</th>
<th>TGA-VSD n=153</th>
<th>Taussig-Bing n=9</th>
<th>( P )</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age,* days</td>
<td>5 (3, 10)</td>
<td>4 (3, 7)</td>
<td>6 (4, 24)</td>
<td>10 (2, 34)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Weight, kg</td>
<td>3.5±0.8</td>
<td>3.5±0.6</td>
<td>3.6±0.8</td>
<td>3.7±2.0</td>
<td>0.7288</td>
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<tr>
<td>Height, cm</td>
<td>51.3±4.5</td>
<td>50.8±3.6</td>
<td>51.8±5.1</td>
<td>53.5±9.4</td>
<td>0.0577</td>
</tr>
<tr>
<td>Female sex, n (%)</td>
<td>123 (30.8)</td>
<td>65 (27.3)</td>
<td>53 (34.6)</td>
<td>5 (55.6)</td>
<td>0.0849</td>
</tr>
<tr>
<td>Ethnicity, n (%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>0.5038</td>
</tr>
<tr>
<td>White</td>
<td>157 (39.3)</td>
<td>86 (36.1)</td>
<td>67 (43.8)</td>
<td>4 (44.4)</td>
<td></td>
</tr>
<tr>
<td>Hispanic</td>
<td>15 (3.8)</td>
<td>10 (4.2)</td>
<td>5 (3.3)</td>
<td>0 (0)</td>
<td></td>
</tr>
<tr>
<td>Black</td>
<td>4 (1.0)</td>
<td>3 (1.3)</td>
<td>1 (0.7)</td>
<td>0 (0)</td>
<td></td>
</tr>
<tr>
<td>Asian</td>
<td>11 (2.8)</td>
<td>5 (2.1)</td>
<td>5 (3.3)</td>
<td>1 (11.1)</td>
<td></td>
</tr>
<tr>
<td>Unknown</td>
<td>213 (53.3)</td>
<td>134 (56.3)</td>
<td>75 (49.0)</td>
<td>4 (44.4)</td>
<td></td>
</tr>
<tr>
<td>Associated malformations, n (%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Aortic arch anomaly(^\d)</td>
<td>26 (6.5)</td>
<td>4 (1.7)</td>
<td>16 (10.5)</td>
<td>6 (66.7)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Multiple VSDs</td>
<td>29 (7.2)</td>
<td>0 (0)</td>
<td>28 (18.3)</td>
<td>1 (11.1)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>LVOT gradient ≥50 mmHg</td>
<td>6 (1.5)</td>
<td>1 (0.4)</td>
<td>5 (3.3)</td>
<td>0 (0)</td>
<td>0.0724</td>
</tr>
<tr>
<td>Abnormal AVV attachment(^\d)</td>
<td>6 (1.5)</td>
<td>0 (0)</td>
<td>4 (2.6)</td>
<td>2 (22.2)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Coronary anatomy, n (%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>0.0664</td>
</tr>
<tr>
<td>Normal</td>
<td>264 (66.0)</td>
<td>167 (70.2)</td>
<td>94 (61.4)</td>
<td>4 (44.4)</td>
<td></td>
</tr>
<tr>
<td>Circumflex from RCA</td>
<td>72 (18.0)</td>
<td>45 (18.9)</td>
<td>25 (16.3)</td>
<td>2 (22.2)</td>
<td></td>
</tr>
<tr>
<td>Single RCA</td>
<td>17 (4.3)</td>
<td>8 (3.4)</td>
<td>8 (5.2)</td>
<td>1 (11.1)</td>
<td></td>
</tr>
<tr>
<td>Single LCA</td>
<td>7 (1.8)</td>
<td>2 (0.8)</td>
<td>5 (3.3)</td>
<td>0 (0)</td>
<td></td>
</tr>
<tr>
<td>Inverted</td>
<td>10 (2.5)</td>
<td>2 (0.8)</td>
<td>8 (5.2)</td>
<td>0 (0)</td>
<td></td>
</tr>
<tr>
<td>RCA from LAD</td>
<td>6 (1.5)</td>
<td>3 (1.3)</td>
<td>2 (1.3)</td>
<td>1 (11.1)</td>
<td></td>
</tr>
<tr>
<td>Intramural LCA</td>
<td>6 (1.5)</td>
<td>2 (0.8)</td>
<td>4 (2.6)</td>
<td>0 (0)</td>
<td></td>
</tr>
<tr>
<td>Intramural LAD, circumflex from RCA</td>
<td>1 (0.3)</td>
<td>0 (0)</td>
<td>1 (0.7)</td>
<td>0 (0)</td>
<td></td>
</tr>
<tr>
<td>Other</td>
<td>16 (4.0)</td>
<td>9 (3.8)</td>
<td>6 (3.9)</td>
<td>1 (11.1)</td>
<td></td>
</tr>
<tr>
<td>Follow-up post ASO*, years</td>
<td>18.7 (14.7, 22.5)</td>
<td>18.7 (14.9, 22.9)</td>
<td>19.0 (14.1, 22.4)</td>
<td>16.1 (13.4, 17.6)</td>
<td>0.2324</td>
</tr>
</tbody>
</table>

ASO indicates arterial switch operation; AVV, atrioventricular valve; IVS, intact ventricular septum; LAD, left anterior descending; LCA, left coronary artery; LVOT, left ventricular outflow tract; RCA, right coronary artery; TGA, transposition of the great arteries; and VSD, ventricular septal defect.

*Non-normally distributed continuous variables are presented as median and interquartile range (25\(^\text{th}\), 75\(^\text{th}\) percentile).

\(^\d\)Includes aortic coarctation, interrupted aortic arch, and hypoplastic aortic arch.

\(^\d\)Includes straddling atrioventricular valves and abnormally attached valves.
recent myocardial infarction resulting from a near-complete ostial occlusion of the single RCA. The only noncardiovascular late death occurred in a 17-year-old who was well until a fatal motor vehicle accident.

**Surgical and Catheter-Based Interventions**

Surgical and catheter-based interventions after ASO are listed in Table 2. The most common interventions were for pulmonary artery stenosis at the site of anastomosis or involving the main branches. Overall, 48 (12.8%) patients had ≥1 cardiac surgical reintervention, with corresponding freedom from surgical reintervention rates of 89.8±1.6% at 10 years and 85.7±2.0% at 25 years of follow-up. Sixty patients (16.0%) had catheter-based procedures (excluding diagnostic studies), with an intervention-free survival rate of 86.8±1.8% at 10 years and 82.1±2.3% at 25 years. Freedom from surgical or catheter-based intervention was 81.8±2.0% at 10 years and 75.5±2.5% at 25 years. Figure 2 depicts intervention-free survival according to whether patients had an intact ventricular septum, ventricular septal defect, or a Taussig-Bing variant. Factors associated with surgical or catheter interventions are listed in Table 3. The only multivariate predictors were an aortic arch anomaly (hazard ratio, 3.25; 95% CI, 1.69-6.27; \( P = 0.0004 \)) and lower weight at the time of ASO (hazard ratio, 0.61 per kg; 95% CI, 0.41-0.91; \( P = 0.0144 \)).

**Cardiovascular Outcomes**

Over the course of follow-up, 21 (5.6%) postoperative survivors had the following cardiac events: atrial flutter/intraatrial reentrant tachycardia (n=4), atrial fibrillation (n=2), bradycardia requiring pacemaker (n=3), myocardial infarction (n=4), heart failure-related hospitalization (n=1), and cerebrovascular accident (n=6). Arrhythmia-free survival was 98.4±0.7% at 10 years and 96.4±0.1% at 25 years (Figure 3A). Freedom from an adverse cardiovascular event was 96.8±0.9% at 10 years and 92.9±1.1% at 25 years (Figure 3B). Associated factors are listed in Table 4. The only multivariate predictors were a single RCA (hazard ratio, 4.58; 95% CI, 1.32-15.90; \( P = 0.0166 \)) and a low cardiac output syndrome in the immediate postoperative period (hazard ratio, 6.93; 95% CI, 1.57-30.62; \( P = 0.0107 \)).

Table 5 summarizes clinical data at the last follow-up. The mean left ventricular ejection fraction was 60.3±8.9% and 97.3% of patients had New York Heart Association (NYHA) class I symptoms. Nineteen (5.2%) patients had documented coronary disease, and 12 (3.3%) had systemic hypertension. At least moderate neoaortic and pulmonary regurgitation were documented in 3.4% and 6.6% of patients, respectively. Some degree of right ventricular outflow tract or pulmonary artery stenosis was present in 62.1% of patients, with a mean gradient of 25±17 mmHg by echocardiography, and at least moderate stenosis in 10.3%. Neoaortic stenosis was present in 11.9% of patients, with an average gradient of 19±7 mmHg and at least moderate stenosis in 3.2%. The mean aortic root size was 30.8±8.3 mm, with 6.5% of patients having an aortic root dimension ≥40 mm. Only 1 patient had an aortic root >50 mm (ie, 51 mm).

A total of 161 patients had cardiopulmonary exercise testing. The peak oxygen uptake was 35.1±7.6 mL/kg/min, corresponding to 86.1±15.1% of predicted values. The percentage of maximum predicted heart rate averaged 90.7±7.0% but was...
<80% in 8 (5.0%) patients. The mean chronotropic index was 83.9±10.9%. Excluding 6 patients with a respiratory exchange ratio <1.05 (indicative of submaximal exercise performance), the chronotropic index fell below 80% in 55 (34.2%) patients. Percent maximum peak oxygen uptake was not significantly associated with the percent maximum predicted peak heart rate ($r=0.04$, $P=0.7130$) or chronotropic index ($r=0.15$, $P=0.2379$).

Discussion

As the first recipients of arterial switch procedures reach their adult years, it is essential to characterize long-term sequelae and outcomes, so as to inform and guide appropriate patient screening and surveillance. To this end, our study is unique in several respects, including the longest follow-up to date (median 18.7 years),12,16,26,27 the comprehensive nature of the dataset (ie, physical examination, noninvasive imaging, hemodynamic studies, cardiopulmonary exercise testing, catheter and surgical interventions), and the arrhythmic and combined adverse cardiovascular outcomes. We deliberately restricted the study population to an early cohort (ie, with ASO between 1983 and 1999) to focus on long-term results. In contrast, most previous longitudinal studies have reported an average follow-up of ≤10 years.12,16,26,27 To maximize

Table 3. Factors Associated With Cardiovascular Surgical or Catheter-Based Intervention

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Hazard Ratio</th>
<th>95% CI</th>
<th>$P$</th>
</tr>
</thead>
<tbody>
<tr>
<td>Univariable</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ventricular septal defect</td>
<td>1.59</td>
<td>1.03, 2.47</td>
<td>0.0376</td>
</tr>
<tr>
<td>Taussig-Bing variant</td>
<td>2.80</td>
<td>0.88, 9.18</td>
<td>0.0819</td>
</tr>
<tr>
<td>Aortic arch anomaly</td>
<td>3.73</td>
<td>2.02, 6.88</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Coronary anomaly</td>
<td>1.37</td>
<td>0.88, 2.12</td>
<td>0.1636</td>
</tr>
<tr>
<td>Weight at time of arterial switch (per 1 kg reduction)</td>
<td>0.48</td>
<td>0.33, 0.70</td>
<td>0.0001</td>
</tr>
<tr>
<td>Height at time of arterial switch (per 1 cm reduction)</td>
<td>0.96</td>
<td>0.90, 1.02</td>
<td>0.1383</td>
</tr>
<tr>
<td>Multivariable</td>
<td></td>
<td></td>
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<tr>
<td>Aortic arch anomaly</td>
<td>3.25</td>
<td>1.69, 6.27</td>
<td>0.0004</td>
</tr>
<tr>
<td>Weight at time of arterial switch (per 1 kg reduction)</td>
<td>0.61</td>
<td>0.41, 0.91</td>
<td>0.0144</td>
</tr>
</tbody>
</table>

Table 4. Factors Associated With the Combined Cardiovascular Outcome in Early Survivors

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Hazard Ratio</th>
<th>95% CI</th>
<th>$P$</th>
</tr>
</thead>
<tbody>
<tr>
<td>Univariable</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Single right coronary artery</td>
<td>5.12</td>
<td>1.50, 17.50</td>
<td>0.0092</td>
</tr>
<tr>
<td>Post-operative course in intensive care unit ≥7 days</td>
<td>2.79</td>
<td>0.94, 8.30</td>
<td>0.0651</td>
</tr>
<tr>
<td>Post-operative low cardiac output syndrome</td>
<td>8.08</td>
<td>1.86, 35.06</td>
<td>0.0052</td>
</tr>
<tr>
<td>Post-operative ventricular tachycardia</td>
<td>4.12</td>
<td>0.55, 30.86</td>
<td>0.1687</td>
</tr>
<tr>
<td>Chest open postoperatively</td>
<td>2.51</td>
<td>0.90, 6.95</td>
<td>0.0777</td>
</tr>
<tr>
<td>Multivariable</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Single right coronary artery</td>
<td>4.58</td>
<td>1.32, 15.90</td>
<td>0.0166</td>
</tr>
<tr>
<td>Post-operative low cardiac output syndrome</td>
<td>6.93</td>
<td>1.57, 30.62</td>
<td>0.0107</td>
</tr>
</tbody>
</table>

CI indicates confidence interval.
completeness of data collection, the catchment area was limited to patients living in New England. Moreover, data were supplemented by directly contacting patients and by acquiring records from secondary sources. To minimize misclassification errors, outcomes were uniformly defined, and detailed standardized case-report forms were subject to data quality checks.

In this early surgical experience, the perioperative mortality rate declined over time. Since the original description of the ASO in 1976, modifications such as the Lecompte procedure, coronary artery relocation, and pulmonary artery reconstruction have likely contributed to improved perioperative outcomes. The association between the Taussig-Bing anomaly and poorer outcomes observed in our study has been previously described, and postoperative complications, including hemorrhage, have been linked to increased...
perioperative mortality. Additional reported risk factors for early death include, but are not limited to, aortic arch repair prior to ASO, right ventricular hypoplasia, lower birth weight, and longer intraoperative support.10

In perioperative survivors, the observed 96.7% actuarial survival rate at 25 years further extends results from previous longitudinal studies.12,16,26,27 With the exception of 1 accidental death, all late fatalities were cardiovascular and attributable to myocardial infarction or sudden death of presumed arrhythmic etiology. Three of the 6 cardiovascular deaths occurred in infants, an observation consistent with studies suggesting a bimodal distribution of coronary events, with most transpiring during the first year of life.16,33 Optimal screening remains a contentious issue, especially considering the fact that patients with ASO and denervated coronary arteries may not experience typical symptoms of angina. Some authors have, therefore, recommended serial coronary angiographic studies to identify potential lesions of concern.33 Although coronary artery disease was identified in 5% of patients in the current study, acute coronary syndromes were far less common and occurred exclusively in infants aged <3.5 months. Late coronary artery events have been reported64 but appear to be rare. The current practice at our institution is not to perform routine coronary angiography in otherwise asymptomatic patients with ASO.

Unexpected deaths of unknown or presumed arrhythmic cause were infrequent events, with an incidence <0.1% per year. Arrhythmias in general were remarkably uncommon, unlike patients with D-TGA and Mustard or Senning baffles.4 Although cavotricuspid isthmus-dependent atrial flutter was the most prevalent atrial tachyarrhythmia, atrial fibrillation was also documented. Only 1 of 4 patients with sustained ventricular tachycardia had more than mild left ventricular dysfunction, and none had coronary artery disease. Freedom from an adverse cardiovascular event, which included arrhythmias along with acute coronary syndromes, heart failure–related hospitalizations, cerebrovascular accidents, and cardiovascular deaths, was 93% at 25 years. A single RCA was independently associated with adverse cardiovascular events. Acute low cardiac output syndrome after ASO was also an independent predictor, a finding consistent with Losay et al’s observation that major intensive care unit complications predict late mortality.12

Whereas previous series have described high surgical reintervention rates during the first 5 years of follow-up,12,16,26,27 we quantified this rate to be nearly 15% by 25 years. In addition, a high catheter intervention rate (ie, 18% at 25 years) was also observed. We identified an aortic arch anomaly to be an independent predictor of reintervention. Similarly, others have reported higher rates of reintervention in patients with left ventricular outflow tract obstruction.17,35 Lower weight at ASO, also an independent predictor of reintervention in the current study, has been associated with increased mortality in earlier reports.17 Pulmonary artery stenosis is consistently reported to be the most frequent cause for reintervention.11,36–38 The obstruction was most commonly located in the main pulmonary artery or proximal branches, but valvular and subvalvular stenoses were also observed. As in former studies, ascending aortic stenosis was far less common.39,40 No aortic dissection or rupture occurred despite 6.5% of patients having a neoaoartic root dimension ≥40 mm at latest follow-up. In this patient population, rupture of a dilated aortic root appears to be unreported, suggesting a low propensity for such. Further studies are required to assess rates of progression of right ventricular outflow tract and neoaoartic complications, and their determinants, to better define optimal follow-up strategies.

At the latest follow-up visit, >97% of patients had NYHA functional class I symptoms and 96% maintained normal left ventricular systolic function. The subgroup of 161 patients with cardiopulmonary exercise testing represents the largest reported series to date. The average peak oxygen uptake of 35 mL/kg/min (86% of predicted values) compares favorably to published data from all other subgroups of patients with complex and simple forms of congenital heart disease.41 Although the peak heart rate averaged 91% of maximum predicted values, chronotropic incompetence, as defined by a chronotropic index <80%, was present in more than one third of patients. Although mechanisms remain to be elucidated, it can be hypothesized that residual cardiac sympathetic denervation after ASO may contribute to a blunted chronotropic response in a manner similar to cardiac transplantation. Interestingly, smaller series have likewise concluded that this impaired chronotropic response does not translate into poorer exercise capacity.42,43

Limitations
The study is retrospective in nature and subject to limitations inherent to observational investigations. As such, therapeutic decisions and follow-up testing were not standardized and reflect best clinical judgment. Standardization of investigations has since been implemented.44 In particular, the prevalence of coronary artery stenoses may be underestimated by the lack of routine invasive testing. Data were derived from a single high-volume institution, which may limit generalizability. Because we sought to describe long-term follow-up, patients in our study underwent the arterial switch procedure before 1999. Thus, their perioperative course and long-term complications may not reflect those of patients with D-TGA undergoing the ASO in the current era. Finally, low event rates for outcomes such as acute coronary syndromes and arrhythmias preclude formal assessment of associated factors.

Conclusion
Excellent overall and arrhythmia-free survival was observed in this early cohort of perioperative survivors with ASO for D-TGA. The few fatalities were predominantly attributable to myocardial infarction or sudden death of presumed arrhythmic etiology. The most common sequelae were stenoses of the main pulmonary artery or its branches, pulmonary regurgitation, neoaoartic stenosis and regurgitation, coronary artery disease, and an impaired chronotropic response. Nearly one quarter of the patients required reintervention by 25 years of follow-up, whether surgical or percutaneous. Adverse cardiovascular events were predicted by a single RCA and acute postoperative low cardiac output syndrome. Despite the prevalent postoperative sequelae and occasional adverse events, the majority of patients remained asymptomatic, with preserved ventricular systolic function, and normal exercise tolerance.
Acknowledgments

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Disclosures

None.

References

As the initial cohort of patients with arterial switch procedures for transposition of the great arteries reach their adult years, it is essential to characterize sequelae and longer-term outcomes to inform and guide screening and surveillance. We, therefore, conducted a retrospective cohort study on 400 patients with arterial switch surgery between 1983 and 1999. Excellent overall (96.7%) and arrhythmia-free (96.6%) survival was observed at 25 years of follow-up. Late fatalities were predominantly attributable to myocardial infarction or sudden death of presumed arrhythmic cause. The few acute coronary events occurred exclusively in infants aged <3.5 months. The most common cardiovascular sequelae were stenoses of the main pulmonary artery or its branches, pulmonary regurgitation, neoaortic stenosis and regurgitation, and coronary artery disease. Nearly one quarter of the patients required reintervention by 25 years of follow-up, whether surgical or percutaneous. Adverse cardiovascular events were predicted by a single right coronary artery and acute postoperative low cardiac output syndrome. Despite the prevalent postoperative sequelae and occasional adverse events, the mean left ventricular ejection fraction was 60.3% at the last follow-up, with 97.3% of patients having New York Heart Association class I symptoms. The peak oxygen uptake was 86.1% of predicted values. Chronotropic incompetence was nevertheless identified in more than one third of patients, perhaps reflecting sympathetic denervation. These results compare favorably with the much higher arrhythmia burden, incidence of sudden death, and prevalence of systemic (right) ventricular dysfunction previously reported in patients with atrial switch (ie, Mustard or Senning) procedures.
Cardiovascular Outcomes After the Arterial Switch Operation for D-Transposition of the Great Arteries
Paul Khairy, Mathieu Clair, Susan M. Fernandes, Elizabeth D. Blume, Andrew J. Powell, Jane W. Newburger, Michael J. Landzberg and John E. Mayer, Jr

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