Long-term Survival for Arterial vs. Atrial Switch in d-Transposition of the Great Arteries: A Report from the Pediatric Cardiac Care Consortium

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B.S.
Emory University, College of Arts and Sciences
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I. Abstract:

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Background: The arterial switch operation (ASO) was introduced in the US in the early 1980's and quickly became the procedure of choice for dextro-transposition of the great arteries (d-TGA). Our objective was to compare the long-term transplant-free survival of patients with d-TGA who underwent ASO vs. atrial switch in the Pediatric Cardiac Care Consortium (PCCC), a large international multi-center registry.

Methods: We performed a retrospective cohort study of d-TGA patients undergoing arterial switch operation (ASO) or atrial switch operation in the US between 1982 and 1991. Long-term transplant-free survival was obtained by linking PCCC data with the National Death Index and the Organ Procurement and Transplant Network. Kaplan-Meier survival plots were constructed and multivariable regression was used to compare long-term transplant-free survival for each procedure, adjusted for sex, complexity, and surgical center. We compared both overall long-term survival and survival conditional on discharge following the initial surgery.

Results: Of 554 d-TGA patients who underwent ASO (n=259) or atrial switch (n=295) the 20-year overall transplant-free survival for children who had surgery for d-TGA was 82.1% for those undergoing ASO and 76.3% for those who had atrial switch procedure. Overall transplant-free survival was initially similar between the two surgical groups, but after 10 years post d-TGA repair, the ASO had better long-term transplant-free survival as compared to the atrial switch (HR=0.07, 95% CI 0.01-0.52, p-value=0.009). During this time period the ASO had higher in-hospital mortality than the atrial switch (21.6% vs 12.9%, p=0.007). After excluding those with post-operative in-hospital mortality, the transplant-free survival 20 years post-repair was 97.7% for the ASO vs. 86.3% for the atrial switch. There were 38 post-hospital discharge deaths (4 ASO, 34 atrial switch) and 4 transplants (1 ASO, 3 atrial switch). Among those with atrial switch procedure, long-term results were similar for Mustard operation vs. Senning operation.

Conclusions: Despite initial higher in-hospital mortality for ASO, there is a significant long-term transplant-free survival advantage for ASO as compared to atrial switch for d-TGA surgery. Ongoing monitoring of this cohort is required to assess late risk of cardiovascular disease.

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II. Manuscript:

Long-term Survival for Arterial vs. Atrial Switch in d-Transposition of the Great Arteries: A Report from the Pediatric Cardiac Care Consortium

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INTRODUCTION:

Dextro-Transposition of the Great Arteries (d-TGA) is the second most common cyanotic congenital heart defect, with an estimated annual incidence of 860 cases in the United States (1). In the late 1950s and early 1960s the Mustard and Senning atrial switch procedures became the first corrective surgeries available for d-TGA (2, 3). Although the atrial switch had good perioperative survival, complications such as baffle obstructions/leaks, atrial arrhythmias, systemic ventricle dysfunction, and tricuspid regurgitation were common (4).

In 1975, Jatene introduced the arterial switch operation (ASO) (5), but his initial experience was notable for a high perioperative mortality (71%), much greater than the well-established atrial switch procedure (4, 6). At this time some surgeons recommended ASO only for complex d-TGA, citing the potential long-term complications of the ASO that would remain unknown for many years (7, 8). Others weighed the perceived benefits of an anatomic correction and sought to perform the ASO in most cases of d-TGA despite poor initial results (9). In the 1990's, with the improved perioperative results as surgeons gained ASO experience, the ASO superseded the atrial switch as the preferred corrective surgery for all forms of d-TGA in the US (10).

Although the ASO has been shown to have better mid-term results, long-term results beyond the second decade of life are unknown for those undergoing the procedure in the US (11-15). Common ASO complications include neo-pulmonary stenosis and neo-aortic dilation which may impact long-term results (10). Additionally, while reports of coronary artery obstruction are not uncommon (12, 13, 16), late deaths due to myocardial infarction and sudden cardiac death in ASO patients are rare (12, 17, 18). Nevertheless, coronary lesions and other ASO complications underlie concerns about the long-term results of the operation. Our objective, therefore, was to compare the long-term transplant-free survival of patients with d-TGA between the ASO and atrial switch performed in the decade when the surgery preference transitioned.

METHODS:

Study Design

We performed a retrospective cohort study using data from the Pediatric Cardiac Care Consortium (PCCC), a large international registry for interventions for pediatric heart diseases (19). The PCCC was established in 1982 to allow collaboration between pediatric cardiovascular centers with the aim to improve outcomes for patients with congenital or acquired heart diseases (20). Cardiovascular centers voluntarily participated in the PCCC, with 47 US centers participating from 1982-2011. Estimates report that the PCCC contains 15-30% of the national volume of pediatric cardiac surgeries during that time period (21).

Patients were included in this study if they were US residents operated for d-TGA with an ASO or an atrial switch (Mustard or Senning) during infancy at a PCCC center in the US during the decade from 1982 to 1991, the time period during which the transition from atrial to arterial switch type of correction for d-TGA took place in the US. The Mustard and Senning procedures were considered together as the atrial switch group in the initial analyses, with supplemental analyses then performed considering these operations separately. Complex d-TGA was defined as d-TGA accompanied by any combination of: ventricular septal defect (VSD), coarctation, native pulmonary outflow tract obstruction (POTO), or native systemic outflow tract obstruction. Simple d-TGA included patients with an atrial septal defect (ASD), patent ductus arteriosus, or no accompanying defects. Presence of accompanying defects was determined by examining PCCC diagnostic or surgical procedure codes for the specified lesions occurring prior to or at the time of d-TGA repair. Available PCCC forms were reviewed for the collection of variables such as cardiopulmonary bypass and cross-clamp times, as well as coronary artery anatomy. In-hospital death were defined as postoperative death during the admission for d-TGA repair. Among hospital survivors, those who had adequate identifiers [first name, middle initial (if available), last name, birth day, birth month, birth year, sex, and state of birth] were submitted to the National Death Index (NDI) and the Organ Procurement and Transplant Network and included in the long-term survival analysis (22). Ascertainment of vital status with NDI was complete through December 31st, 2014. Cause of death analysis was based on International Classification of Disease codes (ICD-9 until 1998 and -10 after that year) among NDI linked patients with general system-based etiology of death categories created based on those used in prior PCCC studies (23). The study was approved by the Institutional Review Board of Emory University.

Statistical Methods

Statistical analyses were conducted using SAS 9.4 (SAS Institute, Cary, NC) and statistical significance was assessed at the 0.05 level, unless otherwise noted. Normality of continuous variables was assessed with histograms, normal probability plots and the Anderson-Darling test for normality. Descriptive statistics are presented as counts and percentages for categorical variables and median (25th-75th percentile) for continuous data with skewed distributions. Continuous data were compared between patients who underwent ASO intervention and those who underwent atrial switch intervention with the use of Wilcoxon rank-sum tests and comparisons between categorical variables were performed with Chi-square tests, or Fisher exact tests when the expected cell counts were <5. Unadjusted and adjusted in-hospital mortality was compared between surgical interventions using generalized linear mixed models (controlling for sex and transposition complexity and treating surgical center as a random effect). Kaplan-Meier survival plots were constructed to display long-term transplant-free survival data, with statistical comparisons performed using the log-rank test. These plots were created for overall transplant-free survival (including in-hospital deaths) and for long-term transplant-free survival, conditional on survival to hospital discharge following d-TGA repair.

Survival without transplant after d-TGA intervention was treated as a time-dependent outcome and analyzed using survival analysis methods. Prior to modeling, the proportional hazard assumption was assessed using log-log survival curves and by formally testing the interaction between time and d-TGA intervention group using an extended Cox model. For both overall and conditional long-term survival, the proportional hazard assumption was violated. As a result, we utilized Heaviside functions in the extended Cox Model. When such a function is used, the hazard ratio (HR) formula yields constant HR for different time intervals. Our intervals were chosen such that a) an event occurred in both groups so that the hazard ratio was estimable and b) the hazard function was relatively stable within each window of time. Stability of the hazard function was assessed using kernel smoothed hazard plots with bandwidth of 2 years. The date of intervention was used as our starting point and the effects of ASO intervention on the probability of survival in the models are given as HR with 95% confidence interval (CI), unadjusted and adjusted. In a supplemental analysis, we further classified atrial switch operations into Mustard and Senning and compared survival among the three groups.

RESULTS:

Baseline Characteristics

There were 554 patients with d-TGA who met the study inclusion criteria. Among those, 259 patients underwent surgical correction with ASO and had a median follow-up time of 24.3 years; there were 295 patients with atrial switch and a median follow-up time of 26.5 years. The Senning procedure accounted for 63.7% (n=188) of all atrial switch procedures. There were 460 patients discharged alive after surgical correction, and 336 of the hospital survivors (73.0%) had sufficient identifiers to be submitted to NDI. The patient flow diagram is depicted in Figure 1. The number of ASO performed each year increased until 1990 when the ASO outpaced the atrial switch (Figure 2). Of the atrial switch procedures, more Senning operations were performed consistently throughout the decade.

The characteristics of all d-TGA patients are shown in Table 1. There were no differences between the two groups with regards to sex, anatomic complexity, or presence of an accompanying VSD or coarctation. Those who underwent ASO were more likely to have an ASD and less likely to have POTO. Of the 116 total patients who had documented coronary artery anatomy, atypical coronary anatomy was present in a similar percentage of ASO and atrial switch patients (18.6% vs 13.0%, p=0.43). Not surprisingly given the nature of the two operations, age and weight at index operation were both lower among patients who underwent ASO compared to those undergoing atrial switch (7 days vs 167 days, p<0.001; 3.6 kg vs 6.0 kg, p<0.001). Patient characteristics stratified by hospital discharge status are shown in Table 2. Hospital survivors were less likely to have an accompanying VSD (24.6% vs 40.4%, p=0.002) or an additional cardiac lesion (complex d-TGA) than those who died prior to discharge (26.3% vs 40.4%, p=0.003). Sex, coronary anatomy, cardiopulmonary bypass time, or cross-clamp time were not significantly different between hospital survivors and those who died in-hospital. Demographic information stratified by hospital discharge status for each specific surgical group is shown in Supplemental Table 1 and Supplemental Table 2.

Overall Survival

As shown in Figure 3, the 20-year overall transplant-free survival for children who had surgery for d-TGA was 82.1% for those undergoing ASO and 76.3% for those who had atrial switch procedure (log-rank p-value=0.14). Given that the hazard of transplant/mortality changed over time, we determined time intervals where the hazard was proportional to establish mortality HRs (Table 3). Overall transplant-free survival was initially similar between the two surgical groups, but after 10 years post d-TGA repair, the ASO had better long-term transplant-free survival as compared to the atrial switch (adjusted mortality HR=0.07, 95% CI 0.01-0.52, p-value=0.009).

In comparing the overall transplant-free survival by type of atrial switch, patients who underwent Mustard and Senning atrial switch procedures had similar long-term results. There was an initial difference in early mortality, with Mustard having a lower hazard of transplant/mortality within the first month after the operation (adjusted mortality HR=0.27, 95%CI 0.09-0.81, p-value=0.02). Beyond this early period there was no difference in overall transplant-free survival, with both atrial switch procedure groups experiencing a steady survival decline (Supplemental Figure 1, Supplemental Table 3).

Conditional Survival

Much of the mortality in this population was in-hospital mortality. For the ASO, in-hospital mortality was 21.6%; for the atrial switch, it was 12.9% (OR=1.87, 95% CI 1.19-2.93, p-value=0.007). Among those who survived to hospital discharge, 20-year transplant-free survival was 97.7% for those with ASO and 86.3% for those with atrial switch as shown in Figure 4 (p-value <0.001). Again, time intervals were established where the hazard of transplant/mortality remained proportional (Table 4). Within the first 10 years after the operation there was no significant difference between the transplant-free conditional survival of the two surgical groups. However, beyond 10 years the advantage of the ASO became clear, with an adjusted mortality HR of 0.07 (95% CI 0.01-0.52, p-value=0.009).

In examining the atrial switch outcomes by subtype, those with a Senning operation had significantly higher in-hospital mortality than those with a Mustard (16.5% vs. 6.5%, OR=2.82, 95%CI 1.19-6.67, p-value=0.02). Among survivors of these initial operations, patients had similar long-term outcomes, with transplant-free survival at 20 years of 87.6% for those with a Senning and 84.0% for those with a Mustard (p-value=0.99, Supplemental Figure 2). When comparing the late conditional survival of the ASO to each individual atrial switch procedure the results were similar (Supplemental Table 4).

Cause of Death

There were 38 post-hospital discharge deaths in our cohort, with four occurring in ASO patients and 34 in atrial switch patients. The deaths were attributed to a cardiac cause in 50% (2/4) of the ASO patients and 68% (23/34) of the atrial switch patients. The other ASO deaths were classified as pneumonia/other respiratory in one patient and external cause of injury (motor vehicle accident) in another. The other atrial switch deaths included sepsis (2), multiple system organ failure (1), pulmonary hypertension (1), pneumonia/other respiratory (2), neurologic (1), external cause of injury (3), and unknown (1). The low numbers of late deaths in the ASO group prohibited any cause of death comparisons between the two groups.

DISCUSSION:

In this study, which to our knowledge is the largest of its kind comparing surgical techniques in d-TGA patients with at least 20 years of follow-up, we found that long-term transplant-free survival among patients with d-TGA was superior in patients who received an ASO as compared to an atrial switch. This finding was true both with and without consideration of the in-hospital mortality associated with the initial operation. Prior survival modeling of the two groups of operations using mortality parameters from this era predicted that the overall survival curves would intersect around 30 years, beyond which ASO survival would be superior (24). Our study reveals that this cross-over point actually took place around 10 years after the operation in the transitional era between the two procedures in the US. Our results are consistent with many other studies of smaller size or shorter duration of follow-up (11-15, 17).

In the current era of the ASO, with extremely low in-hospital mortality, the 20-year survival of d-TGA patients likely approximates the >97% 20-year survival of the ASO hospital survivors shown here. The ASO is clearly the better long-term strategy, but in the 1980's this outcome was not a certainty. The delay between the first successful ASO and its widespread use was primarily due to the concern for the high in-hospital mortality of the operation. The atrial switch procedure had well-established low in-hospital mortality at the time. ASO results improved with the development of the Lecompte maneuver in 1981, the success of the neonatal ASO in 1984, and improvements in coronary implantation techniques (25). Our study shows the gradual increase in number of ASOs performed throughout the decade, as well as the decline in preference for the atrial switch. Over half of the ASOs that were included in this study occurred in 1990 and 1991. However, despite the surgical innovations, our results reveal that during this time period the ASO, compared to atrial switch, remained a risk factor for early mortality. Greater than 20% of patients who underwent an ASO were not discharged from the hospital alive. This in-hospital mortality for the ASO is slightly higher than other reports from the same era (12, 14). This high in-hospital mortality likely reflects the technical learning curve occurring at different points throughout the decade for each center (21). In the current era, in-hospital mortality following ASO is considered a rare event. Villafañe et al. reported that the in-hospital mortality after ASO in the PCCC was only 2.9% from 2003-2007 (10) , similar to other present-day reports consistently below 5% (12, 14).

There are many factors which may contribute to the increased long-term mortality among the atrial switch cohort. The atrial baffles diverting venous inflow to the contralateral ventricle in the atrial switch procedure are prone to baffle leaks and obstructions. In addition, the process of atrial reconstruction predisposes these patients to atrial arrhythmias. Finally, the systemic right ventricular function deteriorates over time, also leading to tricuspid regurgitation (26). These complications give rise to a high rate of re-interventions (4). Likely as a result of these complications, more than two thirds of the long-term deaths in the atrial switch patients in our study involved a cardiovascular etiology. Our study agrees with prior estimates of overall long-term survival in atrial switch patients, with around 70-80% remaining alive 25 years after their operation (26, 27). Despite the difference in in-hospital mortality between the Senning and Mustard procedures, patients undergoing these operations in our study had similar overall survival to beyond 20 years.

The ASO has been shown to have functionally better results than the atrial switch (28). However, these patients are not entirely free of morbidity. Neo-pulmonary outflow tract obstruction and neo-aortic dilation are common problems (10, 15). Coronary lesions have been found to be present by coronary ultrasonography and angiography at an overall rate of 5.2%-6.8% in patients after ASO (13, 16, 29, 30). The risk of myocardial ischemia and sudden death early after ASO is well documented due to the need for coronary re-implantation and complications from technical difficulties or abnormal coronary anatomy (29, 31, 32). The hazard of mortality from coronary complications is highest within the first few months after the operation (32). Nevertheless in our study, the overall survival between the ASO and atrial switch was similar within the first post-operative month. Beyond the reported risk for early coronary events, there is also concern that the surgical manipulation of the coronary arteries during ASO with age becomes a substrate for higher risk for coronary artery disease and sudden cardiac death than the general population (33). Within the time frame of this study, there was only one late death beyond the first postoperative year and this was due to a motor vehicle collision more than 20 years after ASO. Our findings are consistent with a recent systematic review which found that there were only 5 cases of sudden cardiac death (with none having a proven coronary cause) among nearly 8,798 ASO patients after 66,450 patient follow-up years (18). If patients with ASO are at increased risk of sudden cardiac death due to coronary events, this difference is not apparent within the first 20 years post-operatively.

Our study has several limitations in addition to those inherent of a retrospective cohort study. First, a proportion of our hospital survivors did not contain adequate identifiers to be submitted to NDI. Our previous work with this linked registry demonstrated that younger patients were less likely to have adequate identifiers (22). This limitation did not affect our ability to detect a difference in transplant-free survival, but it may have prohibited us from comparing causes of death. Second, in 1990 there was a rapid shift from the atrial switch to the ASO, a shift that resulted in more than half of the ASO group occurring in the last 2 years of our study. This timeframe somewhat limits our ability to compare exactly contemporaneous outcomes between the groups. Third, there was limited data collection or ascertainment for some of our variables of interest such as coronary artery anatomy. However, we feel that this is unlikely to have affected our overall results as this potential misclassification would have been equally distributed between the two groups. Finally, the PCCC database does not collect information regarding long-term complications. Thus, we cannot assess whether there are differences in complications between the surgical groups other than mortality or transplant. Nevertheless, our study describes the late survival of a large nationally representative cohort of d-TGA patients who underwent surgery when the superiority of the ASO was uncertain. As patients with ASO age and are exposed to the cardiovascular complications of aging, future efforts should be directed at continued surveillance of this cohort for coronary artery disease and sudden cardiac death. Such data will help direct patient screening guidelines for late ASO complications.

CONCLUSION:

This study shows that among d-TGA patients, the survival into the third decade of life of those who underwent ASO is superior to that of atrial switch patients. This is particularly true among those who survived to discharge following the initial hospitalization. In the current era of the operation with low ASO perioperative mortality, the overall ASO survival to 20 years of age likely closely approximates the >97% 20-year survival of ASO hospital survivors reported here.

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III. Tables/Figures/Figure Legends:

Table 1. Characteristics of all d-TGA patients (including in-hospital deaths), overall and stratified by operation

	N	Overall n=554	ASO n=259	Atrial Switch n=295	p-value
Sex	554				0.65
Female		157 (28.3%)	71 (27.4%)	86 (29.2%)	
Male		397 (71.7%)	188 (72.6%)	209 (70.8%)	
Genetic defect	554	2 (0.4%)	0 (0.0%)	2 (0.7%)	0.50
Type of transposition	554				0.55
Simple d-TGA		394 (71.1%)	181 (69.9%)	213 (72.2%)	
Complex d-TGA		160 (28.9%)	78 (30.1%)	82 (27.8%)	
Accompanying defect	554				
VSD		151 (27.3%)	76 (29.3%)	75 (25.4%)	0.30
Coarctation		16 (2.9%)	10 (3.9%)	6 (2.0%)	0.20
ASD		115 (20.8%)	65 (25.1%)	50 (16.9%)	**0.02**
POTO		13 (2.3%)	2 (0.8%)	11 (3.7%)	**0.02**
Coronary anatomy	116				0.43
Usual		97 (83.6%)	57 (81.4%)	40 (87.0%)	
Abnormal		19 (16.4%)	13 (18.6%)	6 (13.0%)	
Prior balloon atrial septostomy	554	347 (62.6%)	129 (49.8%)	218 (73.9%)	**<0.001**
Birth weight (kg)	531	3.4 (3.0 – 3.8)	3.4 (3.1 – 3.7)	3.3 (2.9 – 3.8)	**0.009**
Age at index operation (days)	554	72 (7 – 177)	7 (4 – 12)	167 (97 – 215)	**<0.001**
Weight at TGA operation (kg)	489	4.2 (3.5 – 6.1)	3.6 (3.2 – 3.9)	6.0 (4.9 – 7.1)	**<0.001**
Cardiopulmonary bypass time (min)	90	117 (85 – 152)	123 (80 – 150)	106 (88 – 180)	0.35
Cross clamp time (min)	84	66 (56 – 87)	67 (56 – 86)	62 (52 – 94)	0.97
Median length of follow-up (years)	394	25.2 (23.3 – 27.5)	24.3 (23.3 – 25.6)	26.5 (23.4 – 28.7)	**<0.001**

d-TGA = dextro-transposition of the great arteries, ASO = arterial switch operation, VSD = ventricular septal defect, ASD = atrial septal defect, POTO = native pulmonary outflow tract obstruction

Values expressed as N (%) or median (IQR 25^{th}-75^{th})

Continuous variables are compared using Wilcoxon rank sum tests and categorical variables using Chi-square tests or Fisher's exact test if expected cell count <5

Table 2. Characteristics of all d-TGA patients stratified by hospital discharge status

	N	Hospital Survivors n=460	In-hospital Deaths n=94	p-value
Index operation	554			**0.006**
ASO		203 (44.1%)	56 (59.6%)	
Atrial switch operation		247 (55.9%)	38 (40.4%)	
Sex	554			0.34
Female		127 (27.6%)	30 (31.9%)	
Male		333 (72.4%)	64 (68.1%)	
Genetic defect	554	1 (0.2%)	1 (1.1%)	0.31
Type of transposition	554			**0.003**
Simple d-TGA		339 (73.7%)	55 (58.5%)	
Complex d-TGA		121 (26.3%)	39 (41.5%)	
Accompanying defect	554			
VSD		113 (24.6%)	38 (40.4%)	**0.002**
Coarctation		13 (2.8%)	3 (3.2%)	0.74
ASD		90 (19.6%)	25 (26.6%)	0.13
POTO		13 (2.8%)	0 (0.0%)	0.14
Coronary anatomy	116			0.36
Usual		74 (81.3%)	23 (92.0%)	
Abnormal		17 (18.7%)	2 (8.0%)	
Prior balloon atrial septostomy	554	297 (64.6%)	50 (53.2%)	**0.04**
Birth weight (kg)	531	3.4 (3.0 - 3.8)	3.3 (3.0 - 3.7)	0.92
Age at index operation (days)	554	83 (7 - 182)	21 (5 - 134)	**0.02**
Weight at TGA operation (kg)	489	4.5 (3.6 - 6.3)	3.8 (3.2 - 5.2)	**0.001**
Cardiopulmonary bypass time (min)	90	123 (86 - 152)	86 (78 - 146)	0.28
Cross clamp time (min)	84	65 (57 - 88)	67 (43 - 86)	0.42

ASO = arterial switch operation, d-TGA = dextro-transposition of the great arteries, VSD = ventricular septal defect, ASD = atrial septal defect, POTO = native pulmonary outflow tract obstruction

Values expressed as N (%) or median (25^{th}-75^{th})

Continuous variables are compared using Wilcoxon rank sum tests and categorical variables using Chi-square tests or Fisher's exact test if expected cell count <5

Table 3. Effect of treatment strategy on overall survival of d-TGA patients during time periods after surgical correction that have proportional hazards.

	Unadjusted mortality HR (95%CI)	p-value	Adjusted mortality HR (95%CI)*	p-value
ASO (vs atrial switch):				
Between 0 and 1 month	1.39 (0.81-2.37)	0.23	1.62 (0.93-2.85)	0.10
Between 1 month and 10 years	0.45 (0.12-1.64)	0.23	0.52 (0.14-1.90)	0.32
After 10 years	0.06 (0.01-0.46)	**0.007**	0.07 (0.01-0.52)	**0.009**

d-TGA = dextro-transposition of the great arteries, HR = hazard ratio, CI = confidence interval, ASO = arterial switch operation

* adjusted for sex, transposition complexity, and surgical center

Table 4. Effect of treatment strategy on long-term mortality among d-TGA hospital survivors during time periods after surgical correction that have proportional hazards.

	Unadjusted mortality HR (95%CI)	**p-value**	**Adjusted mortality HR (95%CI)***	**p-value**
ASO (vs atrial switch)				
Between 0 and 10 years	0.42 (0.12-1.51)	0.18	0.47 (0.13-1.71)	0.25
After 10 years	0.06 (0.01-0.47)	**0.007**	0.07 (0.01-0.52)	**0.009**

d-TGA= dextro-transposition of the great arteries, HR = hazard ratio, CI = confidence interval, ASO = arterial switch operation

* adjusted for sex, transposition complexity, and surgical center

Figure 1.

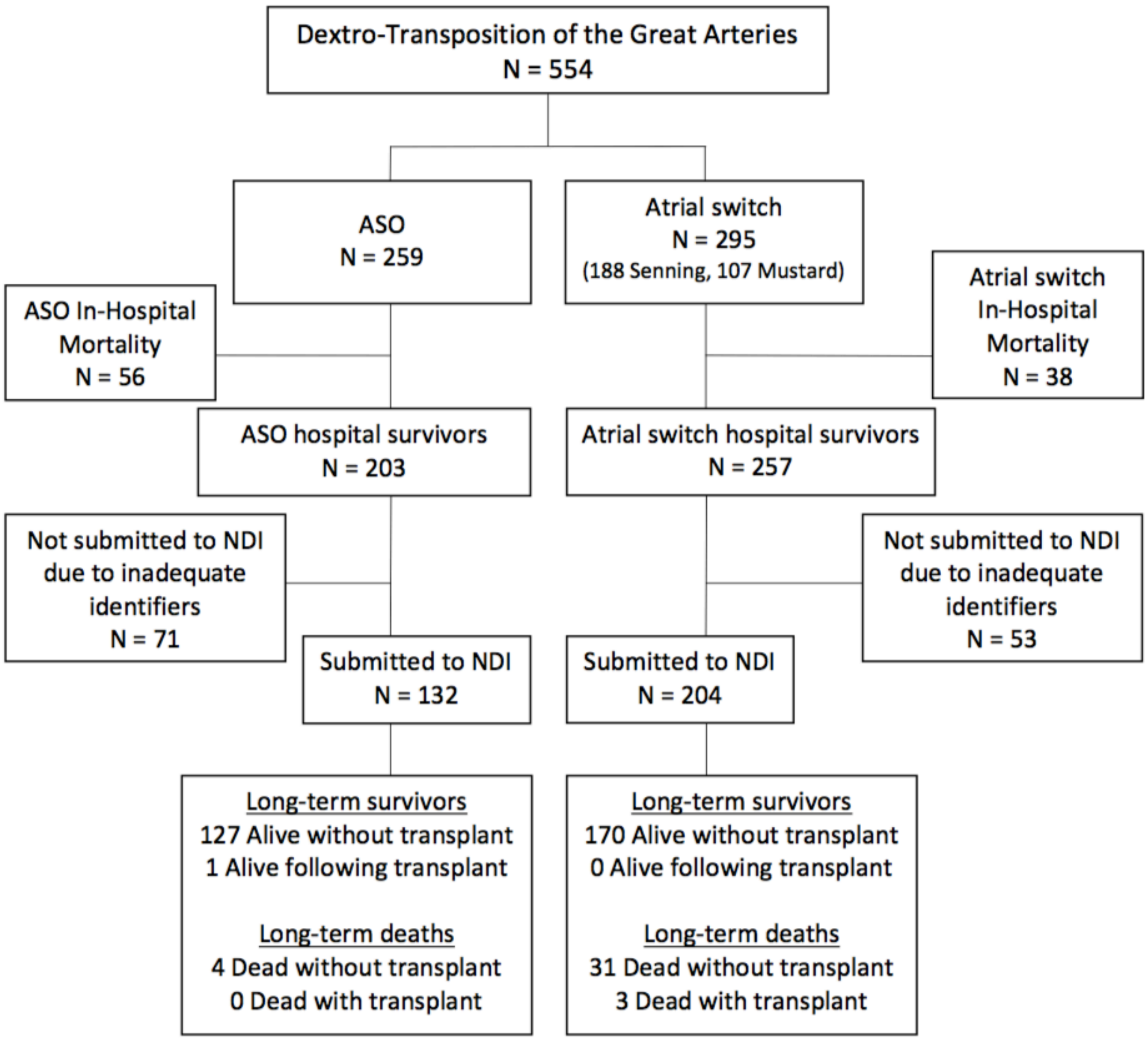
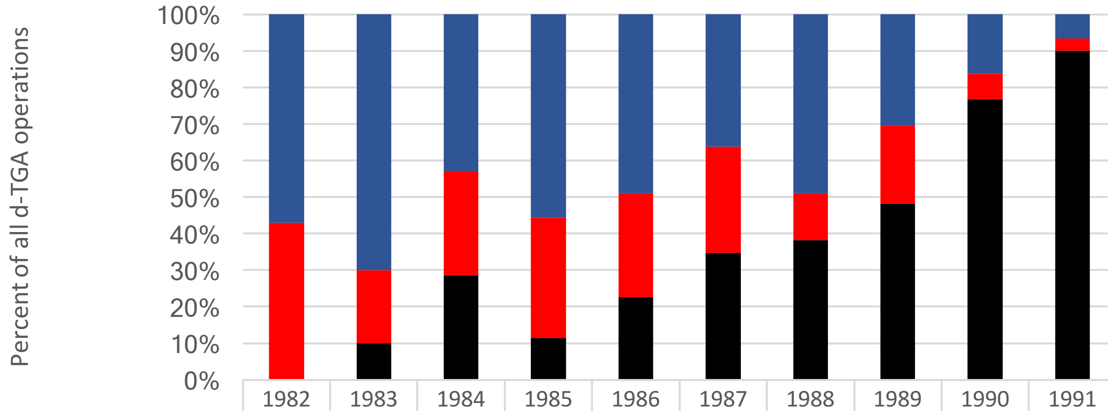


Figure 1. Patient inclusion diagram. NDI = National Death Index, ASO = arterial switch operation.

Figure 2.



	1982	1983	1984	1985	1986	1987	1988	1989	1990	1991
Senning atrial switch	8	7	12	39	26	25	27	24	14	6
Mustard atrial switch	6	2	8	23	15	20	7	17	6	3
Arterial switch	0	1	8	8	12	24	21	38	66	81

Figure 2. Operations for dextro-transposition of the great arteries in the Pediatric Cardiac Care Consortium, expressed as percent of total d-TGA operations in the bar graph as well as raw number of each operation in the underlying table. d-TGA = dextro-transposition of the great arteries.

Figure 3.

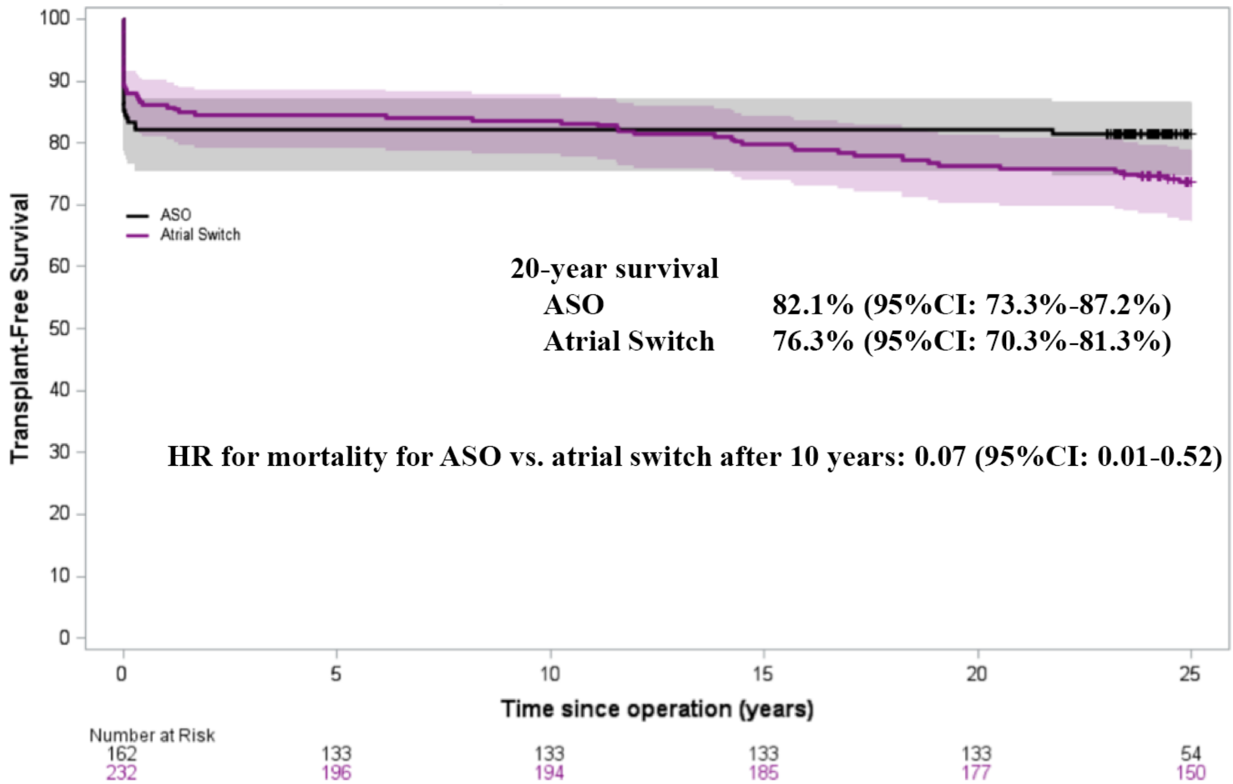


Figure 3. Kaplan-Meier curves for overall transplant-free survival of patients with d-transposition of the great arteries are shown by operation group. For the time period after 10 years, mortality HR for ASO vs. atrial switch is displayed, adjusted for sex, transposition complexity, and surgical center. ASO = arterial switch operation, HR = hazard ratio, CI = confidence interval.

Figure 4.

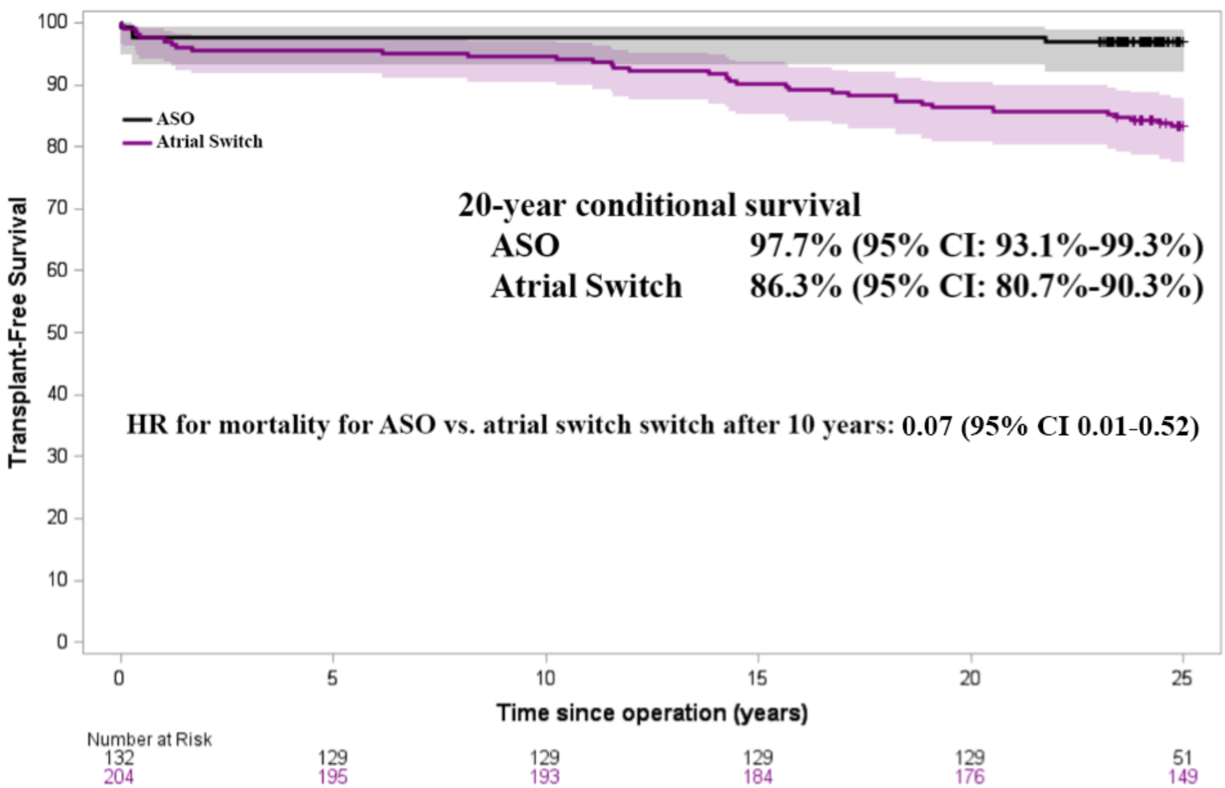


Figure 4. Kaplan-Meier survival curves for transplant-free survival of patients with d-transposition of the great arteries shown by operation group, *conditional on survival to hospital discharge following initial operation*. For the time period after 10 years, mortality HR of ASO vs. atrial switch is displayed, adjusted for sex, transposition complexity, and surgical center. ASO = arterial switch operation, HR = hazard ratio, CI = confidence interval.

IV. Supplemental Tables & Figures:

Supplemental Table 1. Characteristics of arterial switch operation patients stratified by hospital discharge status

	N	Hospital Survivors n=203	In-hospital Deaths n=56	p-value
Sex	259			0.91
Female		56 (27.6%)	15 (26.8%)	
Male		147 (72.4%)	41 (73.2%)	
Genetic defect	259	0 (0.0%)	0 (0.0%)	1.00
Type of transposition	259			0.09
Simple d-TGA		147 (72.4%)	34 (60.7%)	
Complex d-TGA		56 (27.6%)	22 (39.3%)	
Accompanying defect	259			
VSD		54 (26.6%)	22 (39.3%)	0.07
Coarctation		8 (3.9%)	2 (3.6%)	1.00
ASD		48 (23.6%)	17 (30.4%)	0.31
POTO		2 (1.0%)	0 (0.0%)	1.00
Coronary anatomy	70			0.72
Usual		43 (79.6%)	14 (87.5%)	
Abnormal		11 (20.4%)	2 (12.5%)	
Prior balloon atrial septostomy	259	105 (51.7%)	24 (42.9%)	0.24
Birth weight (kg)	251	3.5 (3.1 – 3.8)	3.3 (2.9 – 3.6)	**0.05**
Age at index operation (days)	259	6 (4 – 12)	7 (4 – 18)	0.61
Weight at index operation (kg)	234	3.6 (3.2 – 3.9)	3.4 (3.0 – 3.8)	**0.05**
Cardiopulmonary bypass time (min)	59	127 (83 – 150)	86 (78 – 146)	0.47
Cross clamp time (min)	58	67 (57 – 85)	68 (52 – 86)	0.78

d-TGA = dextro-transposition of the great arteries, VSD = ventricular septal defect, ASD = atrial septal defect, POTO = native pulmonary outflow tract obstruction

Values expressed as N (%) or median (25^{th}-75^{th})

Continuous variables compared using Wilcoxon rank sum tests and categorical variables are compared using Chi-square tests or Fisher's exact test if expected cell count <5

Supplemental Table 2. Characteristics of atrial switch procedure patients stratified by hospital discharge status

	N	Hospital Survivors n=257	In-hospital Deaths n=38	p-value
Type of atrial switch operation	295			**0.01**
Mustard		100 (38.9%)	7 (18.4%)	
Senning		157 (61.1%)	31 (81.6%)	
Sex	295			0.13
Female		71 (27.6%)	15 (39.5%)	
Male		186 (72.4%)	23 (60.5%)	
Genetic defect	295	1 (0.4%)	1 (2.6%)	0.24
Type of transposition	295			**0.01**
Simple d-TGA		192 (74.7%)	21 (55.3%)	
Complex d-TGA		65 (25.3%)	17 (44.7%)	
Accompanying defect	295			
VSD		59 (23.0%)	16 (42.1%)	**0.01**
Coarctation		5 (1.9%)	1 (2.6%)	0.57
ASD		42 (16.3%)	8 (21.1%)	0.47
POTO		11 (4.3%)	0 (0.0%)	0.37
Coronary anatomy	46			0.33
Usual		31 (83.8%)	9 (100.0%)	
Abnormal		6 (16.2%)	0 (0.0%)	
Prior balloon atrial septostomy	295	192 (74.7%)	26 (68.4%)	0.41
Birth weight (kg)	280	3.3 (2.9 - 3.7)	3.3 (3.0 - 3.9)	0.14
Age at index operation (days)	295	169 (105 - 211)	141 (73 - 215)	0.23
Weight at index operation (kg)	255	6.0 (5.0 - 7.2)	5.4 (4.3 - 6.8)	0.09
Cardiopulmonary bypass time (min)	31	106 (88 - 180)	-	-
Cross clamp time (min)	26	62 (58 - 94)	35 (35 - 35)	0.09

d-TGA = dextro-transposition of the great arteries, VSD = ventricular septal defect, ASD = atrial septal defect, PDA = patent ductus arteriosus, POTO = native pulmonary outflow tract obstruction
Values expressed as N (%) or median (25^{th}-75^{th})
Continuous variables compared using Wilcoxon rank sum tests and categorical variables are compared using Chi-square tests or Fisher's exact test if expected cell count <5

Supplemental Table 3. Effect of specific surgical treatment strategy on overall mortality among d-TGA hospital survivors during various time periods after surgical correction that have proportional hazards

	Unadjusted mortality HR (95%CI)	**p-value**	**Adjusted mortality HR (95%CI)***	**p-value**
ASO (vs Mustard)				
Between 0 and 1 month	3.35 (1.17-9.61)	**0.02**	3.42 (1.12-10.45)	**0.03**
Between 1 month and 10 years	0.84 (0.14-5.00)	0.85	0.88 (0.14-5.46)	0.89
After 10 years	0.04 (0.01-0.33)	**0.003**	0.04 (0.01-0.35)	**0.003**
ASO (vs Senning)				
Between 0 and 1 month	1.05 (0.60-1.83)	0.86	1.14 (0.64-2.03)	0.65
Between 1 month and 10 years	0.36 (0.09-1.34)	0.13	0.38 (0.10-1.44)	0.15
After 10 years	0.08 (0.01-0.64)	**0.02**	0.09 (0.01-0.68)	**0.02**
Mustard (vs Senning)				
Between 0 and 1 month	0.30 (0.11-0.88)	**0.03**	0.27 (0.09-0.81)	**0.02**
Between 1 month and 10 years	0.42 (0.09-1.99)	0.28	0.37 (0.08-1.76)	0.21
After 10 years	1.72 (0.77-3.83)	0.19	1.50 (0.65-3.50)	0.34

d-TGA= dextro-transposition of the great arteries, HR = hazard ratio, CI = confidence interval, ASO = arterial switch operation

* adjusted for sex, transposition complexity, and surgical center

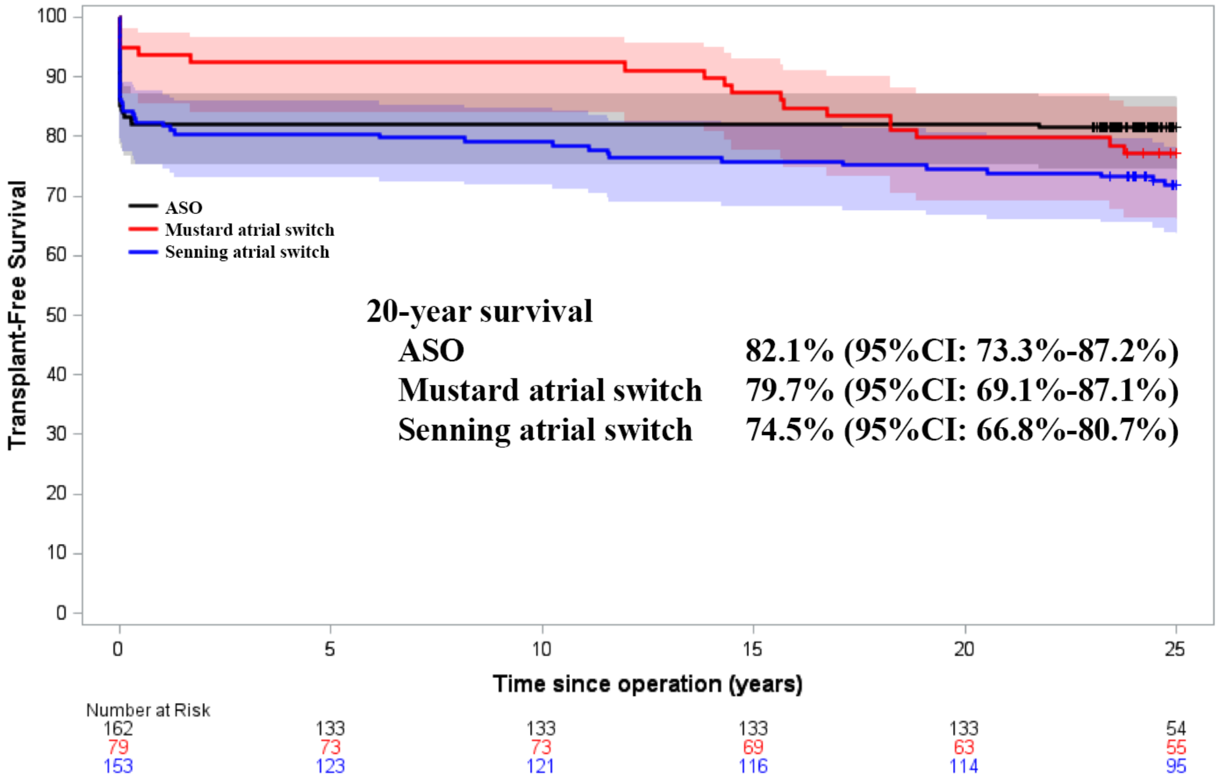
Supplemental Table 4. Effect of specific surgical treatment strategy on long-term mortality among d-TGA hospital survivors during various time periods after surgical correction that have proportional hazards

	Unadjusted mortality HR (95%CI)	**p-value**	**Adjusted mortality HR (95%CI)***	**p-value**
ASO (vs Mustard)				
Between 0 and 10 years	0.86 (0.14-5.16)	0.87	0.80 (0.13-5.07)	0.81
After 10 years	0.05 (0.01-0.34)	**0.003**	0.04 (0.01-0.33)	**0.003**
ASO (vs Senning)				
Between 0 and 10 years	0.32 (0.09-1.19)	0.09	0.35 (0.09-1.32)	0.12
After 10 years	0.08 (0.01-0.65)	**0.02**	0.09 (0.01-0.69)	**0.02**
Mustard (vs Senning)				
Between 0 and 10 years	0.37 (0.08-1.73)	0.21	0.33 (0.07-1.56)	0.16
After 10 years	1.70 (0.76-3.79)	0.19	1.49 (0.62-3.56)	0.37

d-TGA= dextro-transposition of the great arteries, HR = hazard ratio, CI = confidence interval, ASO = arterial switch operation

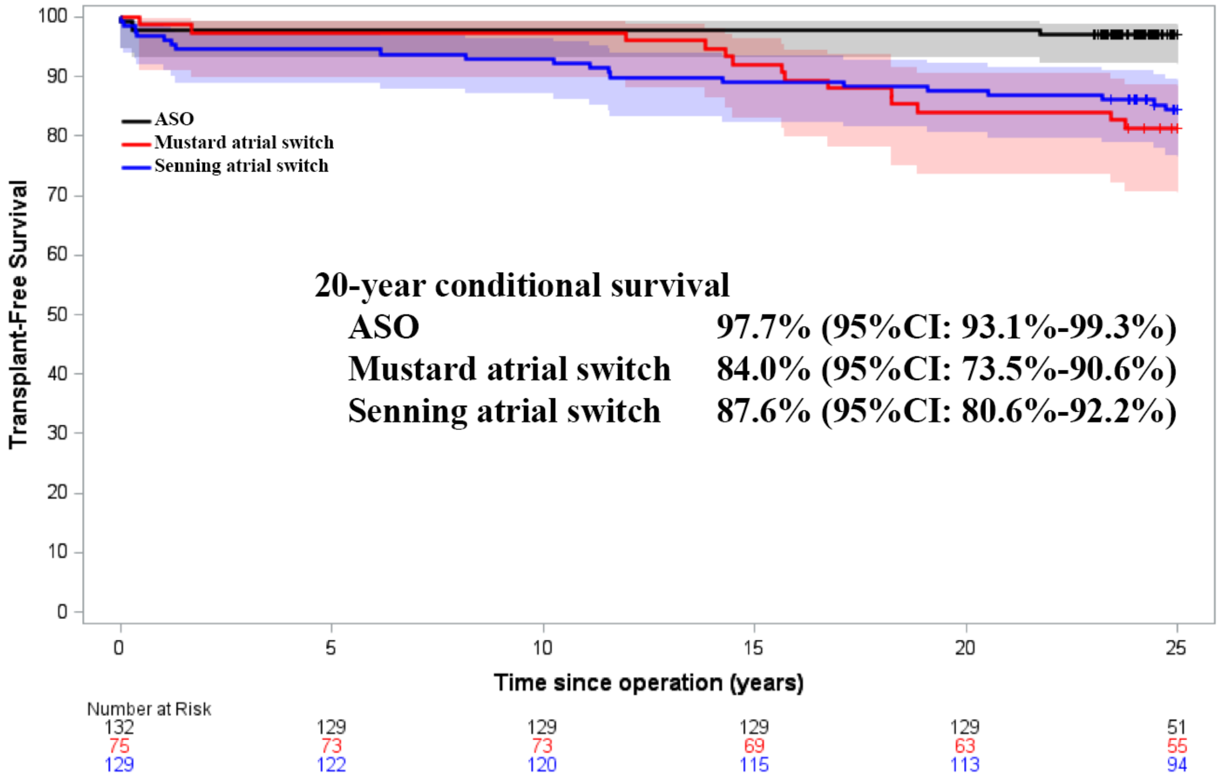
* adjusted for sex, transposition complexity, and surgical center

Supplemental Figure 1.



Supplemental Figure 1. Kaplan-Meier curves for overall transplant-free survival of patients with d-transposition of the great arteries shown by each specific operation. ASO = arterial switch operation, CI= confidence interval.

Supplemental Figure 2.



Supplemental Figure 2. Kaplan-Meier survival curves for conditional survival of hospital survivors with d-transposition of the great arteries shown by each specific operation. ASO = arterial switch operation, CI = confidence interval.