Determinants of repair type, reintervention, and mortality in 393 children with double-outlet right ventricle

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Supplemental material is available online.

Objective: We sought to define the prevalence of definitive end-states and their determinants in children with double-outlet right ventricle.

Methods: We performed a clinical record review of 393 children with double-outlet right ventricle presenting to our institution from 1980 to 2000.

Results: Double-outlet right ventricle classification was as follows: subaortic ventricular septal defect with or without pulmonary stenosis in 47%, subpulmonic ventricular septal defect in 23%, noncommitted ventricular septal defect in 26%, and doubly committed ventricular septal defect in 4%. Hypoplastic ventricles were present in 39%, pulmonary stenosis was present in 65%, and aortic arch obstruction was present in 24%. Biventricular repair was performed in 194 patients (55%) at a median age of 10 months (range: birth to 14.0 years), and the Fontan operation (n = 182; 23%) was performed at a median age of 3.7 years (range: 6 months to 14.9 years). Results improved over time ($P < .001$). Factors discriminating among end-states included younger patient age at presentation ($P < .001$), lower weight ($P < .001$), and adequacy of left-sided heart structures, especially the size of the left ventricle ($P < .001$), aortic arch ($P < .001$), and mitral valve ($P = .004$). For complex double-outlet right ventricle, Rastelli-type repair increased early reintervention risk ($P = .04$) and late post-repair mortality ($P = .02$), whereas the arterial switch operation increased early post-repair mortality ($P = .02$) with a benefit of improved late post-repair survival.

Conclusions: Biventricular repair, especially Rastelli-type reconstruction, is associated with higher late mortality and reintervention than is Fontan repair. The wisdom of extending biventricular repair to borderline anatomic candidates with hypoplastic left-sided structures or a nonsubaortic ventricular septal defect is questionable.

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Double-outlet right ventricle (DORV) defines a ventriculoarterial connection in which 50% of each great artery originates from the morphologic right ventricle.¹ DORV occurs as a heterogeneous group of congenital malformations subclassified by Lev and associates² according to the relationship of the ventricular septal defect (VSD) to the great arteries: (1) subaortic VSD with or without pulmonary stenosis; (2) subpulmonic VSD; (3) doubly committed VSD; and (4) noncommitted VSD.

Innovations in the Fontan operation have led to improved early and midterm results after single-ventricle repair.³⁻⁸ Similarly, innovative techniques coupled with improved perioperative care in the modern era have made biventricular repair achievable even in patients with complex forms of DORV, albeit at a higher early mortality rate compared with single-ventricle repair.^{1,3,9-11} Delius and colleagues³ found that the application of complex biventricular repair resulted in higher reintervention and mortality rates at 3 years compared with single-ventricle repair in a

Abbreviations and Acronyms

DORV	= double-outlet right ventricle
LV	= left ventricle
RVOT	= right ventricular outflow tract
RV-PA	= right ventricle–pulmonary artery
VSD	= ventricular septal defect

similar anatomic group. What remains in question, though, is whether the early hazard of a “risky” biventricular repair is mitigated by an important late benefit. Further, it is unclear across the morphologic spectrum of DORV which patient substrates are best suited for a particular biventricular repair type, and whether there are specific anatomic characteristics that are consistently associated with either a biventricular or single-ventricle approach.

The objectives of this study were, therefore, to (1) characterize the spectrum of presenting clinical and anatomic features in the largest consecutive single institution series of patients with DORV; (2) determine the prevalences of single-ventricle repair, biventricular repair, and pre-repair attrition and their associated factors; and (3) determine the prevalence of death and reintervention after repair and their associated factors.

Materials and Methods**Patients**

After appropriate approval from the Ethics Review Board at the Hospital for Sick Children, all children aged less than 18 years ($n = 444$) presenting to the Hospital for Sick Children with a diagnosis of DORV and born between 1980 and 2000 were identified from computerized databases. Anatomic diagnosis of DORV was confirmed in 393 patients on the basis of fetal and postnatal echocardiography, angiography, surgical inspection, or autopsy findings. A diagnosis of DORV was made if both great arteries originated predominantly from the right ventricle with application of the “50% rule.”¹² VSD location was determined using the classification system developed by Lev and associates.²

Data regarding initial demographic and morphologic characteristics, surgical procedures, and outcomes were abstracted by review of patient records. Echocardiographic and cardiac catheterization reports were reviewed, and clinical status at the last patient clinic visit (mean follow-up 8 ± 6 years) was documented by review of clinic notes.

Statistical Analysis

Data are presented as frequency, median with range, or mean $\pm$ standard deviation as appropriate, with the number of nonmissing values indicated. Percentages, hazard functions, and parametric estimates are presented with confidence limits equivalent to 1 standard error (70%). All data analyses were performed using SAS statistical software (version 9; SAS Institute, Inc, Cary, NC). Categorical variables between groups were analyzed by the chi-square test or Fisher exact test as appropriate. Continuous variables between groups were compared using 2-sample t tests or the

TABLE 1. Reparative procedures ($n = 276$)

Procedure	No.
Single-ventricle repair types ($n = 82$)	
Lateral tunnel Fontan	30 (8%)
Extracardiac Fontan	27 (7%)
Classic atriopulmonary connection	22 (6%)
Kawashima operation	3 (1%)
Biventricular repair types ($n = 194$)	
Simple flat-patch closure VSD	35 (9%)
with RV-PA conduit	$n = 9$
with transannular patch	$n = 5$
with outflow tract patch	$n = 10$
Baffle closure VSD to aorta	133 (34%)
with RV-PA conduit (Rastelli-type)	$n = 28$
with transannular patch	$n = 22$
with outflow tract patch	$n = 36$
Arterial switch with closure VSD to neo-aorta	23 (12%)
with outflow tract patch	$n = 2$
Atrial switch with baffle LV to PA	2 (1%)
Yasui (Damus-Stansel-Kaye anastomosis + Rastelli)	2 (1%)

VSD, Ventricular septal defect; RV-PA, right ventricle–pulmonary artery; LV, left ventricle.

Wilcoxon rank-sum test, depending on the normality of the distribution of the data. Pairwise comparisons of continuous variables within each group were performed using a paired t test or Wilcoxon signed-rank test. Time-related events were analyzed initially using the nonparametric Kaplan–Meier method. Multiphase parametric modeling of the underlying hazard function was then used to determine the rates of transition to time-related events and identify incremental risk factors associated with each transition rate as previously described.^{13–15} Integration of the hazard functions using competing risks methodology^{13–15} was then used to determine the time-related prevalence of 4 mutually exclusive pre-repair end-states: death without repair, achievement of single-ventricle repair, achievement of biventricular repair, and remaining alive without repair. A second competing risk analysis determined the prevalence of 3 mutually exclusive outcomes after repair: death without subsequent initial reintervention, reintervention, and remaining alive without subsequent reintervention. The association of risk factors with each end-state transition rate was explored using multivariable regression analysis with bootstrap bagging^{13,14} to guide variable selection and assess the reliability of inclusion in final regression models.

Results**Patient Characteristics at Presentation**

The initial patient characteristics are shown in Table E1.

Initial Surgical Procedures

Overall. Reparative surgical procedures are shown in Table 1. A flow-chart illustrating the surgical procedures and subsequent outcomes for all 393 patients is shown in Figure E1. Of the 393 patients, 41 had no intervention, only

7 of whom remained alive at the last follow-up. Operative procedures in the remaining 352 patients included biventricular repair in 55% ($n = 194$), single-ventricle repair in 23% ($n = 82$), and palliation alone without subsequent repair in 22% ($n = 76$). Overall time-related survival from birth was 56% (70% confidence interval: 53%–59%) at 15 years (Figure E2).

Single-ventricle repair ($n = 82$). Staged single-ventricle repairs were completed at a median age of 3.7 years (range: 6 months to 14.9 years) and were varied in type (Table 1).

Biventricular repair ($n = 194$). Biventricular repairs were performed at a median age of 10 months (range: birth to 14.0 years) (Table 1). Primary biventricular repair was performed in 109 patients (56%); 51 (26%) had 1 palliative procedure before repair, 27 (14%) had 2 procedures, and 8 (4%) had 3 procedures. Augmentation or reconstruction of the right ventricular outflow tract (RVOT) at repair included right ventricle–pulmonary artery (RV-PA) conduit in 38 patients (Rastelli-type), transannular patch placement in 27 patients, and RVOT patch in 48 patients.

Competing Risks Analysis: Outcomes Before and Including Repair

Patients transitioned to four end-states after birth: death without repair, biventricular repair, single-ventricle repair, and remaining alive without definitive repair. With these transition rates used simultaneously, the time-dependent prevalence of each state was calculated by the competing risks analysis. Five years from birth, 53% had achieved biventricular repair, 14% had achieved single-ventricle repair, 15% had died without definitive repair, and 18% remained alive without repair (Figure 1).

Death without repair. Incremental risk factors associated with an increased risk of death without repair were sought and are shown in Table E2.

Achievement of single-ventricle repair ($n = 82$). Incremental risk factors predictive of achieving a single-ventricle repair included later birth cohort ($P < .001$), prenatal diagnosis, presence of a hypoplastic left ventricle (LV) or double-inlet LV, and VSD type other than subaortic (Table E2).

Achievement of biventricular repair ($n = 194$). Incremental risk factors predictive of achieving a biventricular repair included (1) demographic factors (younger age at surgery); (2) morphologic factors (absence of mitral valve atresia or straddling of the mitral valve, absence of LV hypoplasia, VSD type other than noncommitted); and (3) procedural characteristics (<3 pre-repair interventions, VSD enlargement) (Table E2). The favorable influence of later birth cohort on outcomes for an ideal patient of age 1 year with favorable anatomy is illustrated in a risk-adjusted competing risks nomogram (Figure 2) stratified by 2 different birth decades. In 1980, mortality was 16% with a significant proportion of patients (17%) remaining unrepaired

Figure 1. Non-risk adjusted competing risks estimates for the proportion of 393 children with DORV reaching each of 4 end-states after birth. All patients begin alive and thereafter migrate to 1 of 4 mutually exclusive end-states (achievement of biventricular repair, achievement of single-ventricle repair, death before reaching definitive repair, and remaining alive without repair) at a time-dependent rate defined by the underlying hazard functions. At any point in time, the sum of the proportion of children in each state is 100%. For example, the estimated prevalences after 5 years from birth are as follows: biventricular repair, 53%; single-ventricle repair, 14%; death without repair, 15%; remaining alive without repair, 18%. Parametric point estimates (solid lines); 70% confidence interval (dashed lines); estimated proportion of patients in each state at 5 years from birth (numbers in parentheses). 1-v, Single ventricle; 2-v, biventricular.

at 5 years. Recent birth decade in the year 2000, however, shows a dramatic reduction in pre-repair attrition (1%) concomitant with a significant increase in the proportion of children achieving definitive repair (97%) at 5 years.

Competing Risks Analysis: Outcomes After Repair

After complete repair ($n = 276$), the proportion of children reaching each of 3 end-states (subsequent reintervention, death without reintervention, and remaining alive free of reintervention) were estimated from a second competing risks analysis. The predicted prevalences after 15 years from repair are as follows: 37% reintervention, 26% death without reintervention, and 37% remaining alive without reintervention (Figure 3).

Reintervention after complete repair ($n = 82$). A first reintervention occurred in 82 patients at a median interval of 3.3 years (range: 3 days to 16.4 years) after complete repair. Freedom from first reintervention was 81%, 69%, and 59% at 5, 10, and 15 years after repair. Indications for reintervention by repair type are listed in Table E3. First reintervention was most common in patients undergoing Rastelli-type repairs ($n = 40$; 49%) and least common in patients with tetralogy of Fallot with subaortic VSD undergoing

Figure 2. Risk-adjusted multivariable competing risks depiction of pre-repair end-states stratified by recent birth decade (year 2000) (B) compared with older birth decade (year 1980) (A) for an ideal patient aged 1 year with favorable anatomy. Mortality is increased, with a significant proportion of patients waiting for definitive repair in an earlier era (A), compared with a dramatic reduction in pre-repair attrition (1%) concomitant with a significant increase in the proportion of children achieving definitive repair. Continuous point estimates (*solid lines*) and the predicted proportion of patients achieving each end-state at 5 years from birth (*numbers underneath each caption*). 1-v, Single ventricle; 2-v, biventricular.

simple flat-patch VSD closure ($n = 7$; 9%). Risk factors for reintervention were lower weight at repair ($P = .03$) and Rastelli-type repair with the use of an RV-PA conduit ($P = .02$) (Table E4).

Death after complete repair ($n = 64$). Death after repair but without reintervention was characterized by a constant hazard phase that predominated for 3 years after repair followed by a rapidly increasing late hazard phase that escalated 3 years after repair (Figure E3). Incremental risk factors associated with increased mortality without reintervention varied depending on the time distribution from repair (Table E4). The arterial switch operation increased mortality early after repair ($P = .02$), whereas late attrition was associated with baffle closure of the VSD to the aorta ($P = .02$). The survival curve (Figure 4, A) and hazard function (Figure 4, B) illustrate that although the early risk is higher for the patients undergoing the arterial switch operation, the ongoing late phase risk of death is higher for the group undergoing baffle closure of the VSD to the aorta.

Discussion

We described morphologic factors and determined the prevalence of definitive end-states and their predictive factors in the largest single-institution series of children with DORV. We showed that biventricular repairs, especially Rastelli-type reconstruction using an RV-PA conduit, are associated with higher late mortality and reintervention rates compared with single-ventricle repairs. High early mortality associated with biventricular options such as the arterial switch operation is perhaps attributable to a learning curve because our study circumscribed a broad time interval. However, ongoing late attrition and reintervention associated predominantly with biventricular options are cause for concern. Unless future studies demonstrate a conclusive long-term or health-related quality of life benefit favoring biventricular repair, the wisdom of extending biventricular repair to borderline anatomic candidates with inadequate left-sided structures (especially hypoplastic mitral valves) and a non-subaortic VSD is questionable.

Figure 3. Non-risk adjusted competing risks estimates for the proportion of 276 children with DORV reaching each of 3 end-states after complete repair. All patients begin alive at the time of repair (time 0) and thereafter migrate to 1 of 3 mutually exclusive end-states (subsequent reintervention, death without reintervention, and remaining alive without subsequent reintervention) at a time-dependent rate defined by the underlying hazard functions. At any point in time, the sum of the proportion of children in each state is 100%. For example, the estimated prevalences after 15 years from repair are as follows: reintervention, 37%; death, 26%; and remaining alive without reintervention, 37%. Parametric point estimates (solid lines); 70% confidence interval (dashed lines); estimated proportion of patients in each state at 15 years from repair (numbers in parentheses).

Mortality

Our study, in concordance with previous reports, showed an improvement in outcomes for patients with DORV.^{1,4,16,17} We showed that the favorable influence of contemporary era extends to even those patients with complex forms of DORV (subpulmonary VSD with outflow obstruction). The 15-year overall survival of 56% in this study is lower than that reported by others.^{1,16} However, other reports selected patients with more favorable anatomy (ie, tetralogy of Fallot-type DORV), excluded attrition before repair, or focused on outcomes after biventricular repairs. Belli and colleagues⁹ reported 86% 10-year survival from biventricular repair in 154 patients with concordant ventriculoarterial connection repaired between 1985 and 1996. Although direct comparisons with the figures reported in previous studies are not relevant because we have taken into account the simultaneous competing risks of death without repair and each repair pathway, the estimate reported by Belli and colleagues⁹ is identical to the 86% 10-year survival after repair estimated from the second competing-risks analysis in our study. Brown and colleagues¹ reported 89.5% 15-year survival after repair in their historical experience with 124 patients repaired between 1980 and 2000. Only 20 patients in their series underwent Rastelli-type repair, and

Figure 4. A, Risk-adjusted survival without reoperation in a patient weighing 4 kg, stratified by repair type, either baffle closure of the VSD to the aorta ($n = 133$) or arterial switch operation with baffle closure of the VSD to the neo-aorta ($n = 23$). The arterial switch operation has a higher early attrition after repair but results in improved long-term survival free of operation at 15 years. Parametric point-estimates (solid lines) enclosed by 70% confidence limits (dashed lines). B, Risk-adjusted hazard functions (solid lines) from our multivariable competing risk models stratified by 2 different repair types. The hazard function represents the instantaneous risk of death before reoperation at each moment in time after repair and consisted of a constant phase that predominated until 3 years after repair, followed by an accelerated late-phase mortality risk. VSD, ventricular septal defect.

the median follow-up was slightly shorter than ours (6 years vs 8 years, respectively).

Achievement of Definitive Repair

We found that an adequately sized normal mitral valve and LV are the main determinants of achieving a biventricular

repair, whereas a small LV or abnormalities of an atrioventricular valve were associated with a greater predilection toward single-ventricle repair. The association between hypoplastic left-sided heart structures and mortality at any time-point has been reported,^{9,4,17} but our study is the first to show which morphologic features predict achievement of each repair type. Kleinert and colleagues⁴ documented an association between aortic arch obstruction and mortality before repair, and found that multiple VSDs were associated with late mortality after repair. Belli and colleagues⁹ similarly identified mitral valve anomalies as an independent predictor of death after repair.

VSD location was a crucial determinant of repair type in our study. Patients with subaortic defects were unlikely to undergo single-ventricle repair, whereas those with non-committed VSD were likely to be triaged to a single-ventricle pathway. The presence of a subaortic VSD was also a risk factor for death without definitive repair. This finding may reflect the presence of important concomitant pulmonary stenosis or outflow obstruction within this subset and highlights the heterogeneity that has complicated the development of a standardized nomenclature for DORV.

We also identified later birth cohort to be associated with an increased prevalence of both single-ventricle and biventricular repairs. From our competing risks analysis, we showed that a 1-year old patient with favorable characteristics born in the year 1980 had only a 53% chance of reaching a biventricular repair and a 16% chance of death before reaching repair, whereas the same patient born in the year 2000 had a 97% chance of achieving biventricular repair and a less than 1% chance of death before reaching repair. Undoubtedly, the expanded armamentarium of biventricular options, more precise preoperative imaging, prenatal diagnosis (a protective factor against pre-repair mortality in our study), and improved perioperative care have contributed to the improved outcomes.^{1,18-21}

Outcomes After Repair

Optimism over improved overall outcomes must be tempered by a critical look at post-repair results.^{20,22} The perceived benefit of a biventricular repair may not be justified if biventricular repair increases late death or reintervention compared with single-ventricle repairs.^{1,4-6,20} Although it is true that some reinterventions are anticipated (eg, RV-PA conduit changes in patients undergoing Rastelli-type repairs), morbidity and mortality are associated with any reoperation, whether expected or unplanned. This question is increasingly relevant with improved short- and medium-term results after single-ventricle reconstruction, especially in the presence of 2 functioning ventricles, documented by Jacobs and Norwood⁵ and Pearl and colleagues.⁶

Although standardized functional assessment was not undertaken in this study, neither single-ventricle repair nor

single-ventricle repair type was associated with adverse post-repair outcome. In contrast, biventricular repairs, specifically Rastelli-type repair with the use of an RV-PA conduit, was significantly associated with both post-repair reintervention and death. We also showed that the arterial switch operation with baffle of the LV to the neo-aorta, although associated with an increased risk of early post-repair mortality, mitigates somewhat the risk of late death. Given the historical nature of this report, it is likely that the early risk associated with the arterial switch operation was attributable to a learning curve and may therefore be neutralized in the current era, similar to the paradigm documented in transposition of the great arteries.²³ However, cautious interpretation is warranted because parallel advancements in single-ventricle techniques (eg, extracardiac reconstruction) were not accompanied by a significant fluctuation in early risk in our study.

The need for reintervention after repair remains a considerable challenge in patients with repaired DORV.^{1,3-5,9,17,20} Our competing risks analysis predicted that 37% of patients will undergo reintervention within 15 years from repair. The majority of reinterventions were directed at relief of RVOT obstruction, but residual or recurrent LVOT obstruction was also documented in 11 patients (13%). Our findings agree with those of Kleinert and colleagues.⁴ They reported a 65% freedom from reoperation at 10 years from repair, with the indication being RVOT obstruction in 8 patients (27%) and LVOT obstruction in 4 patients (14%). VSD enlargement at the time of repair, as shown by Belli and colleagues,⁹ was not associated with an increased risk of reintervention in our study. However, it is possible that VSD enlargement may be surrogated by Rastelli-type repair in our study (which was a risk factor for reintervention), because intraventricular baffle construction for transposition-type DORV is nearly always accompanied by generous conal septal resection.

Limitations

The limitations of this study include those of any single-institution retrospective series. Echocardiographic and cardiac catheterization data were gathered from reports rather than standardized review. Designation of morphologic DORV-type and associated abnormalities was based on review of diagnostic reports and surgical (or autopsy) data from a broad time period in which standardized nomenclature did not exist. It is possible, given the anatomic complexity of DORV, that morphologic assignment was incorrect. The heterogeneous nature of our study population is another possible limitation, because we included more “simple” forms of DORV as well as more “complex” forms. However, this was intentional for 3 main reasons: (1) There are no uniform objective criteria that discriminate “simple from complex.” Rather, there are many anatomic factors

that add or subtract from the complexity of a particular phenotype, and therefore the use of morphologic “patterns” may be an oversimplification; (2) nonassignment to a “complex” or “simple” group was necessary to tease out those specific characteristics that led to successful single-ventricle or biventricular repair; and (3) our stated objective was to determine outcomes among the entire population of DORV.

Finally, an important indication for reintervention in DORV is postoperative arrhythmia, whether an early consequence of repair technique or a late consequence of ventricular dilation. Unfortunately, our data regarding postoperative conduction abnormalities are incomplete, although we are aware that complete heart block developed in 5 patients (2 requiring pacemaker implantation), early atrial arrhythmias developed in 42 patients, and ventricular arrhythmias developed in 5 patients.

Conclusions

DORV represents a complex heterogeneous group of congenital anomalies that mandate a morphologically driven treatment algorithm based on the adequacy of the left-sided structures and the location of the VSD. Improved results over time have increased the proportion of children eventually achieving definitive repair, but reintervention and late attrition remain important problems, especially with Rastelli-type repair. Biventricular strategies, such as the arterial switch operation with baffle of the VSD to the neo-aorta, have mitigated some of the adverse post-repair outcomes, but patients with hypoplastic left-sided structures and a nonsub-aortic VSD may fare better with a single-ventricle repair.

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Figure E1. Flow-chart of events after birth in 393 children with anatomically proven DORV. Overall, there were 194 deaths during the duration of the study. There were 41 patients who had no interventional procedure and 76 patients who had only palliative procedures. *DORV*, Double-outlet right ventricle; *1V*, single ventricle; *2V*, biventricular.

Figure E2. Overall survival from birth was 75% at 1 year, 65% at 5 years, and 56% at 15 years (70% confidence intervals: 53%-59%). There was a rapidly declining early risk of death (*inset*) followed by a tapering late risk thereafter. Parametric estimates (*solid lines*) surrounded by their 70% confidence limits (*dashed lines*). Nonparametric estimates (*circles*) with error bars equivalent to 1 standard error. Insert, parametric hazard function (*solid curve*) with 70% confidence limits (*dashed curve*) represents the instantaneous risk of death at any given time up to 15 years after birth.

Figure E3. Death after complete repair ($n = 64$) but without reoperation was 96%, 86%, and 63% at 5, 10, and 15 years after repair, respectively. Mortality risk was characterized by a constant hazard phase that predominated for 3 years after repair followed by a rapidly increasing late hazard phase (*inset*) that escalated 3 years after repair. Parametric estimates (*solid lines*) surrounded by 70% confidence limits (*dashed lines*). Nonparametric estimates (*circles with error bars*) and number of patients traced at that time point (*numbers at the bottom horizontal axis*).

TABLE E1. Initial patient characteristics (n = 393)

Variable	Value	No. Missing
Demographic characteristics		
Gender (female/male)	158:235	0
Age at presentation (median; range)	1 day (birth to 14 y)	
Prenatal diagnosis	36 (9%)	0
Noncardiac anomalies	132 (34%)	2
Chromosomal anomalies	38 (10%)	0
Preterm (<36 wk gestation)	40 (16%)	142
Ventriculoarterial relationship		55
Concordant	143 (42%)	
D-malposed	121 (36%)	
L-malposed	26 (8%)	
Side-by-side (Taussig–Bing)	48 (14%)	
Location of VSD		58
Subaortic	156 (47%)	
Noncommitted	88 (26%)	
Subpulmonary	76 (23%)	
Doubly committed	15 (4%)	
Multiple VSDs	28 (7%)	
Hypoplastic LV	117 (30%)	2
Hypoplastic RV	37 (9%)	2
Aortic arch obstruction	94 (24%)	0
Pulmonary stenosis	257 (67%)	0
Coronary artery anomalies	79 (20%)	0
Right atrial isomerism	24 (6%)	0
Left atrial isomerism	24 (6%)	0
Double-inlet LV	11 (3%)	0
Double-inlet RV	20 (5%)	0
Common atrioventricular valve	97(25%)	0
Mitral valve abnormalities		0
Overriding/straddling	23 (6%)	
Stenosis	34 (9%)	
Atresia	35 (9%)	
Cleft	9 (2%)	
Tricuspid valve abnormalities		0
Overriding/straddling	9 (2%)	
Stenosis or atresia	12 (3%)	
Coronary arterial abnormalities		4
Present (yes/no)	78 (20%)	
Single left coronary artery	13 (17%)	
Left anterior descending from right coronary artery	10 (8%)	
Single right coronary artery	9 (12%)	
Accessory left anterior descending artery	9 (12%)	
Circumflex coronary artery from right coronary artery	9 (12%)	
Conal branches from right coronary artery	7 (9%)	
Unspecified single coronary artery	5 (6%)	
Other or unknown	16 (21%)	

VSD, Ventricular septal defect; LV, left ventricle; RV, right ventricle.

TABLE E2. Incremental risk factors for time-related transition to pre-repair end-states after birth (n = 393)

Variable	Coefficient ($\pm$ SE)	P	Reliability* (%)
1. For death without achieving repair			
Younger age at presentation to HSC (per year)	1.99 $\pm$ 0.30	<.001	96%
Lower weight at first intervention (per kilogram) [†]	3.50 $\pm$ 0.47	<.001	90%
Higher mean PA pressure at initial catheterization (per millimeters of mercury)	0.07 $\pm$ 0.02	<.001	68%
Higher systemic mean arterial pressure at initial catheterization (per millimeters of mercury)	0.05 $\pm$ 0.02	.002	68%
Higher RVSP at initial echocardiography (per millimeters of mercury)	0.06 $\pm$ 0.01	<.001	68%
Unrestrictive ASD at initial echocardiography	0.92 $\pm$ 0.35	.008	68%
Older age at palliation (per year)	2.24 $\pm$ 0.40	<.001	99%
Coarctation of the aorta	1.45 $\pm$ 0.38	<.001	99%
Presence of subaortic VSD	0.63 $\pm$ 0.28	.02	97%
Stenotic or atretic tricuspid valve	2.33 $\pm$ 0.52	<.001	54%
Noncardiac anomalies	1.49 $\pm$ 0.27	<.001	85%
No intervention	6.79 $\pm$ 0.36	<.001	98%
Catheter diagnosis (protective)	2.25 $\pm$ 0.33	<.001	96%
Presence of IVC anomaly (protective)	6.13 $\pm$ 0.90	<.001	78%
Interaction term between IVC anomaly and catheter diagnosis	3.61 $\pm$ 0.87	<.001	—
2. For achievement of single-ventricle repair			
Later birth cohort (per year)	0.10 $\pm$ 0.2	<.001	83%
Hypoplastic LV	0.69 $\pm$ 0.23	.003	84%
Double inlet LV	1.21 $\pm$ 0.42	.003	92%
Absence of subaortic VSD	0.84 $\pm$ 0.31	.007	84%
Absence of hepatic venous anomaly	1.1 $\pm$ 0.40	.008	52%
Fetal diagnosis	1.08 $\pm$ 0.35	.002	65%
3. For achievement of biventricular repair			
Later birth cohort (per year)	0.09 $\pm$ 0.01	<.001	93%
Younger age at first intervention (per year) [‡]	1.08 $\pm$ 0.34	.002	89%
Balanced atrioventricular canal	1.53 $\pm$ 0.48	.001	97%
Nonhypoplastic LV	1.77 $\pm$ 0.35	<.001	89%
Absence of noncommitted VSD	0.75 $\pm$ 0.30	.01	79%
VSD enlargement at first intervention	0.83 $\pm$ 0.35	.02	99%
<3 pre-repair interventions	1.29 $\pm$ 0.42	.002	89%
Taussig-Bing anomaly	0.66 $\pm$ 0.20	.001	86%
Not performing atrial septostomy	0.61 $\pm$ 0.24	.01	99%
Normal mitral valve	0.67 $\pm$ 0.24	.004	100%
Absence of overriding/straddling mitral valve	0.95 $\pm$ 0.43	.03	100%
Interaction term between VSD enlargement and age at first intervention	-1.67 $\pm$ 0.11	.14	—

HSC, Hospital for Sick Children; PA, pulmonary artery; RVSP, right ventricular systolic pressure; ASD, atrial septal defect; VSD, ventricular septal defect; IVC, inferior vena cava; LV, left ventricle; SE, standard error. *Percent refers to the reliability determined by bootstrap bagging (variable resampling) method.

[†]After logarithmic transformation. [‡]After inverse transformation.

TABLE E3. Initial reinterventions after repair

Repair type	No.
Single-ventricle repairs (n = 24)	
Fenestration closure	9
Coil-occlusion of collaterals	4
Tricuspid valve repair/replacement	2
Pacemaker insertion	2
Branch pulmonary artery dilation/arterioplasty	2
Fontan revision	2
Creation of axillary fistula	1
Repair of aortic coarctation	1
Myectomy for subaortic stenosis	1
Biventricular repairs (n = 58)*	
Relief of RVOT obstruction	23
Relief of LVOT obstruction	11
Branch pulmonary artery dilation/arterioplasty	12
RVOT aneurysm repair	4
Pulmonary valve implantation	2
Tricuspid valve repair/replacement	2
Residual VSD closure	2
Pacemaker implantation	1

RVOT, Right ventricular outflow tract; LVOT, left ventricular outflow tract; VSD, ventricular septal defect. *Reason for reintervention in 1 patient unspecified.

TABLE E4. Incremental risk factors for time-related transition to post-repair outcomes (n = 276)

Variable	Coefficient (±SE)	P	Reliability* (%)
1. For death after repair			
Constant phase			
Arterial switch with baffle VSD to neoaorta	3.07 ± 1.29	.02	84%
Late phase			
Lower weight at first intervention (per kilogram)†	0.65 ± 0.34	.06	68%
Intraventricular repair with baffle VSD to aorta	0.63 ± 0.28	.02	84%
2. For reintervention after repair			
Constant phase			
Lower weight at first intervention (per kilogram)†	0.87 ± 0.41	.03	68%
Rastelli-type repair	0.88 ± 0.37	.02	84%
Late phase:			
Two pre-repair interventions	1.16 ± 0.54	.03	71%

VSD, Ventricular septal defect; SE, standard error. *Percent refers to the reliability determined by bootstrap bagging (variable resampling) method. †After logarithmic transformation.