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Outcomes Following Congenital Heart Surgery in Down Syndrome Patients: Analysis of a National Clinical Database

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Abstract

Background—Contemporary outcomes data in Down Syndrome (DS) patients undergoing congenital heart surgery are limited. We describe patient characteristics and post-operative morbidity and mortality in a large multi-center cohort.

Patients and Methods—This retrospective cohort study utilized The Society of Thoracic Surgeons Congenital Heart Surgery Database to compare patient characteristics and postoperative outcomes in DS and non-DS patients (0–18y) undergoing surgery from 2000–2008. Primary analysis focused on the most common surgeries performed in DS patients.

Results—A total of 45,579 patients (n=4,350 DS, 41,229 non-DS) were included: median age 7m [interquartile range (IQR) 47d–4yr]; 56% male. DS patients were younger at surgery, with the exception of those undergoing tetralogy of Fallot (TOF) and atrioventricular septal defect (AVSD) repair. Mortality did not differ significantly in DS vs. non-DS patients. Length of stay was

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prolonged in DS patients undergoing atrial septal defect [4d (IQR 3–5d) vs. 3d (IQR 2–4d), $p<0.0001$] and ventricular septal defect (VSD) closure [5d (IQR 4–8d) vs. 4d (IQR 3–6d), $p<0.0001$], and TOF repair [7d (IQR 5–10d) vs. 6d (IQR 5–9d), $p<0.001$], and was associated with post-operative respiratory and infectious complications. DS patients undergoing VSD closure also had a higher rate of heart block requiring pacemaker placement (2.9% vs. 0.8%, $p<0.0001$).

Conclusion—In this large contemporary cohort undergoing congenital heart surgery, DS does not confer a significant mortality risk for the most common operations performed in this population; however post-operative morbidity remains common.

Keywords

Down syndrome; Congenital heart defects

Introduction

Down syndrome is the most commonly occurring chromosomal abnormality, and recent data suggest the prevalence in the United States has increased over the past two decades by nearly a third (1). Congenital heart disease is reported to occur in 40–60% of patients with Down syndrome, with complete atrioventricular septal defect being the most common defect (2, 3). Other frequently occurring lesions include atrial and ventricular septal defects, and tetralogy of Fallot. Previous studies evaluating outcomes following congenital heart surgery in patients with Down syndrome have shown conflicting results. Some have reported increased mortality, length of stay, and morbidities such as duration of ventilation, and infection, while others have suggested similar or improved outcomes in Down syndrome patients undergoing atrioventricular septal defect repair (2–5). Studies to date have been limited by small sample size, and focus primarily on patients undergoing atrioventricular septal defect repair.

The purpose of this study was to describe post-operative morbidity and mortality in a large, multi-center, contemporary cohort of Down syndrome patients undergoing congenital heart surgery. Primary analysis focused on the most common surgeries performed in Down syndrome patients. Due to the infrequency of Down syndrome patients at any single center undergoing staged palliation for a functionally univentricular heart, we also evaluated outcomes in this more rare subgroup of patients in secondary analysis.

Patients and Methods

Data Source

This retrospective cohort study utilized The Society of Thoracic Surgeons (STS) Congenital Heart Surgery Database. As previously described, the STS Congenital Heart Surgery Database collects operative and peri-operative data on all patients undergoing surgery for congenital heart anomalies at participating centers (6). It is estimated that STS centers currently represent nearly two thirds of all centers performing congenital heart surgery in the United States (7). Data collected include demographic information, cardiac diagnosis, non-cardiac and genetic abnormalities, pre-operative factors, intra-operative details, surgical procedure performed, post-operative complications, and inhospital mortality. The Duke

Clinical Research Institute serves as the data warehouse and analysis center for all of the STS National Databases. This study was approved by the Duke institutional review board, and by the Access and Publications Committee of the STS Workforce for National Databases.

Patient Population

To maximize data integrity, analysis was restricted to 63 STS centers with >90% complete data for all study variables. From these centers, patients 18 years of age who underwent congenital heart surgery between January 1, 2000 and June 30, 2008 were included. Only the first operation of each hospitalization was analyzed. We excluded 15,290 patients with a genetic abnormality other than Down syndrome and 867 patients with missing or invalid data for sex, weight, or type of procedure. This left a final study population of 45,579 patients from 63 centers.

Data Collection

Data collection included demographic information, Down syndrome status, and the presence of any pre-operative risk factors (defined in the database as pre-operative acidosis, shock, arrhythmia, atrioventricular block, pulmonary hypertension, mechanical ventilatory support, endocarditis, sepsis, neurologic deficit, or seizure), cardiac diagnosis and surgical procedure performed. Operative data included duration of cardiopulmonary bypass, cross clamp, and circulatory arrest (if applicable). Outcomes data included inhospital mortality, total post-operative length of stay, and post-operative complications. Post-operative complications were classified as: delayed sternal closure, unplanned re-operation during the hospitalization, renal failure requiring temporary or permanent dialysis, neurologic deficit (transient or permanent deficit, or seizures), infection (sepsis, wound infection or dehiscence, mediastinitis, or endocarditis), pulmonary (phrenic or recurrent laryngeal nerve injury, pneumothorax, pleural effusion requiring drainage, mechanical ventilatory support > 7 days, reintubation, tracheostomy), arrhythmia, atrioventricular block requiring permanent pacemaker, cardiac arrest, use of extracorporeal membrane oxygenation, and pulmonary hypertension. Of note, pulmonary hypertension is currently defined in the database as a pulmonary artery pressure greater than or equal to systemic arterial pressure as estimated by echocardiography or cardiac catheterization.

Analysis

Patient characteristics and outcomes were summarized in Down syndrome and non-Down syndrome patients using frequencies and percentages for categorical variables, and median and interquartile range for continuous variables. Patient weight was plotted on standard growth curves and converted to z-scores (8). Standard growth curves were used for both Down syndrome and non-Down syndrome patients as the purpose was to facilitate comparison of weight between Down syndrome and non-Down syndrome patients normalizing for age at surgery, rather than comparison to their respective normative populations.

The ten most common surgical procedures were described in the Down syndrome and non-Down syndrome groups. Five of the most common procedures in Down syndrome patients

were then evaluated further, including atrial septal defect closure (any type), ventricular septal defect closure (any type), complete atrioventricular septal defect repair, mitral valve repair/replacement, and tetralogy of Fallot repair (including surgeries involving transannular patch, non-transannular patch, or right ventricle to pulmonary artery conduit). For these procedures, patient characteristics, operative data, and outcomes including in-hospital mortality and post-operative length of stay were compared in Down syndrome vs. non-Down syndrome patients using the Pearson Chi-square test for categorical variables and the Wilcoxon rank-sum test for continuous variables. Post-operative complications (as noted above) were similarly evaluated. Finally, in-hospital mortality and post-operative length of stay were evaluated in the rare subgroup of Down syndrome patients with a functionally univentricular heart undergoing staged palliation. This included Stage 1 palliation (Norwood operation or Damus-Kaye-Stansel operation), cavopulmonary anastomosis (bidirectional Glenn or hemifontan operation), and Fontan completion (lateral tunnel or extracardiac).

Missing data were rare (<0.5% for all variables). Patients with missing data were excluded from analysis involving the missing variable. P-values were reported without adjustment for multiple comparisons. In light of the number of endpoints evaluated, a highly stringent criterion ($p < 0.001$) was used for interpreting statistical significance.

Results

Pre-operative and Operative Characteristics

A total of 45,579 patients were evaluated: 4,350 Down syndrome patients and 41,229 non-Down syndrome patients. Patient characteristics are displayed in Table 1. The Down syndrome group included fewer males, and was younger at the time of surgery. As expected, Down syndrome patients also weighed less at the time of surgery after normalizing for age. The ten most common procedures performed in Down syndrome and non-Down syndrome patients are displayed in Table 2. Complete atrioventricular septal defect repair was the most common procedure performed in Down syndrome patients (33%), whereas ventricular septal defect repair was the most common procedure performed in non-Down syndrome patients (8%).

Five of the most common procedures performed in Down syndrome patients were investigated further (atrial septal defect closure, ventricular septal defect closure, complete atrioventricular septal defect repair, mitral valve repair/replacement, and tetralogy of Fallot repair; Table 3). Children with Down syndrome were younger at the time of surgery with the exception of those undergoing tetralogy of Fallot and complete atrioventricular septal defect repair who were similar in age to non-Down syndrome patients. Weight z-scores at the time of surgery were lower in Down syndrome patients compared to non-Down syndrome patients for all procedures.

Down syndrome patients undergoing atrial septal defect and ventricular septal defect closure were more likely to have pre-operative risk factors compared to non-Down syndrome patients (21% vs. 7%, $p < 0.0001$, and 22% vs. 12%, $p < 0.0001$, respectively). There was no difference in the frequency of pre-operative risk factors in Down syndrome patients undergoing other procedures. In patients with an atrial septal defect, these included

significant differences in Down syndrome patients compared to non-Down syndrome patients in pre-operative pulmonary hypertension (6.2% vs. 0.2%, $p<0.0001$) and pre-operative neurologic deficit or seizure (2.8% vs. 0.9%, $p=0.01$, trend). No significant difference was found in pre-operative infection (sepsis or endocarditis 0% vs. 0.1%, $p=0.7$), or pre-operative mechanical ventilation (2.3% vs. 1.4%, $p=0.4$). In patients with a ventricular septal defect, significant differences were found in pre-operative pulmonary hypertension (8.4% vs. 2.0%, $p<0.0001$), and pre-operative neurologic deficit or seizure (1.3% vs. 0.5%, $p=0.008$, trend). No difference was seen in pre-operative infection (0.4% vs. 0.6%, $p=0.4$), or pre-operative mechanical ventilation (1.9% vs. 1.8%, $p=0.8$). Of note, there was no significant difference among patients undergoing atrioventricular septal defect repair in pre-operative pulmonary hypertension (4.1% vs. 4.7%, $p=0.6$)

Operative data are displayed in Table 4. Down syndrome patients undergoing ventricular septal defect closure had longer duration of cardiopulmonary bypass compared to non-Down syndrome patients. No statistically significant differences were seen in duration of cardiopulmonary bypass for the other procedures evaluated.

Outcomes

Outcomes data for those undergoing the most common types of surgery performed in Down syndrome patients are displayed in Table 4. No statistically significant differences were seen in in-hospital mortality in Down syndrome verses non-Down syndrome patients. There were trends toward increased mortality in Down syndrome patients undergoing tetralogy of Fallot repair, and decreased mortality in Down syndrome patients undergoing complete atrioventricular septal defect repair and mitral valve repair/replacement which did not reach statistical significance. Post-operative length of stay was similar for those undergoing complete atrioventricular septal defect repair and mitral valve repair/replacement. Down syndrome patients undergoing atrial septal defect closure, ventricular septal defect closure, and tetralogy of Fallot repair had significantly prolonged length of stay compared to non-Down syndrome patients.

Evaluation of the groups with longer length of stay demonstrated similar postoperative complications across groups. Compared with non-Down syndrome patients, a higher proportion of Down syndrome patients undergoing ventricular septal defect closure had post-operative infection (3.4% vs. 1.1%, $p<0.0001$), respiratory complications (11.3% vs. 5.2%, $p<0.0001$), and pulmonary hypertension (2.2% vs. 0.7%, $p=0.0001$). In addition, a higher proportion of Down syndrome patients undergoing ventricular septal defect closure had atrioventricular block requiring permanent pacemaker placement (2.9% vs. 0.8%, $p<0.0001$). Similarly, these complications were also seen in Down syndrome patients undergoing atrial septal defect closure (with the exception of pacemaker placement): post-operative infection (1.7% vs. 0.5%, $p=0.04$, trend), respiratory complications (5.1% vs. 1.9%, $p=0.005$, trend), and pulmonary hypertension (1.7% vs. 0.2%, $p=0.0002$). Finally, a greater proportion of Down syndrome patients undergoing tetralogy of Fallot repair also had respiratory complications (18.0% vs. 11.5%, $p=0.009$, trend), but there were no significant difference in pulmonary hypertension or post-operative infection. No significant differences were found in these complications in the Down syndrome patients without prolonged length

of stay, with the exception of a trend toward greater respiratory complications in the Down syndrome patients undergoing mitral valve repair/replacement (12.5% vs. 6.8%, $p=0.001$). Finally, the complication of post-operative chylothorax requiring medical or surgical intervention was evaluated. With the exception of those undergoing atrial septal defect repair, a greater proportion of Down syndrome vs. non-Down syndrome patients had post-operative chylothorax (ventricular septal defect repair 3.6% vs. 0.6% $p<0.0001$, complete atrioventricular septal defect repair 6.2% vs. 1.7% $p=0.0006$, tetralogy of Fallot repair 11.8% vs. 2.8% $p<0.001$, and mitral valve repair/replacement 3.1% vs. 0.6% $p=0.0005$).

Outcomes were also evaluated in the more rare subgroup of Down syndrome patients with a functionally univentricular heart undergoing staged palliation (Stage 1 palliation $n=11$, cavopulmonary anastomosis $n=32$, and Fontan operation $n=17$). Down syndrome patients undergoing these operations had greater in-hospital mortality compared with non-Down syndrome patients: Stage 1 palliation (72.7% vs. 19.4%, $p<0.0001$), cavopulmonary anastomosis (18.8% vs. 1.8%, $p<0.0001$), and Fontan operation (23.5% vs. 1.6%, $p<0.0001$). Median length of stay in Down syndrome vs. non-Down syndrome patients undergoing Stage 1 palliation was 27 days (interquartile range 1–32 days) vs. 21 days (interquartile range 12–36 days) $p=0.6$; cavopulmonary anastomosis 10 days (interquartile range 6–22 days) vs. 6 days (interquartile range 4–9 days) $p=0.0002$; and Fontan operation 9 days (interquartile range 8–18 days) vs. 9 days (interquartile range 7–14 days) $p=0.3$.

Discussion

This study is the largest to date evaluating outcomes in patients with Down syndrome undergoing congenital heart surgery. Down syndrome did not confer a significant mortality risk for the most common operations performed in this population. However, patients undergoing atrial septal defect, ventricular septal defect, and tetralogy of Fallot repair had prolonged length of stay and a higher rate of post-operative complications.

The approach to the care of Down syndrome patients with congenital heart diseases has changed over time. In the past, surgical repair of cardiac defects was often not considered due to the long-term natural history and reduced life expectancy, and reports suggesting higher peri-operative morbidity and mortality. Increased postoperative infection, prolonged ventilation, and longer length of stay have been reported in patients with Down syndrome (9). Increased mortality has also been reported (10).

However, over the past three decades, life expectancy and treatment for non-cardiovascular morbidities in Down syndrome patients, such as respiratory and neurodegenerative complications, has improved (10). During this time, outcomes in patients undergoing congenital heart surgery have also improved due to refinements in surgical technique and improvements in peri-operative care (11). Surgical repair of congenital heart defects in patients with Down syndrome is now routinely performed. The distribution of cardiac surgical procedures performed in children with Down syndrome found in our study is similar to that reported by others, with complete atrioventricular septal defect and ventricular septal defect repair being the most common (9).

In evaluation of patient characteristics, we found that children with Down syndrome were younger at the time of surgery for all procedures evaluated with the exception of those undergoing complete atrioventricular septal defect repair and tetralogy of Fallot repair. As expected, even after normalizing for age, weight at the time of surgery was lower in Down syndrome patients for all procedures. This is likely related to both the decreased growth velocity and issues with poor feeding known to impact patients with Down syndrome (12–14). The decision to perform surgical repair earlier in patients with Down syndrome may be related to the upper airway and feeding/growth issues associated with Down syndrome in addition to poor growth and respiratory symptoms associated with congestive heart failure. Alternatively, the concern for development of early pulmonary vascular disease in Down syndrome patients with cardiac defects involving significant left to right shunts may play a role in earlier surgical intervention (14). Irreversible pulmonary vascular occlusive disease has been reported in Down syndrome patients under 6 months of age with complete atrioventricular septal defects (15). Interestingly, we found that a higher proportion of Down syndrome patients undergoing atrial septal defect and ventricular septal defect repair were reported to have pre-operative pulmonary hypertension, but there was no difference in patients undergoing atrioventricular septal defect repair.

Our findings regarding post-operative mortality in this large multi-institutional cohort support the results of recent single-institution studies reporting similar or improved survival in Down syndrome patients. A retrospective study by Simsic and colleagues recently reported no increase in hospital mortality in neonates with genetic abnormalities undergoing congenital heart surgery (17). Formigari and colleagues reported that Down syndrome patients undergoing repair of complete atrioventricular septal defect had decreased mortality in comparison to those with a normal karyotype (3). It is speculated that the improved survival may be attributable to more favorable cardiac anatomy with a lower prevalence of left-sided atrioventricular valve abnormalities and left-sided obstructive lesions (18–21). However, we did find a trend toward increased mortality in Down syndrome patients undergoing tetralogy of Fallot repair. While we did not find any difference in the proportion with pre-operative risk factors compared with non-Down syndrome patients, we did find a higher proportion of Down syndrome patients undergoing tetralogy of Fallot repair had post-operative respiratory complications. Whether this was related to the trend toward increased mortality is unclear. To our knowledge no previous studies have evaluated contemporary outcomes in Down syndrome patients undergoing isolated tetralogy of Fallot repair.

In our secondary analysis of the rare subgroup of Down syndrome patients with a functionally univentricular heart undergoing staged palliation, we found significantly increased in-hospital mortality at all three stages. The small sample size even in this multi-institutional cohort precluded detailed analysis of this population. It is known that factors such as pulmonary hypertension, which we and others have shown to be present in Down syndrome patients, can be associated with a significant mortality risk in the single ventricle population (22).

In addition, we found that Down syndrome patients undergoing atrial septal defect, ventricular septal defect, and tetralogy of Fallot repair had longer length of hospital stay compared to non-Down Syndrome patients. These findings may be attributed to either a

higher proportion of Down syndrome patients with pre-operative risk factors and post-operative complications in these groups. Post-operative complications consisted of respiratory and infectious complications and pulmonary hypertension, similar to previous studies. Malec et al. described a higher rate of postoperative complications including respiratory infections and sepsis in Down syndrome patients undergoing congenital heart surgery, which led to prolonged ventilation and longer intensive care unit length of stay (9). Respiratory complications and infections are known to play a significant role in the morbidity and mortality in patients with Down syndrome in general (23). Chronic upper airway obstruction, increased secretions, and gastroesophageal reflux leading to chronic aspiration may all occur in patients with Down syndrome. Down syndrome patients may also be predisposed to frequent infections as a result of abnormalities in T lymphocyte maturation and function (24). In addition, we also found a greater proportion of Down syndrome patients (with the exception of those undergoing atrial septal defect repair) had the complication of post-operative chylothorax. Abnormalities of the lymphatic system and congenital pulmonary lymphangiectasis have been reported in patients with Down syndrome and may play a role (25).

Finally, we found a higher proportion of Down syndrome patients undergoing ventricular septal defect repair had post-operative complete heart block requiring permanent pacemaker placement. This finding has also been reported by Tucker et al. in an analysis of 4,432 patients in the Pediatric Cardiac Care Consortium Database undergoing surgical repair of a perimembranous ventricular septal defect (26). The presence of Down syndrome was the strongest predictor of post-operative atrioventricular block requiring pacemaker placement, independent of patient age or weight at surgery. The reason for this remains unclear. While anomalies of the conduction system in patients with atrioventricular septal defects have been reported, abnormalities in the conduction system in patients with ventricular septal defects have not been described (27).

Limitations

The limitations of this study are related to the observational and voluntary nature of the database. In our description of patient characteristics and outcomes, we were limited by the variables collected in the STS Congenital Heart Surgery Database. There may be other factors which impact patient pre-operative status or post-operative outcomes. Our analysis may also be limited by the definitions currently utilized in the database. For example, the definition of pulmonary hypertension currently requires systemic or suprasystemic right heart pressures. This may have resulted in a lower proportion of patients in our study identified as having pre- or post-operative pulmonary hypertension in comparison to other studies (14). We were unable to evaluate whether those patients with pulmonary hypertension were treated with pulmonary vasodilator medications as this information is currently not collected in the database. Finally, we were unable to evaluate long-term outcomes (such as subsequent atrioventricular valve surgery following complete atrioventricular septal defect repair) as these data are currently not collected. Plans to expand data collection to include long-term morbidity and mortality will allow these types of analyses to be performed in the future.

Conclusions

In this contemporary multi-institutional cohort, patients with Down syndrome undergoing congenital heart surgery do not have a significant mortality risk in comparison to non-Down syndrome patients for the most common congenital heart surgeries performed in this population. The rare subgroup of Down syndrome patients with a functionally univentricular heart undergoing staged palliation did have significantly increased in-hospital mortality compared with non-Down syndrome patients. Those undergoing atrial septal defect, ventricular septal defect, and tetralogy of Fallot repair appear to have prolonged length of stay, as well as more post-operative complications including infection, respiratory complications, and pulmonary hypertension. A greater proportion of Down syndrome patients undergoing ventricular septal defect repair also developed complete heart block requiring pacemaker placement. Anticipation of and early implementation of prevention and treatment measures may help to reduce these post-operative morbidities in patients with Down syndrome undergoing congenital heart surgery.

Abbreviations

STS	Society of Thoracic Surgeons
ASD	atrial septal defect
VSD	ventricular septal defect
AVSD	atrioventricular septal defect
PDA	patent ductus arteriosus
CPB	cardiopulmonary bypass

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Table 1

Patient characteristics

	Down Syndrome	
	Yes (n=4350)	No (n=41,229)
Gender (male)	2013 (46.3%)	23297 (56.5%)
Age at surgery	5.2m (3.4m, 10.7m)	8m (1.1m, 4.3yr)
Length (cm)	61 (56, 69)	68 (53, 102)
Weight (kg)	5.3 (4.3, 7.6)	7.3 (3.8, 16.3)
Weight z-score	-2.1 (-2.9, -1.2)	-0.9 (-1.9, 0.1)

Table 2

Most common surgical procedures

2a. Down syndrome patients	
Procedure	n (%)
Complete AVSD repair	1430 (33)
VSD closure	832 (19)
Mitral valve repair/replacement	320 (7)
Partial AVSD repair	273 (6)
PDA ligation	184 (4)
Tetralogy of Fallot repair	178 (4)
ASD closure	178 (4)
Coarctation/arch repair	103 (2)
Tricuspid valve repair/replacement	80 (2)
Tetralogy of Fallot-AVSD repair	62 (1)
2b. Non-Down syndrome patients	
Procedure	n (%)
VSD closure	3416 (8)
ASD closure	2773 (7)
Coarctation/arch repair	2636 (6)
PDA ligation	2548(6)
Tetralogy of Fallot repair	2274 (6)
Cavopulmonary anastomosis	2194 (5)
Fontan operation	1952 (5)
Norwood procedure	1615 (4)
Systemic to pulmonary shunt	1461 (4)
Arterial switch operation	1240 (3)

ASD = atrial septal defect, VSD = ventricular septal defect, AVSD = atrioventricular septal defect, PDA = patent ductus arteriosus

Table 3

Patient pre-operative characteristics for selected procedures.

Procedure	Down Syndrome		p-value
	Yes	No	
ASD closure			
Gender, male	76 (43%)	1180 (43%)	0.9
Age at surgery	1.2y (6.6m, 3.0y)	4.1y (2.2y, 7.6y)	<0.0001
Length (cm)	73 (63, 86)	102 (87, 125)	<0.0001
Weight (kg)	8.5 (6.0, 12.2)	16.0 (11.8, 24.9)	<0.0001
Weight z-score	−1.9 (−2.7, −1.1)	−0.4 (−1.3, 0.5)	<0.0001
Pre-operative risk factor	38 (21%)	199 (7%)	<0.0001
VSD closure			
Gender, male	392 (47%)	1730 (51%)	0.07
Age at surgery	4.8m (3.2m, 7.1m)	7.4m (3.8m, 2.1y)	<0.0001
Length (cm)	60 (56, 65)	67 (59, 87)	<0.0001
Weight (kg)	5.1 (4.2, 6.1)	6.6 (4.8, 11.6)	<0.0001
Weight z-score	−2.4 (−3.2, −1.6)	−1.6 (−2.5, −0.5)	<0.0001
Pre-operative risk factor	179 (22%)	419 (12%)	<0.0001
Complete AVSD repair			
Gender, male	621 (43%)	158 (44%)	0.9
Age at surgery	4.4m (3.4m, 5.8m)	4.6m (3.1m, 8.5m)	0.01
Length (cm)	59 (56, 62)	61 (56, 67)	<0.0001
Weight (kg)	4.9 (4.3, 5.6)	5.1 (4.2, 6.8)	0.0004
Weight z-score	−2.4 (−3.1, −1.7)	−2.1 (−2.8, −1.4)	<0.0001
Pre-operative risk factor	256 (18%)	61 (17%)	0.7
Mitral valve repair/replacement			
Gender, male	141 (44%)	466 (48%)	0.2
Age at surgery	2.7y (8.1m, 6.2y)	4.6y (1.4y, 10.5y)	<0.0001
Length (cm)	82 (64, 104)	105 (76, 138)	<0.0001
Weight (kg)	11.6 (6.2, 17.9)	16.8 (9.2, 32)	<0.0001
Weight z-score	−1.9 (−2.7, −0.7)	−0.8 (−2.0, 0.2)	<0.0001
Pre-operative risk factor	63 (20%)	195 (20%)	0.8
Tetralogy of Fallot repair			
Gender, male	109 (61%)	1288 (59%)	0.5
Age at surgery	5.5m (3.6m, 7.5m)	5.2m (3.2m, 8.2m)	0.01
Length (cm)	62 (58, 66)	63 (58, 69)	0.01
Weight (kg)	6.1 (4.9, 7.1)	6.4 (5.3, 7.9)	0.002
Weight z-score	−1.7 (−2.6, −0.9)	−0.9 (−1.9, −0.1)	<0.0001
Pre-operative risk factor	27 (15%)	274 (12%)	0.3

ASD = atrial septal defect, VSD = ventricular septal defect, AVSD = atrioventricular septal defect

Table 4

Operative characteristics

Procedure	Down Syndrome		p-value
	Yes	No	
ASD closure			
CPB (min)	42 (30, 59)	45 (34, 63)	0.03
Cross clamp (min)	19 (12, 29)	22 (14, 32)	0.007
VSD closure			
CPB (min)	77 (60, 95)	72 (55, 92)	<0.0001
Cross clamp (min)	46 (35, 59)	41 (30, 56)	<0.0001
Complete AVSD repair			
CPB (min)	122 (98, 156)	123 (98, 152)	0.9
Cross clamp (min)	88 (68, 113)	86 (63, 111)	0.06
Mitral valve repair/replacement			
CPB (min)	94 (70, 133)	105 (73, 139)	0.02
Cross clamp (min)	57 (41, 84)	63 (43, 90)	0.03
Tetralogy of Fallot repair			
CPB (min)	109 (89, 135)	108 (84, 138)	0.5
Cross clamp (min)	66 (50, 86)	65 (48, 84)	0.2

ASD = atrial septal defect, VSD = ventricular septal defect, AVSD = atrioventricular septal defect, CPB = cardiopulmonary bypass

Table 5

Post-operative outcomes

Procedure	Down Syndrome		p-value
	Yes	No	
ASD closure			
Length of stay (days)	4 (3, 5)	3 (2, 4)	<0.0001
In-hospital mortality	1 (0.6%)	3 (0.1%)	0.1
VSD closure			
Length of stay (days)	5 (4, 8)	4 (3,6)	<0.0001
In-hospital mortality	5 (0.6%)	17 (0.5%)	0.7
Complete AVSD repair			
Length of stay (days)	7 (5, 11)	7 (5, 14)	0.9
In-hospital mortality	27 (1.9%)	14 (3.9%)	0.02
Mitral valve repair/replacement			
Length of stay (days)	5 (4, 8)	5 (4, 8)	0.6
In-hospital mortality	1 (0.3%)	19 (2.0%)	0.04
Tetralogy of Fallot repair			
Length of stay (days)	7 (5, 10)	6 (5, 9)	0.0004
In-hospital mortality	4 (2.3%)	14 (0.6%)	0.02

ASD = atrial septal defect, VSD = ventricular septal defect, AVSD = atrioventricular septal defect