Title

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Association Between Down Syndrome and In-Hospital Death Among Children Undergoing Surgery for Congenital Heart Disease

A US Population-Based Study

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Background—The prevalence of Down syndrome (DS)–affected births has increased during the past 30 years; moreover, children with DS have a higher incidence of congenital heart disease compared with their peers. Whether children with DS have better or worse outcomes after repair of congenital heart disease is unclear. We sought to identify differences in in-hospital mortality after cardiac surgery in pediatric patients with and without DS using a large national database.

Methods and Results—Children aged <18 years who underwent surgical intervention for congenital heart disease were identified using the Kids' Inpatient Database (2000, 2003, 2006, and 2009). Patients were stratified using the Risk Adjustment for Congenital Heart Surgery algorithm. A total of 4231 (8.2%) of the 51 309 patients studied had a diagnosis of DS. In-hospital death for patients with DS was significantly lower than that for patients without DS overall (1.9% versus 4.3%; $P<0.05$) as well as within risk categories 2 (1.0% versus 1.8%; $P<0.05$) and 3 (2.3% versus 5.1%; $P<0.05$). Multivariable logistic regression showed a lower odds of death among children with DS (odds ratio=0.60; 95% confidence interval, 0.47–0.76; $P<0.05$) after adjusting for Risk Adjustment for Congenital Heart Surgery risk category, premature birth, major noncardiac structural anomaly, and age.

Conclusions—In this large national study, children with DS who underwent repair of congenital heart disease were more likely to survive to discharge than children without DS. Future work is needed to better understand the factors underlying these differences. **(*Circ Cardiovasc Qual Outcomes*. 2014;7:445-452.)**

Key Words: death ■ heart defects, congenital ■ pediatrics

Down syndrome (DS) affects 1 to 2 per 1000 live births[1–3] and is the most commonly occurring chromosomal abnormality in live-born infants.[4] Despite increases in antenatal detection, the prevalence of babies born with DS has risen by 25% during the past 30 years and parallels the increase in advanced maternal age pregnancies.[5,6] Forty to fifty percent of children with DS have some form of congenital heart disease (CHD).[1,7–9] Although the average life expectancy for children born with DS has increased from 12 years in the 1940s to 60 years in current times, infant mortality for patients with DS still remains 5× to 8× higher than that of the general population.[3] The relatively greater infant mortality rate in the DS population has been largely attributed to their having a higher incidence of CHD[2,9,10]; however, there are limited data suggesting that children with DS may actually have superior outcomes after CHD repairs compared with their eugenic counterparts.[11–13] Given the relative prevalence of patients with both DS and CHD, additional information with regard to expected cardiac surgical outcomes for this particular population might provide parents and medical providers with important guidance.

Congenital cardiac lesions in patients with DS are more likely to be septal defects, commonly atrioventricular septal defects (AVSDs), rather than conotruncal lesions such as transposition of the great arteries, coarctation of the aorta, and truncus arteriosus.[14–16] The vast majority of infants born with an AVSD also have DS[11–13,17–21]; however, DS is not a known risk factor for morbidity and mortality after biventricular AVSD repair.[12,22] In fact, infants with DS tend to have better outcomes after surgical repair of an AVSD compared with infants without DS.[11–13,23] Surprisingly, little is known about the outcomes of children with DS after surgical correction of congenital cardiac defects other than an AVSD.[24] An enhanced understanding of the association between DS and survival across a broad spectrum of lesions may improve our ability to optimize the care of these infants and children.

Large sources of data are required to confidently report the association between DS and survival after repair of

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WHAT IS KNOWN

- Greater infant mortality rates for children with Down syndrome (DS) are attributed to an increased incidence of congenital heart disease.
- Large sources of data are required to explore the association between DS and in-hospital mortality.

WHAT THE STUDY ADDS

- A large national database, the Kids' Inpatient Database, is used to compare outcomes after cardiac surgery for children with and without DS.
- After multivariable logistic regression analysis controlling for Risk Adjustment for Congenital Heart Surgery (RACHS-1) risk category, premature birth, presence of ≥1 major noncardiac structural anomalies, and age, a diagnosis of DS is associated with a lower odds of in-hospital death (odds ratio=0.60; 95% confidence interval, 0.47–0.76; $P<0.05$).
- That DS is associated with increased survival across an extensive list of repairs rather than for only a few select repairs is unexpected and warrants further investigation.

congenital cardiac abnormalities. In the current study, we use a large national database, the Kids' Inpatient Database (KID), to compare outcomes after cardiac surgery for children with and without DS. The KID's large sample size enables analysis of both rare conditions such as DS and uncommon treatments such as cardiac surgery.[25,26] In-hospital mortality for patients with and without DS was compared after stratifying complexity with the Risk Adjustment for Congenital Heart Surgery (RACHS-1) tool. In the final model, multivariable logistic regression was used to test for the association between DS and in-hospital death after CHD repair after adjusting for RACHS-1 risk category, premature birth, major noncardiac structural anomaly, and age.

Methods

Data Sources

Data were obtained from the KID for years 2000, 2003, 2006, and 2009. Developed by the Healthcare Cost and Utilization Project through a federal, state, and industry partnership sponsored by the Agency for Healthcare Research and Quality (https://www.hcup-us.ahrq.gov/kidoverview.jsp), the KID includes nationwide samples of inpatient pediatric discharges. Hospital discharge data are collected by designated state agencies and compiled by Healthcare Cost and Utilization Project; 2784 hospitals from 27 states participated in 2000, 3438 hospitals from 36 states participated in 2003, 3739 hospitals from 38 states participated in 2006, and 4121 hospitals from 44 states participated in 2009. Data sets from each individual version of the KID contain a 10% random sample of uncomplicated in-hospital births and an 80% sample of complicated births and other pediatric discharges for patients aged <20 years. Available information includes patient demographics, admission characteristics, discharge status, and ≤15 procedure codes categorized using *International Classification of Disease, Ninth Revision*, *Clinical Modification* (*ICD-9-CM*) and Current Procedural Terminology codes.

Study Design

The current study is a retrospective cohort analysis of US population-based samples of pediatric hospital admissions during which surgical repair of CHD was performed. Patients enter the cohort at the time of hospital admission and are followed until discharge or in-hospital death, whichever occurs first.

Study Population

All patients aged <18 years with *ICD-9-CM* and Current Procedural Terminology codes indicating surgical repair of CHD were considered for inclusion in this study. The final data set included only those children for whom there were sufficient data to assign a specific RACHS-1 risk category.[27] Cardiac transplantation and catheter-based interventions were excluded, as were newborns aged <30 days who underwent ligation of a patent ductus arteriosus as their sole cardiac procedure.

Outcome

The primary outcome was in-hospital death after repair or surgical palliation of CHD as determined by designations of patient discharge status reported in the KID.

Risk Adjustment

The RACHS-1 method[1,27–29] was used to adjust for differences in patient mix when comparing in-hospital death. Surgical procedures were assigned to 1 of 6 risk categories. Risk category 1 has the lowest risk for in-hospital death, whereas risk category 6 has the highest risk. Risk categories 5 and 6 were combined for reporting purposes because of the low numbers of patients in each of these groups. Patients with >1 cardiac surgical procedure were placed in the category of the highest risk procedure.

Statistical Analysis

KID data were pooled across the 4 years studied. Descriptive statistics were expressed as percentages. Data from the KID were used to compare patients with and without DS (*ICD-9-CM* code: 758.0) who had undergone repair or palliation of CHD. Factors studied included age at surgery (<30 days, 30 days to 1 year, and >1 year), sex, premature birth (*ICD-9-CM* codes: 765.0x and 765.1x), presence of a major noncardiac structural anomaly (*ICD-9-CM* codes: 740.0, 740.1, 740.2, 741.0, 741.9, 742.0, 742.1, 742.2, 742.3, 742.4, 742.5x, 742.9, 748.0, 748.2, 748.3, 748.4, 749.0x, 749.1x, 749.2x, 750.3, 751.1, 751.2, 751.4, 751.61, 753.0, 753.15, 753.2, 753.5, 756.6, and 756.7), and race/ethnicity (white, black, Hispanic, Asian or Pacific Islander, Native American, others, and not documented). All comparisons of children with and without DS were performed using the χ^2 test. A multivariable logistic regression analysis was used to estimate the association between in-hospital death and DS among children undergoing surgical repair for CHD while adjusting for other covariates in the model including RACHS-1 risk category, premature birth, the presence of ≥1 major noncardiac structural anomalies, and age. Data were reported as odds ratios and 95% confidence intervals. All hypotheses were tested at a 2-tailed 0.05 significance level and were performed using Stata software (version 12).

Institutional Review Board Approval

The University of California Davis Health System Institutional Review Board approved this study.

Results

A total of 51 309 patients underwent surgery to correct CHD during the 4 years studied (Table 1). Of these, 2114 (4.1%) died while hospitalized. There was no difference in sex when comparing survivors with nonsurvivors; there were, however, significant differences in age, RACHS-1 risk category,

Table 1. Characteristics of the Study Population

Characteristics, n (%)	Overall (n=51 309)	In-Hospital Death (n=2114)	Discharged Alive (n=49 195)
Sex			
Males	27 818 (54.2)	1145 (54.2)	26 673 (54.2)
Females	23 491 (45.8)	969 (45.8)	22 522 (45.8)
Age*			
<30 d	8784 (17.1)	1024 (48.4)	7760 (15.8)
30 d to 1 y	12 959 (25.3)	300 (14.2)	12 659 (25.7)
>1 y	29 566 (57.6)	790 (37.4)	28 776 (58.5)
RACHS-1 risk category*			
1	10 585 (20.6)	203 (9.6)	10 382 (21.1)
2	16 859 (32.9)	286 (13.5)	16 573 (33.7)
3	16 040 (31.3)	756 (35.8)	15 284 (31.1)
4	6118 (11.9)	495 (23.4)	5623 (11.4)
5 and 6	1707 (3.3)	374 (17.7)	1333 (2.7)
Premature birth*			
Yes	2958 (5.8)	358 (16.9)	2600 (5.3)
Major noncardiac structural anomaly*			
Yes	2647 (5.2)	197 (9.3)	2450 (5.0)
Race*			
White	21 260 (41.4)	742 (35.1)	20 518 (41.7)
Black	4926 (9.6)	266 (12.6)	4660 (9.5)
Hispanic	9815 (19.1)	419 (19.8)	9396 (19.1)
Asian or Pacific Islander	1517 (3.0)	46 (2.2)	1471 (3.0)
Native American	314 (0.6)	12 (0.6)	302 (0.6)
Other	3130 (6.1)	170 (8.0)	2960 (6.0)
Not documented	10 347 (20.2)	459 (21.7)	9888 (20.1)

RACHS-1 indicates Risk Adjustment for Congenital Heart Surgery.
*$P<0.05$.

premature birth, presence of major noncardiac anomalies, and race. The percentage of patients for whom information with regard to race and ethnicity was not documented was similar for both groups.

Of the 51 309 total patients who underwent surgery to correct CHD during the 4 years studied, 4231 (8.2%) had DS (Table 2). When comparing patients with and without DS, we found significant differences in sex, age, RACHS-1 risk category, premature birth, presence of a major noncardiac anomaly, and race. The majority of patients with DS were female, whereas the majority of patients both overall and within the non-DS population were male. The majority of patients in the DS population were in the 30 days to 1 year age group, whereas the majority of children in the non-DS population were in the >1 year age group. The majority of patients in both groups were in RACHS-1 risk categories 1, 2, and 3; however, there were differences in the distribution of patients with and without DS within these 3 groups. For patients with DS, the proportion of patients in risk categories 1, 2, and 3 increased with increasing surgical complexity, whereas the distribution for patients without DS within these same 3 risk categories was more even. Patients with DS were less likely to have been born prematurely but more likely to have a coexisting major noncardiac structural anomaly. Finally, the majority of patients in both categories were white.

As shown in Table 3, when measured across all 6 categories, in-hospital death was lower for patients with DS compared with patients without DS (1.9% versus 4.3%; $P<0.05$). In-hospital death was also significantly lower for patients with DS within risk categories 2 (1.0% versus 1.8%; $P<0.05$) and 3 (2.3% versus 5.1%; $P<0.05$).

Separate analyses focused on the differences in in-hospital mortality for individual repairs within risk categories 2 and 3. Of the 17 individual repairs in risk category 2 (Table 4), the rate of in-hospital death for DS and non-DS populations was significantly different for only 2 repairs: ventricular septal defect closure and placement of a bidirectional Glenn (BDG) shunt. There was a decreased incidence of in-hospital death among patients with DS who underwent ventricular septal defect closure (0.3% versus 1.0%; $P<0.05$); however, there was an increased incidence of in-hospital death among patients with DS who underwent the BDG procedure (15.6% versus 2.1%; $P<0.05$).

Of the 21 individual repairs in risk category 3 (Table 5), the rate of in-hospital death for DS and non-DS populations was significantly different for 4 repairs: placement of a systemic to pulmonary artery shunt, repair of a transitional or complete AVSD with or without mitral valve repair, mitral valvuloplasty, and annuloplasty. There was an increased incidence of in-hospital mortality death among patients with DS who

Table 2. Characteristics of the Down Syndrome Population

Characteristics, n (%)	Overall (n=51 309)	Down Syndrome (n=4231)	Non–Down Syndrome (n=47 078)
Sex*			
Males	27 818 (54.2)	1987 (47.0)	25 831 (54.9)
Females	23 491 (45.8)	2244 (53.0)	21 247 (45.1)
Age*			
<30 d	8784 (17.1)	208 (4.9)	8576 (18.2)
30 d to 1 y	12 959 (25.3)	2203 (52.1)	10 756 (22.9)
>1 y	29 566 (57.6)	1820 (43.0)	27 746 (58.9)
RACHS-1 risk category*			
1	10 585 (20.6)	482 (11.4)	10 103 (21.5)
2	16 859 (32.9)	1315 (31.1)	15 544 (33.0)
3	16 040 (31.3)	2357 (55.7)	13 683 (29.1)
4	6118 (11.9)	68 (1.6)	6050 (12.9)
5 and 6	1707 (3.3)	9 (0.2)	1698 (3.6)
Premature birth*			
Yes	2958 (5.8)	79 (1.9)	2879 (6.1)
Major noncardiac structural anomaly*			
Yes	2647 (5.2)	256 (6.0)	2391 (5.1)
Race*			
White	21 260 (41.4)	1700 (40.2)	19 560 (41.6)
Black	4926 (9.6)	397 (9.4)	4529 (9.6)
Hispanic	9815 (19.1)	884 (20.9)	8931 (19.0)
Asian/Pacific Islander	1517 (3.0)	92 (2.2)	1425 (3.0)
Native American	314 (0.6)	21 (0.5)	293 (0.6)
Other	3130 (6.1)	228 (5.4)	2902 (6.2)
Not documented	10 347 (20.2)	909 (21.5)	9438 (20.1)

RACHS-1 indicates Risk Adjustment for Congenital Heart Surgery.
*$P<0.05$.

underwent placement of a systemic to pulmonary artery shunt (16.8% versus 10.8%; $P<0.05$), whereas there was a reduced incidence of in-hospital death among patients with DS who underwent repair of a transitional or complete AVSD with or without mitral valve repair (1.4% versus 4.6%; $P<0.05$), mitral valvuloplasty (0.8% versus 2.5%; $P<0.05$), and annuloplasty (0.0% versus 5.2%; $P<0.05$).

The negative association between DS and in-hospital death was also seen in our multivariable logistic regression analysis (Table 6). When controlling for RACHS-1 risk category, premature birth, presence of ≥1 major noncardiac structural anomalies, and age, a diagnosis of DS was associated with a lower odds of in-hospital death (odds ratio=0.60; 95% confidence interval, 0.47–0.76; $P<0.05$).

Table 3. In-Hospital Death (Mortality) Rates Stratified by RACHS-1

	Down Syndrome (n=4231)	Non–Down Syndrome (n=47 078)
RACHS-1 category, n (%)		
1	8 (1.7)	195 (1.9)
2*	13 (1.0)	273 (1.8)
3*	54 (2.3)	702 (5.1)
4	4 (5.9)	491 (8.1)
5 and 6	1 (11.1)	373 (22.0)
RACHS-1 (1–6)*	80 (1.9)	2034 (4.3)

RACHS-1 indicates Risk Adjustment for Congenital Heart Surgery.
*$P<0.05$.

Discussion

This is the largest and most contemporary examination of in-hospital death among patients with DS after surgical repair of CHD. We examined outcomes from a large population-based US sample using a well-validated risk adjustment tool. A diagnosis of DS was associated with differences in in-hospital mortality for the overall population, 2 RACHS-1 risk categories, and 6 specific repairs. The results of multivariable logistic regression analyses indicate that the lower observed rate of in-hospital death among patients with DS persists even after adjusting for RACHS-1 risk category, premature birth, presence of ≥1 major noncardiac structural anomalies, and age.

Previous studies assessing the mortality of patients with DS after cardiac surgery have included much smaller numbers and have not used risk stratification.[1,2,11–13,19,22,23,30] In a study using the 2000 version of the KID to examine the role of sex as a risk factor for in-hospital mortality after pediatric cardiac surgery, DS was 1 of 4 comorbidities used as

Table 4. In-Hospital Death Rates for RACHS-1 Risk Category 2 Stratified by Specific Cardiac Procedure (n=16 859)

	Down Syndrome		Non–Down Syndrome	
RACHS-1	No. of Records	In-Hospital Death, n (%)	No. of Records	In-Hospital Death, n (%)
VSD repair*	897	3 (0.3)	5558	58 (1.0)
ASD and VSD repair	604	3 (0.5)	2356	21 (0.9)
Total repair of TOF	169	3 (1.8)	2782	56 (2.0)
Glenn shunt*	45	7 (15.6)	2258	48 (2.1)
Coarctation repair, <30 d	44	1 (2.3)	1439	54 (3.8)
Aortic valvuloplasty, >30 d	31	1 (3.2)	1195	12 (1.0)
Pulmonary valve replacement	32	0 (0.0)	971	11 (1.1)
Pulmonary valvuloplasty	20	1 (5.0)	757	15 (2.0)
Sub-AS resection	33	0 (0.0)	669	1 (0.2)
Repair of TAPVC, >30 d	1	0 (0.0)	617	24 (3.9)
RV infundibulectomy	28	0 (0.0)	560	8 (1.4)
ASD primum repair	94	0 (0.0)	215	4 (1.9)
VSD closure and pulmonary valvotomy/ infundibular resection	12	0 (0.0)	207	3 (1.5)
Pulmonary valvotomy	5	0 (0.0)	125	3 (2.4)
Repair of AP window	2	0 (0.0)	95	6 (6.3)
Repair of unspecified septal defect	6	0 (0.0)	88	3 (3.4)
Aortic valvotomy	0	0 (0.0)	32	0 (0.0)

AP indicates aorticopulmonary; AS, aortic stenosis; ASD, atrial septal defect; RACHS-1, Risk Adjustment for Congenital Heart Surgery; RV, right ventricular; TAPVC, total anomalous pulmonary venous connection; TOF, tetralogy of Fallot; and VSD, ventricular septal defect.

*$P<0.05$.

independent, nonprocedural variables. The findings of this study are consistent with our findings and demonstrate lower odds of in-hospital mortality for patients with DS. Unlike the current study, the authors did not include a direct comparison of in-hospital mortality between patients with and without DS.[25] In contrast, a 2010 study using the Society of Thoracic Surgeons (STS) Congenital Heart Surgery Database did not identify differences in mortality between patients with and without DS after specific 5 repairs: repair of atrial and ventricular septal defects, AVSD repair, mitral valve repair, and repair of tetralogy of Fallot. Unlike the STS study, the current study compares in-hospital mortality for patient with and without DS across an extensive list of surgical repairs for using RACHS-1 risk stratification. Moreover, the STS database study included only the first CHD repair for each admission and did not include subsequent CHD repairs. Finally, the STS study also excluded 15 290 patients with a genetic abnormality other than DS.[24]

Differences in in-hospital mortality for patients with and without DS may be explained, in part, by observed variations in in-hospital death for 6 individual lesions: ventricular septal defect closure, placement of BDG shunt, placement of a systemic to pulmonary artery shunt, repair of a transitional or complete AVSD with or without mitral valve repair, mitral valvuloplasty, and annuloplasty. It is possible that differences in cardiac surgical outcomes for patients with and without DS might be associated with subtle differences in cardiac structure. In a prospective study of 147 consecutive children undergoing AVSD repair, chromosomally normal children were more likely to have a dysplastic atrioventricular valve; moreover, having a dysplastic atrioventricular valve was a risk factor for reoperation. Of note, even after controlling for the presence of a dysplastic atrioventricular valve, a diagnosis of DS was associated with a decreased 30-day mortality after AVSD repair.[11] In a similar study of 476 children undergoing surgery for an AVSD, patients with DS had a lower incidence of reoperation to repair the left-sided atrioventricular valve.[12] In a prospective study of 206 children undergoing cardiac surgery, children without DS who underwent an AVSD repair were more likely to require reoperation because of abnormalities of either the left-sided atrioventricular valve or the left ventricular outflow tract.[13] Finally, in small retrospective study of 44 infants aged <1 year who underwent AVSD repair, infants with DS had significantly larger preoperative aortic valve diameters and left atrioventricular valve areas and significantly fewer adverse outcomes.[23]

Another possible explanation as to why children with DS fare better than their peers is that children with DS may be more resistant to oxidative stress associated with ischemia reperfusion injury and cardiopulmonary bypass. Blood levels of the antioxidant enzymes superoxide dismutase, catalase, and glutathione reductase have recently been shown to be 47.2%, 24.7%, and 49.6% greater in healthy children and teenagers with DS as compared with healthy age-matched chromosomally normal controls.[31]

There are risk factors that would be expected to be associated with less favorable outcomes for children with DS who undergo cardiac surgical repairs. The latter include their increased likelihood of having cervical spine instability and airway abnormalities, including subglottic stenosis, laryngomalacia, tracheomalacia, tracheal bronchus, and bronchomalacia.[32,33] Because of their increased incidence of postoperative

Table 5. In-Hospital Death for RACHS-1 Risk Category 3 Stratified by Specific Cardiac Procedure (n=16 040)

	Down Syndrome		Non–Down Syndrome	
RACHS-1	No. of Records	In-Hospital Death, n (%)	No. of Records	In-Hospital Death, n (%)
Systemic to PA shunt*	113	19 (16.8)	3150	340 (10.8)
Repair of transitional or complete AVC with/without MVR*	1672	23 (1.4)	1427	65 (4.6)
Fontan procedure	14	0 (0.0)	2520	58 (2.3)
Mitral valvuloplasty*	386	3 (0.8)	1100	27 (2.5)
RV to PA conduit	35	2 (5.7)	1337	57 (4.3)
Tricuspid valvuloplasty	152	2 (1.3)	879	28 (3.2)
Aortic valve replacement	12	0 (0.0)	950	32 (3.4)
Arterial switch operation	1	0 (0.0)	729	36 (4.9)
Pulmonary artery band	63	5 (7.9)	444	32 (7.2)
Repair of coarctation and VSD	19	2 (10.5)	455	32 (7.0)
Annuloplasty*	76	0 (0.0)	387	20 (5.2)
Ross procedure	6	0 (0.0)	442	20 (4.5)
Repair of TOF with RV to PA conduit	27	2 (7.4)	345	12 (3.5)
Atrial switch operation	4	0 (0.0)	352	9 (2.6)
Mitral valve replacement	31	2 (6.5)	289	24 (8.3)
Repair of TOF with pulmonary atresia	10	1 (10.)	175	11 (6.3)
TV reposition for Ebstein anomaly, >30 d	1	0 (0.0)	111	3 (2.7)
Tricuspid valve replacement	4	0 (0.0)	99	2 (2.0)
Repair of cor triatriatum	3	0 (0.0)	48	2 (4.2)
Mitral valvotomy	2	0 (0.0)	2	0 (0.0)
Tricuspid valvotomy	0	0 (0.0)	4	0 (0.0)

AVC indicates atrioventricular canal; MVR, mitral valve repair; PA, pulmonary artery; RACHS-1, Risk Adjustment for Congenital Heart Surgery; RV, right ventricle; TOF, tetralogy of Fallot; TV, tricuspid valve; and VSD, ventricular septal defect.

*$P<0.05$.

airway obstruction, children with DS tend to experience delays in extubation and sometimes require reintubation.[34] For this reason, children with DS would be expected to have worse outcomes after operations for which passive pulmonary blood flow and early extubation are essential. Children with DS also have increased pulmonary reactivity compared with their non-DS counterparts[12,35]; thus, they would be expected to have worse outcomes after operations in which the postoperative physiology is dependent on having low pulmonary vascular resistance. Finally, there are limited data suggesting that patients with DS have an increased incidence of pulmonary vein stenosis, a rare and often fatal risk factor for pulmonary hypertension.[36] Future studies are needed to further investigate other underlying causes behind the observed differences in in-hospital mortality between patients with and without DS.

It is difficult to draw conclusions with regard to the association between DS and outcome after the 3-staged single-ventricle repairs, the Norwood palliation, the BDG shunt, and the Fontan operation. Patients with DS and single-ventricle anatomy are almost exclusively patients with an unbalanced AVSD and either right or left ventricular hypoplasia. Survival after these repairs, especially the BDG and Fontan surgeries, is highly dependent on having low transpulmonary pressures. As mentioned previously, patients with DS have an increased incidence of elevated pulmonary vascular resistance and are therefore at increased risk for postoperative mortality.[12,35] The number of patients with DS who undergo these repairs is extremely small; however, the current study provides preliminary information that may lay the groundwork for future investigations.

As shown in our analysis of specific lesions within RACHS-1 risk category 3 (Table 5), in-hospital mortality for patients with DS who underwent placement of a systemic to pulmonary shunt, a major component of the Norwood single-ventricle palliation, was significantly greater than that for patients without DS (16.8% versus 10%; $P<0.05$).

In our analysis of specific lesions within RACHS-1 risk category 2 (Table 4), in-hospital mortality for patients with DS who underwent placement of a BDG shunt was significantly greater than that for patients without DS (15.6% versus 2.1%; $P<0.05$). In a 2008 study by Wada et al,[37] 263 patients underwent the BDG procedure, 6 of whom had DS. All 6 patients had an unbalanced AVSD with right or left ventricular dominance. There were no operative deaths in patients with DS who underwent BDG surgery; however, 1 patient required takedown of the BDG shunt. Only 2 of the remaining 5 patients went on to have Fontan surgery, 1 of whom died from acute cardiac insufficiency associated with pulmonary hypertension. The remaining 3 patients were not thought to be suitable candidates for Fontan surgery because of severe atrioventricular regurgitation and pulmonary hypertension.[37]

In a 2010 study, Gupta-Malhotra et al[38] reported increased in-hospital mortality for children with DS who underwent the

Table 6. Multivariable Logistic Regression Analyses of In-Hospital Death (n=51 309)

Variable	Odds Ratio	95% Confidence Interval	*P* Value
Down syndrome			
No	Ref	…	…
Yes	0.6	0.47–0.76	<0.05
RACHS-1 risk category			
1	Ref	…	…
2	0.92	0.76–1.11	0.4
3	2.45	2.07–2.89	<0.05
4	3.25	2.70–3.92	<0.05
5 and 6	8.96	7.29–11.00	<0.05
Premature birth			
No	Ref	…	…
Yes	3.29	2.88–3.77	<0.05
Major noncardiac structural anomaly			
No	Ref	…	…
Yes	1.44	1.22–1.68	<0.05
Age			
<30 d	Ref	…	…
30 d to 1 y	0.43	0.37–0.50	<0.05
>1 y	0.42	0.37–0.46	<0.05

RACHS-1 indicates Risk Adjustment for Congenital Heart Surgery.

Fontan operation (35%; n=17) compared with children without DS (10%; 204). A 1998 report by Campbell et al[30] examined 533 children who underwent Fontan surgery, 4 of whom carried a diagnosis of DS. Three of the children with DS survived, and 1 died of endocarditis.[30] In a 2013 study, Furukawa et al[39] identified 8 patients with DS of a total of 235 patients who had undergone Fontan surgery. Mortality was greater in the DS group (1/8 patients, 12.5%) compared with the non-DS group (5/227 patients, 2.2%).[39] The general consensus is that children with DS who are not suitable candidates for 1.5- or 2-ventricle repairs may be considered for BDG and Fontan procedures; however, they are at increased risk relative to their peers, and therefore their caretakers must be counseled accordingly.

The current study describes significant differences in outcome between children with and without DS who underwent placement of either systemic to pulmonary or BDG shunts. The lack of a significant difference in in-hospital mortality between patients with and without DS who underwent Fontan surgery in the current study may be attributable to insufficient numbers of patients. We and others have been unable to adequately assess in-hospital mortality for this group of patients because there are insufficient numbers to make any firm conclusions.

The KID is the only all-payer inpatient care database for children in the United States. It includes a sample of pediatric discharges from 2500 to 4000 US hospitals and 2 to 3 million unweighted hospital discharges per year. Results of the current study are subject to the limitations of administrative databases including their disposition to misclassification. The latter would not be expected to favor patients with DS versus patients without DS, thus minimizing its impact on our conclusions. The inability to access other clinical data that may or may not impact in-hospital death may also confound our findings. Adjustment for RACHS-1 risk category, premature birth, major noncardiac structural anomalies, and age reduce the influence of other comorbidities

RACHS-1 risk stratification is a well-validated approach in the analysis of KID data relating to CHD subsets.[26,28,40,41] The current study includes a comprehensive list of surgical repairs. Existing reports do not use RACHS-1 risk stratification, include smaller numbers of patients, and focus on survival after a limited number of repairs.[1,27,28] That DS is associated with increased survival across an extensive list of repairs rather than for only a few select repairs is unexpected. More work is required to further explore the mechanisms underlying this advantage.

Disclosures

None.

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