Pediatr Cardiol 13:80–84, 1992

Pediatric Cardiology

Down's Syndrome Affects Results of Surgical Correction of Complete Atrioventricular Canal

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SUMMARY. **From 1981 through June 1989, 59 children had surgery for a complete atrioventricular (AV) canal defect at Oregon Health Sciences University. We compared the morbidity, mortality, and hemodynamic status of 47 children with and 12 without Down's syndrome through review of operative, clinical, and cardiac catheterization records. Overall, 10 children with Down's syndrome have died, nine from cardiac cause within 90 days of surgery. The 2-year survival of these children was 77 ± 6% as compared to 100% in children without Down's syndrome ($p = 0.08$). Early age at surgery, the surgical anatomy of the AV canal, and gender had no significant effect on survival. Before surgery, the hemodynamic status of Down's syndrome and non-Down's syndrome children did not differ; in a small group of post-operative catheterization, right heart pressures and pulmonary vascular resistance remained significantly higher in the Down's syndrome as compared to non-Down's syndrome children. These trends to higher mortality and poorer postoperative hemodynamics in children with Down's syndrome may necessitate closer follow-up if confirmed in other cohorts.**

KEY WORDS: **Down's syndrome—Atrioventricular canal—Cardiac surgery—Survival**

Complete atrioventricular (AV) canal defects are among the most complex congenital heart defects for which surgical repair is possible. The aim of operative intervention is to reduce symptoms of congestive failure and to avoid the development of pulmonary vascular disease and premature death. While surgical repair improves the length and quality of life for most children [1, 5], the appropriateness of routinely repairing complete AV canal defects in children with Down's syndrome has been questioned [2]. This is an important issue as more than 50% of children with AV canal defects also have Down's syndrome [16]. Specifically, Bull and coworkers [2] argued that in their experience in London, children with Down's syndrome and a complete AV canal with medical management have a survival rate of 80% at 10 and 15 years of age, and therefore an operative mortality rate of less than 20% would be necessary for surgery to improve survival. This view was challenged by others [10, 13, 16], and children with Down's syndrome are not denied reparative cardiac surgeries in most centers. Although these children may not receive equal cardiac care by referral at older ages as compared to children without Down's syndrome [13], a more contemporary report from the Baltimore–Washington Infant Study suggested that care was comparable [12]. Because of the earlier development of pulmonary vascular disease in Down's syndrome, referral at older than 12 months of age often renders the AV canal defect inoperable.

A recent report by Vet and Ottenkamp indicated that operative mortality of children with complete AV canal and Down's syndrome tended to be better than in those without Down's syndrome [15]. However, there remain questions as to whether correction of a complete AV canal achieves the same results in Down's syndrome and non-Down's syndrome children because of the predisposition to pulmonary hypertension and pulmonary vascular obstructive disease. We compared morbidity, mortality, and hemodynamic status in all children who had surgical correction of a complete AV canal defect at Oregon Health Sciences University (OHSU) from 1981 to June 1989 to examine the effect of Down's syndrome on these variables.

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Materials and Methods

A computerized search of medical records was performed at OHSU to identify children who underwent surgical repair of a complete AV canal defect between 1981 and June 1989. This period was selected because the surgical approach remained consistent; one surgical team performed all operative repairs. Patients with significant cardiac defects in addition to a complete AV canal were excluded from this study. Specifically, children with tetralogy of Fallot, double-outlet right ventricle, or hypoplastic left ventricle in addition to an AV canal were excluded. Children with a muscular ventricular septal defect or patent ductus arteriosus were included.

At chart review, data abstracted included cardiac signs and symptoms, and the presence of associated problems. Operative reports were reviewed to determine the anatomical type of the AV canal defect (Rastelli type A, B, or C), the surgical technique, and intraoperative or postoperative events. The pre- and postoperative hemodynamics from cardiac catheterization were also reviewed. For the calculation of pulmonary vascular resistance, standard calculations were used, including direct measurements of mean pulmonary arterial pressure and left atrial pressure preoperatively, and pulmonary capillary wedge pressure postoperatively. Pulmonary blood flow was estimated using standard Fick calculations and measured oxygen consumption. The following formula was used to estimate oxygen content: oxygen content = hemoglobin × 1.34 × % saturation. Pulmonary venous or left atrial saturations were directly measured in preoperative catheterizations, and systemic arterial saturations were used in postoperative catheterizations. Assessment of pulmonary vascular bed reactivity (i.e., with hyperoxia, tolazoline) was not consistently obtained.

Survival was calculated using the Kaplan-Meier method and comparisons between stratified samples were made using the Mantel-Cox statistic. Discrete variables were compared with chi-square and continuous variables with an unpaired t statistic. Pre- and postoperative hemodynamic variables were compared using paired nonparametric statistics.

Results

From 1981 to June 1989, 59 patients had surgical repair of a complete AV canal at OHSU. Forty-seven (80%) of these patients had Down's syndrome. Of the 12 non-Down's syndrome children, two children had a chromosomal anomaly (trisomy 47XXX, chromosome 10q23 deletion). One child had α_1-antitrypsin deficiency in addition to Down's syndrome. Extracardiac defects were present in one child with Down's syndrome (cleft palate) and in one child without Down's syndrome (microcephaly). There were 36 females and 23 males, 57% of the Down's syndrome subgroup were female as were 75% of the non-Down's syndrome subgroup.

This cohort was observed for a median of 24 months after correction of the AV canal (range, 1 day–81 months). Overall, 10 deaths occurred from 1 day to 16 months after surgery, nine from cardiac disease or complications of surgery. Six of these were operative deaths within 30 days of surgery. Three deaths occurred in children from 30–70 days after operation from sepsis developing after surgery, from cardiac failure after two additional attempts to repair the mitral valve, and from persistent pulmonary hypertension. One child died of acute lymphocytic leukemia associated with Down's syndrome 16 months postoperatively. Overall, 30-day survival was 0.90 ± 0.04, 1-year survival was 0.84 ± 0.05, and 2-year survival was 0.82 ± 0.05. No deaths occurred after 2 years postoperatively.

The presence of Down's syndrome was the most significant predictor of survival. All deaths occurred in children with Down's syndrome; their 30-day survival was 0.87 ± 0.05 and 2-year survival was 0.77 ± 0.06 as compared to a 30-day and 2-year survival of 1.00 in non-Down's syndrome children ($p = 0.08$). Average age at surgery in Down's syndrome children was 5.9 ± 6.1 months (range, 1.4–34.0 months) and 4.9 ± 3.7 months (range, 1.5–13.5 months) in non-Down's syndrome children (p = NS). We also attempted to identify other predictors of survival. Categorizing the population into 3-month intervals did not detect a significant effect of age at surgery; 2-year survival was 0.76 ± 0.10 in children with surgery at <3 months of age, 0.84 ± 0.07 at 3–6 months of age, 1.0 at 6–12 months of age, as compared to 0.67 ± 0.19 with surgery at >12 months of age. Fifty-two (88%) of the 59 children were younger than 12 months of age at operation. The anatomic type of AV canal defect did not affect survival, although the sample sizes were small: 64% had a Rastelli type A defect, 7% type B, 24% type C, and for 5% the anatomy was unclear. Gender did not influence the rate of death with a 2-year survival of 0.82 ± 0.08 for males and 0.82 ± 0.07 for females.

Information on functional status was collected at a median of 32 months after surgery. There was no significant difference in signs and symptoms reported by children with and without Down's syndrome at the most recent clinic visit. Of the three children who were symptomatic, two with Down's syndrome have persistent pulmonary hypertension and one non-Down's child was a mitral valve abnormality. Subaortic stenosis has been noted postoperatively in three patients with Down's syndrome and in one non-Down's syndrome child. Repeat cardiac surgery has been required in six children with Down's syndrome and in one without Down's syndrome (p = NS). Reasons for reoperation included: mitral valve repair ($n = 2$), correction of acquired subaortic stenosis ($n = 4$), and repair of coarctation of the aorta discovered after the initial surgery to repair the AV canal.

As seen in Table 1, the hemodynamic status of children with and without Down's syndrome did not

Table 1. Hemodynamic data from preoperative cardiac catheterizations

	Children with Down's syndrome (n = 35)	Children without Down's syndrome (n = 11)
Right atrial pressure	a:10 ± 3, v:8 ± 3, m:6 ± 3	a:11 ± 4, v:7 ± 5, m:6 ± 3
Right ventricular pressure	75 ± 15/9 ± 4	69 ± 22/8 ± 3
Pulmonary artery pressure	67 ± 15/27 ± 10, m:44 ± 2	64 ± 25/26 ± 13, m:43 ± 20
Left atrial pressure	a:11 ± 4, v:12 ± 3, m:8 ± 3	a:11 ± 3, v:10 ± 5, m:6 ± 3
Left ventricular pressure	78 ± 13/9 ± 3	84 ± 17/7 ± 4
Pulmonary vascular resistance	4.0 ± 2.8	4.0 ± 3.3
Pulmonary/systemic flow	4.0 ± 3.4	3.8 ± 2.0

a, a wave; v, v wave; m, mean. Values are given as mean ± SD.

Table 2. Hemodynamic pressures from pre- and postoperative cardiac catheterizations

	Children with Down's syndrome (n = 10)		Children without Down's syndrome (n = 5)	
	Preoperative catheterization	Postoperative catheterization	Preoperative catheterization	Postoperative catheterization
Right atrial				
a-wave	10 ± 2 (6–13)	11 ± 3 (8–17)	13 ± 3 (10–18)	8 ± 2 (5–11)
v-wave	9 ± 4 (4–13)	10 ± 2 (8–13)	10 ± 6 (5–18)	6 ± 3 (2–9)
Mean	7 ± 2 (4–9)	6 ± 3 (1–9)	8 ± 3 (5–12)	5 ± 2 (2–8)
Right ventricular				
Systolic	76 ± 13 (60–95)	47 ± 20 (26–80)	74 ± 17 (50–8)	26 ± 3 (24–30)
Diastolic	8 ± 3 (5–12)	8 ± 3 (2–11)	10 ± 1 (9–12)	5 ± 1 (3–6)
Pulmonary artery				
Systolic	73 ± 12 (55–95)	41 ± 19 (16–79)	70 ± 12 (45–93)	28 ± 10 (24–38)
Diastolic	32 ± 10 (17–45)	18 ± 10 (8–35)	29 ± 10 (15–37)	12 ± 4 (8–18)
Mean	49 ± 9 (34–60)	23 ± 14 (12–51)	46 ± 15 (27–60)	17 ± 4 (14–22)
Left ventricular				
Systolic	76 ± 11 (66–90)	99 ± 26 (70–136)	76 ± 14 (60–93)	112 ± 32 (91–160)
Diastolic	9 ± 2 (7–12)	10 ± 3 (6–14)	10 ± 4 (6–15)	6 ± 4 (2–11)
Pulmonary vascular resistance	4.9 ± 3.1 (2.1–11.8)	3.6 ± 1.7 (1.8–6.2)	4.1 ± 2.7 (1.6–8.3)	1.4 ± 0.5 (0.9–1.9)

Values are given as means ± SD, with ranges in parentheses.

differ significantly at the preoperative cardiac catheterization. Data were available in 35 of 47 children with Down's syndrome and in 11 of 12 children without Down's syndrome. Pre- and postoperative catheterizations were performed in 10 children with and five without Down's syndrome, 21% and 42% of the populations, respectively (Table 2). Overall, right atrial mean, right ventricular, and pulmonary artery pressures decreased significantly after surgery, as did pulmonary vascular resistance (all $p < 0.05$); left ventricular systolic pressure increased significantly ($p = 0.02$). In children with Down's syndrome, right atrial a wave ($p < 0.07$) and v wave ($p = 0.02$), right ventricular systolic ($p = 0.03$) and diastolic pressure ($p = 0.10$), and pulmonary vascular resistance ($p = 0.01$) remained higher after surgery as compared to those without Down's syndrome (Table 2), despite an equal length of time between surgery and the postoperative catheterization (27 months; range, 1–68 months). After surgery, none of the non-Down's syndrome children and four of 10 with Down's syndrome had a pulmonary vascular resistance in excess of 3.0 u. Pulmonary artery pressures were somewhat higher in Down's syndrome children after surgery, although not significantly.

Discussion

The data in this study indicate that surgery for a complete AV canal tends to be associated with a higher operative mortality and less improvement in hemodynamics in Down's syndrome than in non-Down's syndrome children. Although the hemodynamic status of the two groups in this study were comparable before surgery, the occurrence of a complete AV canal with Down's syndrome has been reported to be associated with an unusually high incidence of pulmonary hypertension and pulmonary vascular obstructive disease [4, 17]. Children with Down's syndrome may have a predisposition to more operative complications with correction of congenital heart defects as compared to their counterparts without Down's syndrome. These include more pulmonary atelectasis and pulmonary edema, requiring a longer duration of mechanical ventilation, intensive care, and hospitalization [11].

This difference in operative survival differs from a report by Vet and Ottenkamp who reported 73% survival in Down's syndrome and 54% in non-Down's syndrome children at mean follow-up times of 42 and 37 months, respectively [15]; actuarial analysis of survival was not performed. However, Losay and colleagues recently reported increased late mortality in Down's syndrome as compared to non-Down's syndrome children with AV canal [9]. This difference in survival between the cohort reported by Vet and Ottenkamp [15] and ours and that of Losay et al. [9] may result from the composition of the non-Down's syndrome cohort. In the report by Vet and Ottenkamp, the non-Down's syndrome children had a high prevalence of other serious cardiac and extracardiac anomalies which increase mortality, particularly complete AV canal with hypoplastic left ventricle, tetralogy of Fallot, and double-outlet right ventricle. These children were specifically excluded from our cohort.

Cardiac mortality after surgery was limited to the 90-day period following surgery and occurred in Down's syndrome children only. One additional noncardiac death was reported in a patient with Down's syndrome. Because of the comparatively short period of observation and the small sample size, additional follow-up is necessary to determine if the trend for poorer long-term survival in Down's syndrome children continues, and to determine the late mortality and morbidity in all children who survive surgery for complete AV canal. Other than the presence of Down's syndrome, no factors were evident that might be viewed as prognostic indicators. Specifically, age at surgery, gender, year of surgery, and the surgical anatomy of the AV canal defect had no significant effect on operative mortality. Previous studies have demonstrated that older age at surgery is associated with poorer surgical outcomes because of the development of pulmonary vascular disease with age [1, 7], and as a result surgical repair of complete AV canal is recommended in the first 12 months of life [7]. In this report, the small sample size and the predominance of surgery at an early age limited our ability to evaluate this effect. However, there was no obvious gradient of effect of age on mortality in children younger than 12 months at surgery.

Children with Down's syndrome had higher right heart pressure and pulmonary vascular resistance after surgery as compared to their counterparts without Down's syndrome, although overall the postoperative catheterizations showed a decrease in pressures compared to the preoperative values. These data confirm an improvement in hemodynamic status after surgery as reported by Castaneda and colleagues [3] and Clapp and coworkers [5], though conclusions in our population are limited by the small number of patients with both pre- and postoperative catheterizations, and by their unequal distribution in the Down's and non-Down's syndrome groups. During this period of study there was a policy of routine recatheterization of all patients after surgery regardless of their clinical status. However, it is apparent that this policy was not followed as only 25% of this population had a postoperative catheterization. Because of the similarity of preoperative hemodynamics from those with and without postoperative catheterizations, we believe there is no evidence that either referral for catheterization nor these results is biased.

Our findings demonstrate that the pulmonary vascular resistance at the postoperative catheterization was significantly higher in Down's syndrome children as compared to those without Down's syndrome. Although the etiology of this finding is unclear, it has previously been noted that pulmonary vascular disease can develop in children with Down's syndrome in the absence of congenital heart defects [8, 14]. This predisposition can result from chronic upper airway obstruction from adenoidal and tonsillar hypertrophy or midfacial hypoplasia resulting in alveolar hypoventilation, hypoxemia, and hypercapnia. Also, lung parenchyma may be abnormal in Down's syndrome with a diminished number of alveoli and decreased surface area, resulting in pulmonary hypertension [6]. Yamaki and coworkers [18] examined intimal changes and medial thickness of pulmonary arteries of children with congenital heart defects in the presence and absence of Down's syndrome. Retarded development of medial hypertrophy in response to higher pulmo-

nary artery pressures made these small pulmonary arteries more susceptible to a pressure load in Down's syndrome, promoting the development of severe intimal changes. Once present, pulmonary vascular disease may be aggravated by the increased incidence of pulmonary infection in children with Down's syndrome [14].

In summary, these data indicate that our policy of surgical repair of complete AV canal for all children has been associated with somewhat higher mortality, greater need for reoperation, and persistently poorer hemodynamics for the Down's syndrome children. Additional follow-up to determine long-term morbidity, mortality, and hemodynamic status will be important to confirm these differences and demonstrate if these trends continue.

Acknowledgments. This study was funded by NIH R29 39052, NIH R23 HL36856, and by a summer research fellowship program supported by the American Heart Association, Oregon Affiliate. The authors would like to thank Karen McCracken for her help with this study.

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