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Early childhood health, growth, and neurodevelopmental outcomes after complete repair of total anomalous pulmonary venous connection at 6 weeks or younger

Gwen Y. Alton, RN, BSN,[a,c] Charlene M. T. Robertson, MD, FRCP(C),[a,c] Reg Sauve, MD, FRCP(C),[d] Abhay Divekar, MD, FRCP(C),[f] Alberto Nettel-Aguirre, PhD,[d,e] Sharon Selzer, RN,[g] Ari R. Joffe, MD, FRCP(C),[a] Ivan M. Rebeyka, MD, FRCS(C),[a,b] David B. Ross, MD, FRCS(C),[b] and the Western Canadian Complex Pediatric Therapies Project Follow-Up Group*

Supplemental material is available online.

Objective: This interprovincial inception cohort study explores early childhood outcomes and their operative and perioperative predictors after total anomalous pulmonary venous connection repair, simple (patent ductus arteriosus, atrial septal defect, or both) or complex (any associated major cardiac anomalies).

Methods: From 1996 through 2004, a total of 41 consecutive neonates with total anomalous pulmonary venous connection underwent complete repair with deep hypothermic circulatory arrest. Multidisciplinary health and neurodevelopmental outcomes (Bayley Scales of Infant Development II [1993], Mental and Psychomotor Developmental Indices) were assessed at 18 to 24 months of age. Regression analyses explored potentially modifiable predictors of outcome.

Results: Survival after simple total anomalous pulmonary venous connection repair was 31 of 32 (97%); that after complex repair was 3 of 9 (33%). Relative risk of death was higher for complex (21.3) and obstructive (8.4) total anomalous pulmonary venous connections. Those who died had longer deep hypothermic circulatory arrest times ($P < .001$). For 34 survivors, Mental Developmental Index was 87 ± 16 and Psychomotor Developmental Index was 89 ± 13. Among survivors, 24.6% of variability in Mental Developmental Index was explained by its linear relationship with socioeconomic status, whereas 35.5% of variability in Psychomotor Developmental Index was explained by its linear relationship with weight at surgery and highest plasma lactate level after surgery. North American native peoples made up 38% of survivors, a higher than expected number.

Conclusion: Mean developmental scores were in the low average range of normative data. Socioeconomic factors predicted mental outcome. High postoperative lactate level on day 1 predicted low motor scores. Other potentially modifiable variables will need to be explored. Further epidemiologic study relating race to occurrence of total anomalous pulmonary venous connection is suggested. Early neurodevelopmental assessment is recommended.

From the Departments of Pediatrics[a] and Surgery,[b] University of Alberta, Edmonton, Alberta, Canada, Neonatal and Infant Follow-up Clinic, Glenrose Rehabilitation Hospital, Edmonton, Alberta, Canada,[c] the Department of Pediatrics,[d] and Research Methods Team, Faculty of Medicine,[e] University of Calgary, Calgary, Alberta, Canada, the Division of Pediatric Cardiology, University of Manitoba, Winnipeg, Manitoba, Canada,[f] and the Department of Pediatrics, General Hospital, Regina, Saskatchewan, Canada.[g]

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Address for reprints: Charlene M. T. Robertson, MD, FRCP(C), Room 242A Glen East, Glenrose Rehabilitation Hospital, 10230 111 Ave, Edmonton, Alberta, Canada T5G 0B7 (E-mail: croberts@cha.ab.ca).

*D. Moddemann, Winnipeg, Manitoba, P. Blakley, Saskatoon, Saskatchewan, and A. Ninan, Regina, Saskatchewan.

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Total anomalous pulmonary venous connection (TAPVC) accounts for approximately 2% of congenital heart disease.[1-4] Reported mortality for simple TAPVC is 4.9% to 6.8%,[5,6] whereas that for complex TAPVC with other associated cardiac anomalies is greater than 50%.[7] Survivors after simple TAPVC repair have good long-term school attendance and employment.[8] Parental reports suggest good general health, with 69% of survivors having average or above school performance.[9] School-aged assessments report full-scale and verbal intelligence to be similar to population norms, but survivors have reduced performance scores,

Abbreviations and Acronyms

MDI = Bayley Scales of Infant Development II Mental Developmental Index
PDI = Bayley Scales of Infant Development II Psychomotor Developmental Index
TAPVC = total anomalous pulmonary venous connection

visual–motor integration, and fine motor skills.[10] Little has been published about early childhood neurodevelopmental outcomes after TAPVC repair.

There is increasing awareness of the importance of assessing neurodevelopmental outcomes after neonatal cardiac surgery for complex congenital heart disease, and mechanisms for adverse outcomes have been proposed.[11] Assessments after neonatal cardiac surgery allow standardized results of neurodevelopmental outcomes and identification of those needing early childhood educational interventions.[12]

The objectives of this study were to describe the 18- to 24-month health, growth, and neurodevelopmental outcomes for all infants 6 weeks or younger undergoing intracardiac repair for simple (patent ductus arteriosus, atrial septal defect, or both) or complex (other associated major cardiac anomalies) TAPVC and to explore the proportions of variability in outcomes explained by demographic, operative, and perioperative variables.

Materials and Methods

This interprovincial inception cohort outcomes study was conducted in three provinces in Western Canada. As previously described,[13,14] from September 1996 through August 2004, infants 6 weeks or younger were identified at time of surgery for TAPVC (simple and complex). Surgery was performed at the Stollery Children's Hospital, Edmonton, Alberta, Canada. Although reporting outcomes for those with simple TAPVC only would provide a cleaner study, there is need for information about those with complex abnormalities. Data for both simple and complex TAPVC are therefore given.

The operative management for the repair of TAPVC at our institution during this time was to cool the patient's blood to 20°C or lower for a minimum of 20 minutes before deep hypothermic circulatory arrest. We report here both the lowest blood temperature immediately before deep hypothermic circulatory arrest (in °C) and the lowest rectal temperature on cardiopulmonary bypass for longer than 10 minutes (also in °C). A modified pH-stat cooling strategy was used. The hematocrit during cooling for this cohort was greater than 0.20L, whereas current levels are greater than 0.25L. Preoperative, intraoperative, and postoperative variables that had been agreed on previously were collected prospectively and have been described elsewhere.[13,14] Of particular interest was plasma lactate level as an indicator of outcome; levels were regularly measured twice daily as part of clinical management as well as obtained routinely with blood gas values. Long-term follow-up was discussed with parents or guardians once survival was probable. With appropriate consent, contact was made with the respective follow-up clinic at the tertiary site of origin.

Subjects

All 41 consecutive patients admitted with TAPVC from September 1996 through August 2004—28 (68%) boys, 28 (68%) referred from out of region, and 14 (34%) North American native peoples—were registered. There were no exclusions to enrollment. All 34 survivors (31 with simple TAPVC and 3 with complex) received multidisciplinary neurodevelopmental assessments through existing neonatal follow-up clinics: 25 (74%) in Calgary, Alberta, Regina and Saskatoon, Saskatchewan, or Winnipeg, Manitoba, and 9 (26%) at the Neonatal and Infant Follow-up Clinic at the Glenrose Rehabilitation Hospital, Edmonton, Alberta. Ethics board approvals were obtained from each site before onset of the study. All parents or guardians signed individual consent forms.

Early Childhood Assessments

Outcomes assessment was completed at 18 to 24 months (mean 21 months). At assessment, a research nurse recorded history of hospitalizations, illnesses, medication use, and need for supplemental oxygen. Physical measurements were obtained as described previously.[13,14] The family socioeconomic status was determined according to the Blishen Index, a formula that considers the relative income, education requirement, and prestige factor of employment with a population mean (± SD) of 43 ± 13.[15] Maternal education was indicated by years of schooling. Race was coded according to National Institutes of Health specifications.[16] Pediatricians experienced in neurodevelopmental follow-up examined each child for evidence of cerebral palsy[17] or visual impairment, defined as corrected visual acuity in the better eye worse than 20/60.[13,14] Hearing was evaluated by experienced certified pediatric audiologists in soundproof environments as described elsewhere.[13,14] Hearing impairment was defined as binaural or bilateral sensorineural hearing loss greater than 40 dB at any frequency from 250 to 4000 Hz.[13,14] Certified pediatric psychologists and psychometrists administered The Bayley Scales of Infant Development II,[18] a widely accepted standardized outcome measure used in neonatal follow-up clinics that yields separate Mental Developmental Index (MDI) and Psychomotor Developmental Index (PDI) scores, each with a mean of 100 and SD of 15. Developmental indices lower than 70 (2 SD below mean) indicated mental or motor delay.

Statistical Analysis

Descriptive variables for outcomes were analyzed with the univariate *t* test, χ^2 test, and Fisher exact test (2-sided) analyses. Bonferroni correction was applied. The relative risk for death was calculated. Sequential stepwise multiple regressions for variables from each of the five stages—preoperative, operative, postoperative day 1, postoperative days 2 to 5, and postoperative days 6 and after—were used to explore the overall greatest proportion of outcome explained by a combination of predictors to a significance level of .05. Because numbers of survivors with complex TAPVC were small, analysis of variables predictive of outcome for this

TABLE 1. Descriptive anatomic and operative characteristics of 41 infants 6 weeks or younger undergoing complete repair for total anomalous pulmonary venous connection

Descriptor	Total (n = 41)	Survivors (n = 34)	Deaths (n = 7)	χ^2 or 2-sided *t* test	*P* value
Complex total anomalous pulmonary venous connection (No.)	9 (21.9%)	3 (8.8%)	6 (85.7%)	20.032	<.001
Male sex (No.)	28 (68%)	21 (61.8%)	7 (100%)	3.919	.048
Anatomy (No.)				10.598	.014
Supracardiac	17 (41.5%)	15 (44.1%)	2 (28.6%)		
Infracardiac	19 (46.3%)	17 (50.0%)	2 (28.6%)		
Cardiac	1 (2.4%)	1 (2.9%)	0 (0%)		
Mixed	4 (9.8%)	1 (2.9%)	3 (42.9%)		
Obstructive	17 (41.5%)	11 (32.4%)	6 (85.7%)	6.810	.009
CPB time (min, mean ± SD)	70 ± 30	64 ± 22	100 ± 48	−1.967	.083
Lowest mean arterial pressure on CPB for >10 min (mm Hg, mean ± SD)	24 ± 7	24 ± 7	25 ± 7	−0.439	.663
Lowest flow on CPB for >10 min (mL/[kg · min], mean ± SD)	129 ± 23	129 ± 24	128 ± 23	0.166	.869
Lowest rectal temperature for >10 min on CPB (°C, mean ± SD)	24.3 ± 3.1	24.2 ± 3.2	24.9 ± 2.4	−0.571	.571
Lowest blood temperature immediately before DHCA (°C, mean ± SD)	19 ± 2.4	19 ± 3.3	20 ± 2.8	−1.444	.157
Crossclamp time (min, mean ± SD)	37 ± 18	36 ± 16	48 ± 19	−2.004	.052
DHCA time (min, mean ± SD)	29 ± 11	27 ± 9	41 ± 14	−3.408	.002

After Bonferroni correction, only differences of <.005 remain significant. *CPB*, Cardiopulmonary bypass; *DHCA*, deep hypothermic circulatory arrest.

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group could not be completed separately. SPSS version 12.0 for Windows (SPSS, Inc, Chicago, Ill) was used for analyses.

Results

Of the 41 children, 32 had simple TAPVC (14 supracardiac, 15 infracardiac, 1 cardiac, and 2 mixed; 11 obstructive and 21 not obstructed) and 9 had complex TAPVC (3 supracardiac, 4 infracardiac, and 2 mixed; 6 obstructive and 3 not obstructed). Table E1 gives the anatomic diagnoses of the 9 infants with complex TAPVC.

The anatomic and operative variables for all 41 infants undergoing repair (32 simple, 9 complex) at 6 weeks or younger are given in Table 1. The relative risks for death among the 41 children were as follows: complex TAPVC, 21.3, and obstructive anatomy, 8.4. Of the 7 children who died, all were boys, 6 had complex TAPVC, 6 had obstruction, 2 had supracardiac TAPVC, 3 had mixed TAPVC, and 6 received postoperative extracorporeal membrane oxygenation. The child with simple TAPVC who died had associated bilateral pulmonary artery stenosis and disseminated intravascular coagulation. Of the patients with complex TAPVC, 4 died with multiple organ dysfunction, 1 with septic shock, and 1 with pulmonary hypertension. Six died in the hospital at 8 to 144 days post-operatively; the single late out-of-hospital death occurred at 63 postoperative days.

Table E2 shows the descriptive variables for the 34 surviving children, 31 with simple TAPVC and 3 with complex. The mean ± SD levels of plasma lactate for all surviving children for the time periods were as follows: preoperatively, 2.5 ± 2.0 mmol/L (range 0.8-8.4 mmol/L); first 24 hours postoperatively, 6.2 ± 3.3 mmol/L (range 1.8-14.2 mmol/L); days 2 through 5 postoperatively, 3.5 ± 3.1 mmol/L (range 1.0-12.6 mmol/L); and day 6 and later postoperatively, 1.3 ± 0.45 mmol/L (range 0.1-2.5 mmol/L). The highest plasma lactate level for each child occurred within 24 hours after surgery, except for 1 child with a level of 8.4 mmol/L before surgery, normal levels postoperatively, and a normal outcome. There were 7 of 34 children (21%) with plasma lactate levels on day 1 elevated by at least 1 SD for that period (>9.5 mmol/L). After Bonferroni correction, no differences were seen for demographic, preoperative, operative, or postoperative variables. Children with a racial background described by National Institutes of Health classification[16] as of North American native peoples made up 13 (38%) of the 34 assessed. Of these 13 children, infracardiac anatomy occurred in 8 (61.5%) and obstruction in 5 (38.5%). There were no statistically significant differences, however, in anatomic, operative, or perioperative variables between North American native and white children.

Growth and health outcomes for 34 survivors are described in Table 2. No child had ongoing hypoxia or known episodes of desaturation. The majority of hospitalizations and doctor visits were for pulmonary illnesses. Race, socioeconomic status, mother's schooling, and location of family home did not affect growth and health outcomes (data not shown).

There were no cases of cerebral palsy, visual impairment, or sensorineural hearing loss among the 34 survivors. No survivors were considered medically fragile, defined as

TABLE 2. Growth and general health outcomes at 18 to 24 months of 34 survivors in relation to anatomic complexity of heart defect after total anomalous pulmonary venous connection repair

Variable	Total (n = 34)	Simple (n = 31)	Complex (n = 3)
Length <3rd percentile	0 (0%)	0 (0%)	0 (0%)
Weight <3rd percentile	1 (3%)	1 (3%)	0 (0%)
Microcephaly	0 (0%)	0 (0%)	0 (0%)
Gastrostomy feeds	2 (6%)	2 (7%)	0 (0%)
Hospitalization after initial discharge	18 (53%)	18 (58%)	0 (0%)
Visited doctor (except checkup)	29 (85%)	27 (87%)	2 (67%)
Supplemental oxygen	0 (0%)	0 (0%)	0 (0%)
Chronic pulmonary medication	6 (18%)	5 (16%)	1 (33%)
Chronic cardiac medication	3 (9%)	2 (7%)	1 (33%)
Tracheostomy	1 (3%)	1 (3%)	0 (0%)

All values represent numbers and percentages of patients. Analyses not done because of low numbers within complex cardiac anomaly group.

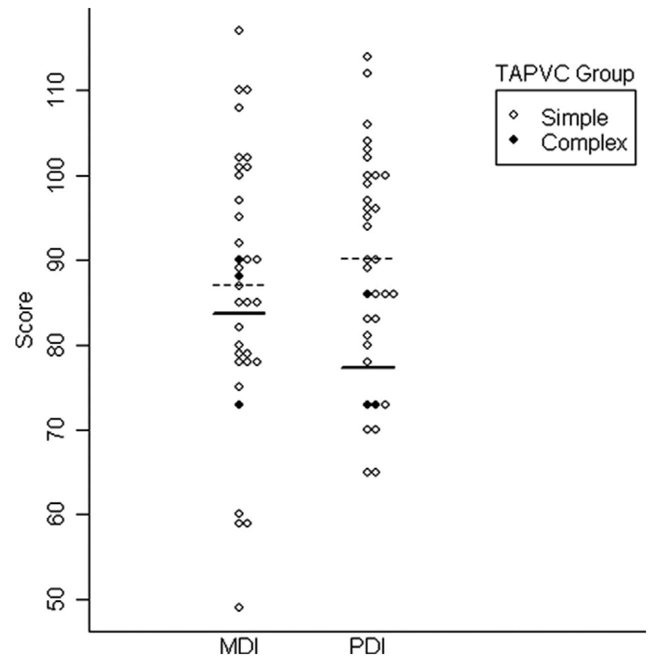

Figure 1. Distribution of individual 18- to 24-month mental and psychomotor developmental indices for 34 survivors (*open circles* for 31 simple and *closed circles* for 3 complex) after total anomalous pulmonary venous connection repair *(TAPVC)* at 6 weeks or younger, with *broken line* indicating mean scores after simple repair and *solid line* indicating mean scores after complex repair. *MDI,* Bayley Scales of Infant Development II (1993) Mental Developmental Index; *PDI,* Bayley Scales of Infant Development II (1993) Psychomotor Developmental Index.

requiring long-term hospitalization or in-home nursing care. One child with simple TAPVC had cat-eye syndrome; growth and developmental scores were not in the delayed range. No other child had a chromosomal abnormality or neurologic syndrome. Mean scores for the 34 survivors were as follows: MDI 87 ± 16 and PDI 89 ± 13. MDI scores did not differ in relation to TAPVC anatomic complexity (simple 87 ± 16 vs complex 84 ± 9, $t = 0.362$, $P > .2$). Although there were almost 14 points of difference on PDI scores between the 31 children with simple TAPVC and the 3 with complex TAPVC, the small number of children in the latter group resulted in no significant difference in the scores (simple 91 ± 13.1 vs complex 77 ± 8, $t = 1.642$, $P = .110$). Scores show a shift to the left relative to population norms of 100 ± 15. The distributions of neurodevelopmental scores for survivors of simple and complex TAPVC repair are seen in Figure 1.

Among the 34 survivors with TAPVC, 5 had delays (scores <70) according to the MDI, PDI, or both. In the simple TAPVC group, 4 of 31 infants (13%) had MDI scores lower than 70, and 2 (7%) had PDI scores lower than 70. None of the 3 children in the complex TAPVC group had scores lower than 70. With all variables listed in Table E2, comparisons were made between children with scores of at least 70 and children with delays. The only significant differences ($P < .05$) found were as follows: weight at surgery, not delayed 3.6 ± 0.62 versus delayed 2.9 ± 0.37; weight in kilograms, $t = 2.372$, $P = .024$; and lowest flow on cardiopulmonary bypass for longer than 10 minutes, not delayed 127.9 ± 27.6 versus delayed 145 ± 11.2 mL/(kg · min), $t = -2.708$, $P = .019$. With Bonferroni correction, there were no longer any significance differences. Similarly, considering only the 31 patients with simple TAPVC, there were no significant differences between children with scores above and below 70.

All variables from Table E2 with a correlation ($P < .10$) with MDI or PDI for all 34 survivors are shown in Table 3, first for all 34 survivors and then for the 31 survivors with simple TAPVC. Stepwise multiple regressions were used to determine combinations of variables predictive of MDI and PDI for all 34 survivors. Only those variables of significance ($P < .05$) from Table 3 were entered for each regression. The only variable to contribute to MDI was socioeconomic status, which explained 24.6% of the variability (slope 0.535, SE 0.166, $t = 3.227$, $P = .003$). The only variables to contribute to the variability of PDI were weight at surgery, which explained 25.1% (slope 8.600, SE 3.746, $t = 2.296$, $P = .029$), and highest plasma lactate on day 1, which contributed another 10.4% to the variability of PDI, for a combined 35.5% explained variability (slope 1.432, SE 0.675, $t = 2.121$, $P = .043$). Repeating the correlations of predictor variables with MDI and PDI for the 31 survivors after simple TAPVC resulted in the same variables showing significance ($P < .1$; Table 3). The results of the stepwise

TABLE 3. Two-tailed Pearson product–moment correlations (*r*) with *P* values of less than .10 for predictor variables in relation to developmental indices for all 34 survivors after complete repair at 6 weeks or older for total anomalous pulmonary venous connection and for those 31 with simple anatomy

	All assessed (n = 34)				Simple (n = 31)			
	MDI		PDI		MDI		PDI	
Predictor variables	*r*	*P* value	*r*	*P* value	*r*	*P* value	*r*	*P* value
Demographic								
Socioeconomic index	0.496	.003	—	—	0.518	.003	—	—
Mother's schooling (y)	0.397	.020	—	—	0.392	.029	—	—
Race	0.340	.049	—	—	0.372	.040	—	—
Weight at surgery	—	—	0.496	.003	—	—	0.501	.003
Preoperative								
Highest oxygenation index	—	—	−0.347	.054	—	—	0.332	.068
Highest creatinine (μmol/L)	—	—	−0.315	.070	—	—	−0.340	.061
Postoperative day 1								
Highest plasma lactate (mmol/L)	—	—	−0.468	.005	—	—	0.456	.010
Highest creatinine (μmol/L)	—	—	−0.369	.032	—	—	−0.409	.022
Postoperative days 2-5								
Highest dopamine used (μg/[kg · min])	—	—	−0.367	.033	—	—	0.379	.036
Lowest base deficit (mmol/L)	—	—	0.299	.097	—	—	0.362	.054
Overall								
Dialysis used	−0.374	.055	−0.332	.091	0.374	.055	0.332	.091

Variables that had no correlation ($P \leq .1$) with either Mental or Psychomotor Developmental Index for all assessed or for the 31 simple cases are not given and include demographic variables of 2-parent family, English as first language, location, sex, cardiac and obstructive anatomy, complexity, 5-minute Apgar score, gestational age at birth, and age at surgery; operative variables of cardiopulmonary bypass time, lowest mean arterial pressure for more than 10 minutes on cardiopulmonary bypass, lowest flow on cardiopulmonary bypass for more than 10 minutes, lowest rectal temperature (°C) during cardiopulmonary bypass for more than 10 minutes, lowest blood temperature immediately before deep hypothermic circulatory arrest, crossclamp time, deep hypothermic circulatory arrest time, and repeated cardiopulmonary bypass in operating room; variables at any time of lowest PaO_2 and lowest arterial pH; preoperative variables of lowest base deficit, highest dopamine used, lowest PaO_2, lowest arterial pH, highest plasma lactate, and duration of ventilation; postoperative, day 1 variables of highest dopamine used, lowest PaO_2, lowest base deficit, lowest arterial pH, and highest oxygenation index; postoperative days 2 through 5 variables of lowest PaO_2, lowest arterial pH, highest lactate, highest creatinine, and highest oxygenation index; postoperative day 6 variables listed in Table 2; and overall variables of duration of hospitalization, duration of ventilation, time sternum was open, presence of convulsions, and need for cardiopulmonary resuscitation. *MDI,* Bayley Scales of Infant Development II Mental Developmental Index; *PDI,* Bayley Scales of Infant Development II Psychomotor Developmental Index; *CPB,* cardiopulmonary bypass.

multiple regressions were also similar. Socioeconomic status explained 24.3% of the variability of MDI (slope 0.654; SE 0.156; $t = 4.196$; $P < .001$). For PDI, weight at surgery explained 22.6% of the variability; highest plasma lactate on day 1 contributed another 8.5%, for a total of 31.1% of the variability explained (slope 1.416; SE 0.645; $t = 2.196$; $P = .036$).

Because of the large proportion of the variability in MDI explained by socioeconomic status, correlations between this predictor variable and other demographic variables were completed for 34 children. Significant univariate correlations of socioeconomic status were mother's schooling ($r = 0.776$, $P < .001$) and race ($r = 0.616$, $P < .001$).

Discussion

This is the first report of early childhood outcomes of standardized neurodevelopmental assessment for survivors after early infant TAPVC repair. This indication in early childhood of the need for early developmental and educational intervention supports previous recommendations that early intervention would benefit some children with TAPVC repair.[10] Kirshbom and colleagues[9] initially reported that most school-aged survivors of simple TAPVC can expect good functional outcomes, with 69% having average to above average school performance according to parent questionnaires. The need for educational support of TAPVC survivors was shown in a later study that used age-appropriate standardized tests; Kirshbom and associates[10] reported that 58% of the 6- to 19 year- old- children had delays in one or more domains tested: performance intelligence, mathematics achievement, attention, fine motor function, and visual motor integration. Through the early identification of children at risk for these school-related difficulties and the provision of educational intervention as indicated, we hope to be able to reduce adverse outcomes.[10,12]

Direct comparisons between a developmental test for 18- to 24-month-old children, as we have done, and formal intellectual testing for school-aged children, as reported by

Kirshbom and associates,[10] cannot be completed because of the different ages of the children and the low socioeconomic status found in our population. For those surviving after repair of simple TAPVC, Kirshbom found the verbal IQ at a median of 11 years for 30 children to be 98.6 ± 20.2, not differing from population norms. For the comparable anatomic lesion, the MDI mean score for our 31 children after repair of simple TAPVC was 87 ± 16. Mean motor score for our 31 survivors of simple TAPVC, 91 ± 13, was below population norms. Although we cannot compare our data directly with those of Kirshbom and associates,[10] the performance IQ of children in that study was also below population normative data.

The lack of prediction of low mental scores in our study beyond unmodifiable variables related to socioeconomic status suggests that further exploration of other variables might be of benefit. Modifiable predictive variables of mental scores after TAPVC may yet be identified and should be a priority for future research. Our study identifies the potentially modifiable predictor of PDI to be higher plasma lactate within the first 24 hours after surgery. We have previously shown that postoperative plasma lactate may help to differentiate developmental outcomes.[19] Delayed motor scores occurred in the simple and complex TAPVC groups, supporting the literature that documents lower fine motor and performance scores in this population.[10] We have had similar findings in survivors after surgery for transposition of the great arteries.[14] The particularly low mean motor score in our 3 children with complex anatomy, 77 ± 8, is similar to our findings in a previous study of 16 children after surgery for hypoplastic left heart syndrome (68 ± 19).[13]

The important role of socioeconomic status in the outcomes of infants with congenital heart surgery has been documented previously.[20-23] We sought factors that contributed to the lower socioeconomic status in this study: maternal education level and race were associated; however, we have not identified all contributing variables. The significant predictive value of socioeconomic status for the MDI in this study is in contrast to our previous publication on development after arterial switch operation, in which socioeconomic status and mother's education did not predict outcome.[14] Although it is common in the literature for socioeconomic status to relate to the developmental outcome of young children, it is unusual for it to be the only predictor. The usual method of addressing the effect of wide variations of socioeconomic status affecting outcome is to control for this variable.[24,25] Such control was not possible in this outcome study. A combination of postsurgical TAPVC and low socioeconomic status strongly predicted neurodevelopmental delay. We recommend early intervention and education for all children with delays. Early individual assessment helps to identify children in need of additional neurodevelopmental or educational help.

We used The Bayley Scales of Infant Development II[18] to assess the developmental level of these survivors at 18 to 24 months because this commonly used tool provides benefit to the children by outlining developmental strengths and weaknesses, thus assisting in planning individual developmental intervention as required. With this test, correlations with later outcome are best for the oldest children within the range of the test, which is up to 42 months of age. It is important to point out that The Bayley Scales of Infant Development II[18] is not an intelligence test. Severe delay of more than 3 SD below mean on mental developmental tests is associated with a persistent mental delay.[26] After neonatal cardiac surgery, there have been few long-term studies done comparing developmental testing with intelligence testing at school age, but one study after repair of transposition of the great arteries suggested 1-year developmental testing had only modest correlation with later performance. We plan to assess these children at 5 years. Thus far, only 13 have been assessed. The Pearson product correlation (2-sided) of the MDI with full-scale intelligence is 0.663. Further testing is needed, however, to determine the utility of developmental tests in young children after neonatal intracardiac repair.

Fifty-eight percent of our 34 children with TAPVC repair required rehospitalization, whereas 9% of 82 children after the arterial switch operation,[14] from this site and under the same system of medical care, required rehospitalization. In this study, these hospitalizations were largely for pulmonary illnesses regardless of demographic background, suggesting that children after TAPVC repair require close medical follow-up for pulmonary complications. These patients' general health was good, as supported by other studies.[8-10] There was no microcephaly reported in our study, in contrast to 28% reported by Kirshbom and associates[10] and 30% in a population of young children of similar age after complex heart surgery of several types.[27] One child with simple TAPVC and a weight less than the 3rd percentile had a gastrostomy tube.

Our study of consecutive admissions to our regional heart center with TAPVC shows a high incidence of children of native peoples (14 of 41 children, 34%). This proportion of native children is 3.6 times higher than that among our population of children 6 weeks or younger with all types of severe complex cardiac anomalies cared for in 1996 through 1999 and previously published.[13] This finding of a higher than expected incidence of TAPVC among native Canadians has been previously described.[28] We were unable to show that native children had more complicated operative or perioperative periods.

One of the major strengths of this study is its 100% follow-up of all survivors and accountability for all 41 children that underwent surgery. The major limitation to our study is the small number of survivors with complex TAPVC. This precluded the ability to test modifiable variables in that group. In addition, the significantly large number of subjects with low socioeconomic status may have acted to limit the determination of predictive variables.

Conclusions

An increased survival of children with TAPVC during recent decades suggests a need to enhance our understanding of their neurodevelopmental outcomes. We strongly recommend that children who have been treated for this life-threatening condition undergo early developmental assessments that may assist in planning early intervention programs to enhance their future skills. In this study, after evaluation of a wide variety of predictor variables, we found few modifiable predictors, suggesting that alternative predictors should be sought. The observation of a high prevalence of TAPVC among North American native peoples warrants further epidemiologic study.

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TABLE E1. Anatomic diagnoses of the 9 infants with complex total anomalous pulmonary venous connection

Case	Pulmonary vein stenosis or atresia	Double-outlet right ventricle	VSD, multiple VSDs	Mitral valve obstruction	Atrioventricular canal	Aortic stenosis	Pulmonary arterial stenosis	Dextrocardia
1	Yes							Yes
2	Yes	Yes						
3	Yes							
4	Yes						Yes	
5		Yes		Yes				
6*†		Yes	Yes		Yes			
7*			Yes	Yes				
8*			Yes			Yes		
9			Yes					

VSD, Ventricular septal defect. *Surviving at 2 years. †Reintervention for bidirectional cavopulmonary anastomoses at 13 months.

TABLE E2. Demographic, operative, and perioperative descriptors for surviving 34 infants after surgery at 6 weeks or younger for total anomalous pulmonary venous connection mean (SD), n (%)

	Total (n = 34)	Simple (n = 31)	Complex (n = 3)	Statistical test*	P value
Demographic					
Socioeconomic index† (mean ± SD)	38.6 ± 14.6	37.6 ± 14.7	48.7 ± 9.1	−1.272	.213
Mother's schooling (y, mean ± SD)	12.3 ± 3.1	12.3 ± 3.2	12.7 ± 2.1	−0.214	.852
Two-parent family	26 (77%)	23 (74%)	3 (100%)	—	.603
English as first language	30 (88%)	28 (90%)	2 (67%)	—	.322
Race				—	.27
White	20 (59%)	18 (58%)	2 (67%)		
Asian	1 (3%)	0 (0%)	1 (33%)		
North American native	13 (38%)	13 (42%)	0 (0%)		
Location				2.606	.919
Large city (>100,000)	15 (44%)	13 (42%)	2 (67%)		
Town (1000-30,000)	13 (38%)	12 (39%)	1 (33%)		
Farm or village (<1000)	6 (18%)	6 (19%)	0 (0%)		
Male sex	21 (62%)	19 (61%)	2 (67%)	—	1
Apgar score at 5 min (mean ± SD)	8.3 ± 0.97	8.2 ± 0.95	9.3 ± 0.58	−2.033	.05
Birth gestation (wk, mean ± SD)	39.2 ± 1.7	39 ± 2	40 ± 2	0.491	.627
Preoperative					
Age at surgery (d, mean ± SD)	15 ± 15	15 ± 14	15 ± 19	−0.006	.995
Body weight at surgery (g, mean ± SD)	3.5 ± 6.1	3.5 ± 0.64	3.4 ± 0.26	0.426	.673
Supracardiac anatomy	15 (44%)	14 (45%)	1 (33%)	—	>.999
Obstructive anatomy	11 (32%)	10 (32%)	1 (33%)	—	>.999
Highest dopamine used (μg/[kg · min], mean ± SD)	2.7 ± 5.6	2.7 ± 5.7	3.3 ± 5.8	−0.196	.846
Epinephrine used	4 (12%)	4 (13%)	0 (0%)	—	>.999
Lowest PaO_2 (mm Hg, mean ± SD)	41.2 ± 15.2	41.6 ± 15.8	37.0 ± 5.3	0.493	.625
Lowest base deficit (mmol/L, mean ± SD)	−2.8 ± 4.2	−2.6 ± 4.4	−4.7 ± 0.6	0.796	.433
Lowest arterial pH (mean ± SD)	7.33 ± 0.09	7.33 ± 0.1	7.34 ± 0.05	−0.100	.921
Highest plasma lactate (mmol/L, mean ± SD)	2.5 ± 2.0	2.6 ± 2.1	1.8 ± 0.8	0.624	.537
Highest serum creatinine (μmol/L, mean ± SD)	61.4 ± 2.7	60.8 ± 21.9	68.3 ± 34.1	−0.545	.589
Highest oxygenation index (mean ± SD)	14.3 ± 19.6	15.0 ± 20	7 ± 1.7	0.667	.510
Duration of ventilation (d, mean ± SD)	2.1 ± 3.3	1.5 ± 1.7	8.3 ± 8.5	−1.399	.296
Operative					
CPB time (min, mean ± SD)	63.8 ± 21.5	59.4 ± 13.9	109 ± 37.3	−2.289	.146
Lowest mean arterial pressure on CPB for >10 min (mm Hg, mean ± SD)	24.2 ± 6.9	24.6 ± 6.6	20.3 ± 10.5	1.007	.322
Lowest flow on CPB for >10 min (mL/[kg · min], mean ± SD)	129.5 ± 23.6	132 ± 21.8	100 ± 25	2.432	.021
Lowest rectal temperature for >10 min on CPB (°C, mean ± SD)	24.2 ± 3.2	24.4 ± 3.2	22.3 ± 2.6	1.096	.281
Lowest blood temperature immediately before DHCA (°C, mean ± SD)	19.0 ± 2.3	19.1 ± 2.4	18.4 ± 1.5	0.510	.614
Crossclamp time (min, mean ± SD)	34.5 ± 15.7	31.7 ± 8.1	63 ± 41.7	−1.297	.323
DHCA time (min, mean ± SD)	27 ± 8.7	27.1 ± 7.9	26 ± 17.6	.107	.924
Repeat CPB in operating room	2 (6%)	2 (6%)	0 (0%)	—	>.999
Postoperative day 1					
Highest dopamine used (μg/[kg · min], mean ± SD)	6.8 ± 6.4	6.7 ± 6.6	8.3 ± 2.9	−0.424	.674
Lowest PaO_2 (mm Hg, mean ± SD)	73.2 ± 52.5	74.6 ± 54.6	59.3 ± 21.9	0.474	.639
Lowest base deficit (mmol/L, mean ± SD)	−1.0 ± 3.5	−1.1 ± 10.3	−0.67 ± 4.0	−0.184	.855
Lowest arterial pH (mean ± SD)	7.37 ± 0.07	7.33 ± 0.07	7.29 ± 0.1	1.079	.289
Highest plasma lactate (mmol/L, mean ± SD)	6.2 ± 3.3	6.3 ± 3.4	5.2 ± 1.6	0.568	.574
Highest serum creatinine (μmol/L, mean ± SD)	64.4 ± 18.3	64.6 ± 18.8	63.0 ± 13.1	0.141	.889
Highest oxygenation index (mean ± SD)	7.9 ± 4.2	7.9 ± 4.2	8.3 ± 5.1	−0.180	.859
Postoperative days 2-5					
Highest dopamine used (μg/[kg · min], mean ± SD)	8.6 ± 20.8	8.6 ± 21.8	8.3 ± 3.8	0.023	.982
Lowest PaO_2 (mm Hg, mean ± SD)	64.1 ± 24.8	64.5 ± 25.5	60 ± 19	0.297	.768
Lowest base deficit (mmol/L, mean ± SD)	−0.344 ± 3.6	−0.448 ± 3.8	0.667 ± 1.5	−0.502	.619

CHD

TABLE E2. Continued

	Total (n = 34)	Simple (n = 31)	Complex (n = 3)	Statistical test*	*P* value
Lowest arterial pH (mean ± SD)	7.34 ± 0.07	7.35 ± 0.07	7.29 ± 0.09	1.394	.173
Highest plasma lactate (mmol/L, mean ± SD)	3.5 ± 3.1	3.6 ± 3.1	2.5 ± 0.8	0.605	.549
Highest serum creatinine (μmol/L, mean ± SD)	79 ± 33.9	78.7 ± 35.2	71.3 ± 18.6	0.404	.689
Highest oxygenation index (mean ± SD)	4.8 ± 2.5	4.65 ± 2.4	6 ± 2.6	−0.912	.368
Postoperative day 6 and later					
Highest dopamine used (μg/[kg · min], mean ± SD)	1.5 ± 3.4	1.3 ± 3.1	3.3 ± 5.8	−0.991	.329
Epinephrine used	6 (18%)	5 (15%)	1 (33%)	—	.464
Lowest $Pa{O_2}$ (mm Hg, mean ± SD)	66.8 ± 16.4	66.8 ± 17.3	56.3 ± 11.7	1.013	.319
Lowest base deficit (mmol/L, mean ± SD)	0.065 ± 4.7	−1.07 ± 4.8	1.7 ± 3.2	−0.620	.540
Lowest arterial pH (mean ± SD)	7.37 ± 0.06	7.37 ± 0.06	7.36 ± 0.06	0.078	.938
Highest plasma lactate (mmol/L, mean ± SD)	1.3 ± 0.45	1.3 ± 0.46	1.3 ± 0.46	−0.038	.970
Highest serum creatinine (μmol/L, mean ± SD)	59.7 ± 28.7	61.6 ± 27.9	40.0 ± 17.3	1.30	.203
Highest oxygenation index (mean ± SD)	2.7 ± 2.1	2.7 ± 2.2	2.7 ± 1.5	0.033	.974
Overall					
Duration of hospitalization (d, mean ± SD)	18.9 ± 12.9	18.3 ± 13.1	26.1 ± 4.4	−0.987	.331
Duration of ventilation (d, mean ± SD)	8.5 ± 7.5	8.3 ± 7.8	10.3 ± 4.0	−0.444	.660
Duration sternum open (d, mean ± SD)	2.7 (5.8)	2.6 (5.9)	4 (4.6)	−0.401	.691
Convulsions at any time	3 (10%)	3 (10%)	0 (0%)	—	>.999
Cardiopulmonary resuscitation at any time	2 (6%)	2 (6%)	0 (0%)	—	>.999
Dialysis at any time	1 (3%)	1 (3%)	0 (0%)	—	>.999

After Bonferroni correction, only differences of <.0001 remain significant. *CPB*, Cardiopulmonary bypass; *DHCA*, deep hypothermic circulatory arrest. *Statistical tests: χ^2, *t* test, 2-sided Fisher exact test. †Blishen BR. The 1981 socioeconomic index for occupations in Canada. *Can Rev Sociol Anthropol.* 1987;24:465-88.