Developmental and Functional Outcomes at School Entry in Children with Congenital Heart Defects

Annette Majnemer, PhD, Catherine Limperopoulos, PhD, Michael Shevell, MD, CM, Charles Rohlicek, MD, CM, Bernard Rosenblatt, MD, CM, and Christo Tchervenkov, MD, CM

Objective To describe developmental and functional outcomes of children with congenital heart defects (CHDs) at school entry after open heart surgery.

Study design Infants with CHDs who underwent surgical repair in infancy were recruited and assessed prospectively for developmental progress. At 5 years of age (64.2 ± 11.3 months), 94 subjects were evaluated in a blind fashion by using a variety of standardized measures.

Results Mean IQ scores were in the low average range (90-94). Receptive language was in the average range (103.6 ± 14.4). Behavioral difficulties were common (27.1%), with internalizing problems being more frequent. Functional limitations in socialization (93.0 ± 17.1), daily living skills (94.6 ± 16.4), communication (90.0 ± 14.1), and adaptive behavior (92.1 ± 15.8) were noted in 11% to 17% of children. With the Functional Independence Measure for Children, 20% to 22% of subjects were more dependent than their peers in self-care and social cognition, although few (4.5%) had mobility restrictions. Predictors of developmental and functional limitations included: abnormal postoperative neurologic examination, microcephaly, deep hypothermic circulatory arrest time, palliation, acyanotic heart lesion, age at surgery, and maternal education.

Conclusions After infant open-heart surgery, children with CHDs may exhibit a range of developmental difficulties at school entry that enhances risk for learning challenges and decreased social participation. *(J Pediatr 2008;153:55-60)*

It is increasingly appreciated that brain injury may occur in infants with congenital heart defects (CHDs) and that the causes are multifactorial. Before surgery, both prenatally and postnatally, there may be poor oxygen delivery because of arterial hypoxemia, impaired cerebral perfusion, or both.[1] Intraoperatively, surgical procedures may be associated with hypoxic-ischemic reperfusion brain injury.[1-3] Postoperatively, medical complications may contribute to further risk for brain injury. Furthermore, a subset with CHDs may also have subtle brain malformations.[1,3]

There is accumulating evidence that infants with CHDs requiring surgical correction or palliation early in life are at high risk for developmental disability.[3-5] These survivors of open-heart surgery may exhibit delays across developmental domains and subtle neurologic deficits. However, severe disability is uncommon (<5%). These deficits persist throughout childhood, and the extent and range of these impairments are still being clarified. Few prospective studies have followed a cohort from initial surgical intervention to school age.

We prospectively followed a consecutive sample of newborns and infants who underwent open-heart surgery (fall of 1994 to spring of 1998). We used a wide range of outcome measures and documented a variety of medical, surgical, and clinical factors as possible determinants of developmental sequelae. Preoperative and acute postoperative developmental status[6,7] and 12- to 18-month outcomes have already been reported.[8,9] We now report on the developmental (cognitive, receptive language, behavior) and functional (activity limitations) outcomes of our cohort. Furthermore, we also determined the relationship between medical, surgical, and clinical risk factors and these outcomes.

CHD	Congenital heart defect	WeeFIM	Functional Independence Measure for Children
VABS	Vineland Adaptive Behavior Scale		

From the School of Physical and Occupational Therapy (A.M., C.L., M.S.), Departments of Neurology and Neurosurgery (A.M., C.L., M.S., B.R.), Pediatrics (A.M., C.L., M.S., C.R., B.R., C.T.), Cardiovascular and Thoracic Surgery (C.R., C.T.), McGill University, Montreal Children's Hospital, Montreal, Quebec, Canada.

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Reprint requests: Dr Annette Majnemer, Montreal Children's Hospital, Division of Pediatric Neurology, Room A-509, 2300 Tupper St, Montreal, Quebec, H3H 1P3, Canada. E-mail: annette.majnemer@mcgill.ca.

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METHODS

Subjects and Procedures

As part of a prospective study, 2 groups of newborns and infants with CHDs who underwent open-heart surgery early in life were sequentially recruited at the Montreal Children's Hospital before their first open-heart surgery and followed longitudinally. Exclusion criteria were: 1) diagnosis of hypoplastic left heart syndrome; 2) preterm birth; 3) perinatal asphyxia; 4) objective evidence of brain malformation; and 5) clinical documentation of chromosomal anomalies or specific genetic syndromes associated with developmental disability. These infants were excluded because of a greater risk for developmental sequelae that could bias our outcome data. Of subjects recruited, those who had surgery in the first month of life constituted the newborn group, and the infant group included those who had surgery between 1 and 24 months of age, most before 6 months of age. Of 131 subjects recruited, 16 died, 16 were lost to follow-up, and 5 refused further follow-up at school entry, leaving 94 available for the study. Subjects were examined in a blind fashion by an occupational therapist, psychologist, and neurologist. The hospital's institutional review board approved this study, and parents of subjects gave written informed consent at recruitment.

Outcome Measures

Developmental assessments included: 1) the Wechsler Preschool and Primary Scale of Intelligence (WPPSI-R)[10] for cognitive performance; 2) the Peabody Picture Vocabulary Test (PPVT)[11] for receptive language skills; and 3) the Child Behavior Checklist (CBCL)[12] for identification of behavior problems. Functional performance was evaluated by using the Vineland Adaptive Behavior Scale (VABS),[13] which measures a child's typical performance in everyday activities (ie, socialization, communication, daily living skills, adaptive behavior), and the Functional Independence Measure for Children (WeeFIM),[14] which assesses the level of assistance required to carry out everyday activities independently (ie, self-care, cognition, mobility). All outcome measures are age-appropriate, have sound psychometric properties, and are routinely used in clinical practice.

Predictor Variables

A wide range of factors, evident either before, during, or after surgical intervention, were analyzed as possible predictor variables. These included: 1) preoperative and postoperative neurologic examination; 2) presence of microcephaly after surgery before hospital discharge; 3) type of surgery (corrective/palliative); 4) preoperative arterial oxygen saturation (<85% or >85%); 5) deep hypothermic circulatory arrest time (minutes); 6) cardiopulmonary bypass time (minutes); 7) days in intensive care unit after first surgery; 8) days hospitalized; and 9) parental stress measured by using the Parenting Stress Index.[15] Variables that may have had a confounding influence on outcomes were also considered and included the age at surgery (newborn/infant, age in months), maternal education, and type of heart lesion (cyanotic or acyanotic). We used the common categorization of CHD as cyanotic (potential for inadequate pulmonary blood flow) or acyanotic (potential for inadequate systemic blood flow).

Table I. Group characteristics

Descriptive characteristics	Group mean values
Age at assessment (months)	64.2 ± 11.3
Months since open-heart surgery	61.5 ± 10.1
Deep hypothermic circulatory arrest time (minutes)	21.0 ± 23.5
Cardiopulmonary bypass time (minutes)	152.8 ± 73.3
Days in intensive care unit after first surgery	1.7 ± 10.4 (median, 9; range, 1-58)
Number of hospitalizations	1.5 ± 0.9 (median, 1; range, 1-6)

Median values provided for skewed distributions.

Statistical Analysis

Descriptive statistics were used to characterize performance on the developmental and functional outcome measures at school entry. Cut-off values for each measure that are of clinical significance in identifying children with difficulties in particular domains were used to determine percentage of children with delays or limitations. Univariate analyses were first conducted to determine which predictors were significantly associated with the outcomes and to verify co-linearity among variables. A stepwise selection procedure was then conducted by entering variables found to be associated on univariate analyses in a multiple linear regression model, and then adding potential confounders, to derive the best possible predictive models. The authors had full access to the data and take responsibility for its integrity. All authors have read and agree to the manuscript as written.

RESULTS

At 5 years of age, 94 subjects (39 newborn group, 55 infant group) were examined. Descriptive characteristics appear in Table I. The most common defects were transposition of the great arteries, tetralogy of fallot, ventricular septal defect, univentricular heart variants, and double outlet right ventricle. Cyanotic lesions were present in 64 subjects, with 30 subjects having acyanotic lesions. In our original sample, deep hypothermic circulatory arrest was used in 83% of newborns and 30% of infants. There were no significant differences between subjects assessed at 5 years and subjects not followed in type of heart lesion, days in intensive care unit and duration of hospitalization, deep hypothermic circulatory arrest time, type of surgery, preoperative oxygen saturation, preoperative or postoperative neurological examination, or developmental findings. The age at surgery was younger in

Table II. Performance on developmental and functional outcome measures

Outcome measures (cut-off)	Mean ± SD (median)	% Below cut-off
Developmental measures		
Wechsler Preschool and Primary Scale of Intelligence (<80)		
Verbal IQ	90.2 ± 19.3 (92)	19.4%
Performance IQ	93.7 ± 20.9 (97)	20.6%
Full Scale IQ	91.0 ± 20.7 (93)	22.4%
Peabody Picture Vocabulary Test (<1.5 SD)	103.6 ± 14.4 (104)	5.3%
Child Behavior Checklist (borderline, abnormal; >60)		
Internalizing behaviors	52.4 ± 9.8 (51.5)	31.3%
Externalizing behaviors	53.0 ± 10.4 (54.0)	16.7%
Total score	53.9 ± 11.3 (54.0)	27.1%
Functional measures		
WeeFIM (<75)		
Self-care	86.9 ± 19.4 (89)	22.2%
Cognition	86.3 ± 20.2 (91)	20.0%
Mobility	97.4 ± 16.6 (102)	4.5%
Total score	89.7 ± 17.4 (93)	11.0%
Vineland Adaptive Behavior Scale (<78)		
Socialization	93.0 ± 17.1 (95)	13.3%
Communication	90.0 ± 14.1 (91)	17.1%
Daily living skills	94.6 ± 16.4 (97)	10.8%
Adaptive behavior	92.1 ± 15.8 (93)	14.6%

subjects examined compared with subjects lost to follow-up; however, this variable was adjusted for in the regression models.

Mean scores on the developmental measures are presented in Table II. IQs are in the low-normal range, with approximately one-fifth of children experiencing cognitive difficulties. Receptive language skills were age-appropriate for most children. Behavioral problems were common in this cohort, with internalizing problems (eg, withdrawn, anxious, sad, somatic symptoms) being particularly prevalent.

Functional scores were in the low-average range overall; however, 15% to 20% of subjects exhibited activity limitations in particular domains (Table II). Few children had mobility restrictions; however, a subset was more dependent than their peers in self-care and social cognition (eg, problem solving, memory).

The best predictive models (ie, highest percentage variance explained by the combination of independent variables in the model) for each outcome measure appear in Table III. Deep hypothermic circulatory arrest time (especially >40 minutes of exposure) was significantly associated with lower IQ and poor receptive language skills. Higher maternal education was significantly associated with higher performance IQ. Subjects with acyanotic lesions had significantly lower IQ scores (mean range, 86.2-88.0) than subjects with cyanotic lesions (mean range, 91.3-96.6), with the greatest differences for performance IQ. Children who had surgery in infancy had significantly lower IQ scores (88.6-92.1) than those requiring surgery in the newborn period (92.2-95.6). None of the biomedical factors considered were significantly associated with behavioral difficulties, suggesting that other variables (eg, environmental) may have a greater influence on behavior.

Table IV provides the best predictive models for functional outcomes. Results indicated that maternal education emerged as the most important predictor of a child's ability to perform everyday activities expected for age and stage of development as measured with the VABS. There is a small but significant association between increasing age (in months) and cardiopulmonary bypass time and better communication skills. For the level of functional independence as measured with the WeeFIM, abnormalities on postoperative neurological examination were significantly associated with greater assistance required in basic self-care activities. Presence of microcephaly at the time of open-heart surgery and the need for palliation together predicted mobility restrictions and a lower overall score in functional independence. These predictors (neurologic examination, microcephaly, palliation) are similar to those found in our cohort to be predictive of neuromotor impairments.[16] Maternal education was also significantly associated with social cognition.

The developmental measures and functional assessments were highly correlated with each other (most with r values >0.5, $P < .0001$), with the exception of the Child Behavior Checklists scores. For the latter, only the externalizing behaviors correlated with performance and full scale IQ (−.31-−.32, $P < .05$), and this subscale and total scores also correlated with Vineland daily living skills, adaptive behavior, and socialization (−.38-−.56, $P < .01$). As part of this study, the Parental Stress Index was used to describe family well-being.[17] High levels of stress were significantly associated (r^2 range, 0.12-0.23; $P \leq .01$) with lower IQ scores, poor receptive language skills, behavior problems (internalizing and total scores), socialization, and adaptive behavior as measured with the VABS.

DISCUSSION

Our work confirms earlier studies that have demonstrated that children undergoing early open heart surgery and subsequently evaluated at preschool age, school age, or adolescence have mean IQ scores in the low-normal range (90-99, generally).[4,5,18-26] Most investigators have noted that performance IQ is lower than verbal IQ. This was not the case in our cohort. This may be because English (the language in which this test was developed) was not the primary language for many of our subjects, having somewhat of an impact on verbal IQ performance. Although most children who had infant cardiac surgery score in the "normal" range, these children may experience particular difficulties with visual-spatial and visual-motor skills and have impaired executive functions such as memory and problem solving and are at risk for learning disabilities.[21,23,27] As in this study, socioeconomic status and prolonged deep hypothermic circulatory

Table III. Best predictive models for cognitive, language, and behavioral outcomes

Outcome measure Predictor variables	*P* value (model)	r^2 (% variance)	Parameter estimate	*P* value (variable)
Performance IQ	.0003	42%		
Cyanotic/Acyanotic			11.3	.0374
DHCA (minutes)			−0.40	.0006
Maternal Education			12.5	.0226
Verbal IQ	.0034	17%		
Newborn/Infant			−10.8	.0030
DHCA (minutes)			−0.36	.0001
Full scale IQ	.0004	23%		
Newborn/Infant			−12.8	.0138
DHCA (minutes)			−0.45	.0002
Peabody Picture Vocabulary Test	.0159	11%		
DHCA (minutes)			−0.21	.0159
Child Behavior Checklist				
No significant predictors	NS			

DHCA, deep hypothermic circulatory arrest; *NS*, not signficant.

Table IV. Best predictive models for functional limitations

Outcome measure Predictor variables	*P* value (model)	r^2 (% variance)	Parameter estimate	*P* value (variable)
Socialization (VABS)	.0383	9%		
Maternal education			9.4	.0383
Adaptive behavior (VABS)	.0145	13%		
Maternal education			10.8	.0145
Communication (VABS)	.0243	9%		
Age at surgery			0.80	.0426
CPB (minutes)			0.08	.0189
Daily living skills (VABS)	NS			
No significant predictors				
Self-care (WeeFIM)	.0282	7%		
Postoperative Neurologic Exam			−11.3	.0282
Mobility(WeeFIM)	.0001	25%		
Postoperative microcephaly			−8.5	.0500
Corrective/Palliative			−25.8	.0003
Cognition (WeeFIM)	.0135	13%		
Maternal education			11.3	.0135
Total Score (WeeFIM)	.0009	20%		
Postoperative microcephaly			−9.5	.0359
Corrective/Palliative			−21.3	.0035

CPB, cardiopulmonary bypass.

arrest (>40) have been found to be associated with lower IQ.[19-21,25,27] In a recent review, Wray[26] suggested that older age at repair and acyanotic lesions may be associated with cognitive deficits long-term. Our results support this. We found that children who had surgery delayed to infancy had lower IQ scores than children who had surgery in the first days of life. Subjects with acyanotic lesions in our cohort had lower IQ than subjects with cyanotic lesions. These types of heart lesions may be associated with poor cerebral blood flow because of poor systemic perfusion, beginning in the fetal period and extending until surgical correction. Other predictors of low IQ noted by other studies include prolonged bypass time,[22] seizures,[4,23] and length of hospital stay.[24] We did not find bypass time or hospital stay to be predictive.

We found receptive language skills to be age-appropriate in the most of our subjects, but did not evaluate expressive or complex language skills. Language was evaluated in detail in the Boston Circulatory Arrest study at preschool and school age. That study demonstrated that although receptive language was acceptable, as in this investigation, there were higher order language skills in the expressive domain that were often impaired. This included oromotor apraxia and

abnormalities of speech production such as fluency and phonological awareness. Other studies have also found expressive language difficulties.[22,23] The only predictor variable identified for language ability is deep hypothermic circulatory arrest time, which was further validated in our study.[4,27]

The evidence to date on behavioral outcomes has been somewhat conflicting. Some studies found no differences in this domain compared with that in typically developing peers,[18,21,28] whereas other studies obtained mean scores on the Child Behavior Checklist that were elevated (deviant) compared with normative data.[5,23,29,30] Our study supports the latter by showing that behavioral difficulties, particularly internalizing behaviors, are commonly observed at school entry. Poor attention span was noted in more than half the children with hypoplastic left heart syndrome in 1 study, with 18% having deviant scores on the Child Behavior Checklist (CBCL).[23] Ellerbeck et al[29] reported frequent behavioral concerns in school-age children, with internalizing (29%) and externalizing (22%) behaviors (total score deviant in 33%) that were of comparable frequency to our cohort. In our study, none of the biomedical, surgical, or clinical predictor variables were associated with behavioral outcome. It is conceivable that parental over-protectiveness, anxiety, and stress and frequent and recurrent negative experiences in hospital settings may have contributed to some extent to these behavioral manifestations. There is some evidence that increased bypass time may be associated with impulsive behaviors.[27] Severity of hemodynamic status and low socioeconomic status were collectively associated with withdrawn behaviors and somatic complaints in another study.[31]

There is growing evidence to suggest that survivors of infant open-heart surgery are at risk for learning disabilities and academic failure, which include activities such as mathematics and reading.[5,23,32] Children with CHDs and other chronic health conditions may perceive that they have physical activity restrictions, and preliminary evidence supports a lack of vigorous physical activity experiences when compared with age-matched adolescent peers.[33] 1 study reports on functional status comparable with our cohort.[21] Overall, children in our cohort appeared to adapt fairly well to their developmental deficits, with few demonstrating important activity limitations at this time. However, with entry to the school environment and the community for most activities, it is possible that these children will experience greater challenges in everyday activities (eg, social relationships, oral and written communication, recreation). Children in our cohort who were more dependent in self-care and mobility (WeeFIM) than their peers, were likely to have had microcephaly, abnormal neurologic examination results after open-heart surgery, or both and were more likely to have been palliated. Early postoperative neurologic impairment should therefore be viewed as a risk factor for future disability in functional activities.

We found that high levels of parental stress were significantly correlated with IQ scores, receptive language ability, internalizing and total behavioral scores, adaptive behavior, and socialization skills. It is difficult to ascertain whether children with developmental or psychosocial difficulties "caused" their parents to be stressed or whether the highly stressed parental context contributed in part to the developmental difficulties their child was experiencing. It is conceivable that this relationship is bidirectional, and therefore efforts to support families to enhance coping and adaptive responses would be as important as early interventions to promote developmental progress in the child. The strong relationship between parental stress and behavior problems has been documented previously in this population.[17,28,30] Families in 1 study that had greater social supports had less stress,[28] reinforcing the potential for modification.

Limitations in this study include missing data on some children and lack of follow-up on the entire cohort. Exclusion of hypoplastic left heart syndrome limits our ability to generalize the findings to this population. Furthermore, data collection at a single-site may have unique attributes and therefore needs validation at other centers. We did not control for any rehabilitation treatments that may have optimized outcomes in the small subset of children that received intensive early interventions.

The relationship between age at surgery and type of defect with IQ provide some clues for prevention strategies to potentially diminish brain injury, by minimizing chronic exposure to ischemia. Early clinical markers of neurologic insult after surgery such as an abnormal neurologic examination results or microcephaly may help target a subgroup at high risk for persisting neuromotor impairment[16] and functional limitations who may benefit from early, intensive rehabilitation intervention. Finally, families of children with CHDs continue to be highly stressed years after surgical repair, which may have an impact on the functioning and well-being of the child and family unit. This is potentially modifiable, and therefore needs to be addressed by the health service providers.

Acknowledgements available at www.jpeds.com.

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