Neurodevelopmental and neuroradiologic outcomes in patients with univentricular heart aged 5 to 7 years: Related risk factor analysis

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Objective: Despite improved survival and neurodevelopmental outcome, children with hypoplastic left heart syndrome and other forms of univentricular heart remain at increased risk for cognitive, motor, and other neurologic deficits.

Methods: We examined 27 children with hypoplastic left heart syndrome or other forms of univentricular heart at a median age of 5.70 years (range 4.99–7.51 years) and performed brain computed tomography or magnetic resonance imaging on 20. Possible risk factors were correlated with outcome.

Results: Mean full-scale IQ among patients with hypoplastic left heart syndrome was 86.7; that among patients with other forms of univentricular heart was 89.1, with both differing significantly from the expected population mean ($P = .015$ and $P = .029$, respectively). Cerebral palsy was diagnosed in 1 of 7 patients with hypoplastic left heart syndrome and 2 of 20 with other forms of univentricular heart. Brain computed tomography or magnetic resonance imaging revealed ischemic changes and infarcts or atrophy in 5 of 8 patients who had undergone the Norwood procedure and in 2 of 12 of those who had not ($P = .062$). Abnormal computed tomographic findings correlated significantly with lower full-scale IQ ($P = .045$) and verbal IQ ($P = .02$). In the multiple linear regression model, diuresis the third day after the primary operation and cardiopulmonary bypass time in the bidirectional Glenn operation correlated significantly with the primary outcome of full-scale IQ.

Conclusion: In children with univentricular heart, intellectual and neurologic deficits are common. Perioperative and postoperative risk factors related to the primary phase and bidirectional Glenn operation contribute to these deficits.

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Supported by grants from Arvo and Lea Ylppö foundation, Lastenlinna Foundation, and the Foundation for Pediatric Research, Finland.

Received for publication Sept 18, 2006; revisions received Nov 24, 2006; accepted for publication Dec 13, 2006.

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J Thorac Cardiovasc Surg 2007;133:1524-32

0022-5223/$32.00

doi:10.1016/j.jtcvs.2006.12.022

Because of increased survival rates, the focus in congenital heart surgery is increasingly on quality of life. Patients with univentricular heart (UVH) remain at increased risk for neurodevelopmental sequelae caused by several brain mechanisms.[1-3] Hypoplastic left heart syndrome (HLHS) is associated with the poorest outcome.[4-7] Because of developments in surgical methods and preoperative and postoperative care, recent results are better than those of the first reports, which noted that most patients with HLHS have mental retardation.[4,8] Reported mean full-scale IQ (FIQ) of patients with HLHS has ranged from 86 to 94, remaining clearly below the mean level of the normal population, unlike the 93 to 107 seen in patients with other forms of UVH. In most studies, prevalences of mental retardation have ranged from 10% to 18% for HLHS and from 0% to 8% for other forms of UVH.[5-7,9-11] Cerebral palsy was present in 17% of the children with HLHS examined by Mahle and colleagues,[10] and problems with both gross and fine motor development occurred in almost half. The same study reported a high

Abbreviations and Acronyms

BDG = bidirectional Glenn
CPB = cardiopulmonary bypass
CT = computed tomography
DHCA = deep hypothermic cardiac arrest
FIQ = full-scale IQ
HLHS = hypoplastic left heart syndrome
MRI = magnetic resonance imaging
PIQ = performance IQ
TCPC = total cavopulmonary connection
UVH = univentricular heart
VIQ = verbal IQ

incidence (69%) of attention deficit hyperactivity disorder among children with HLHS.

Patients and Methods

Patient Population

All children aged 5 to 7 years who had previously undergone surgery for UVH at the Hospital for Children and Adolescents of Helsinki University Central Hospital had the option of taking part in a neurodevelopmental and neuroradiologic evaluation between October 2002 and April 2004 as part of follow-up. The study protocol was approved by the ethics committee of our hospital.

During the visits, parents were interviewed regarding such topics as socioeconomic status,[12] occurrence of possible neurodevelopmental problems in the family, and use of any rehabilitation. Patient records were analyzed thoroughly concerning perinatal and preoperative, perioperative, and postoperative clinical factors and laboratory results: Apgar scores at 1, 5, and 10 minutes; weight, height, and head circumference at birth; preoperative use of alprostadil infusion and inotropic agents, age at diagnosis; and cardiac ejection fraction and ductal flow on echocardiography before the primary operation. Figures on durations of cardiopulmonary bypass (CPB), deep hypothermic cardiac arrest (DHCA), aortic crossclamp time, hypothermia, cooling, and rewarming; on level of hypothermia; and on occurrence of any perioperative or postoperative complications were collected for every operation. Preoperative heart failure was assessed according to the New York Pediatric Heart Failure Index.[13] The following postoperative data were collected: times spent on a respirator and in the intensive care unit (ICU), amount of diuresis in the first 3 postoperative days (milliliters per kilogram per hour), use of inotropic agents, and number of days of nitric oxide inhalation needed. The following laboratory values were collected during the periods of 0 to 6, 6 to 24, 24 to 48, and 48 to 72 postoperative hours: the lowest and highest arterial pH values, lowest venous oxyhemoglobin saturation, and the lowest and highest blood glucose levels. The normalization time of arterial pH was recorded. Follow-up echocardiographic data were analyzed for cardiac function (ejection fraction >55% regarded as normal), nonphysiologic atrioventricular valve regurgitation, recoarctation of the aorta, and other possible abnormal findings. Possible catheterization complications were recorded, as well as any clinical seizures or resuscitations during any phase. Cumulative CPB, DHCA, and aortic crossclamp times were recorded. All these data were analyzed for association with the primary outcome of FIQ in the univariate analysis.

Neurologic Examination

All children (n = 27) were examined according to a routine neurologic examination modified from Bax and Whitmore.[14] The gross motor section was complemented with tasks of ball kicking and throwing, squatting, walking on tiptoe and heels, jumping with both feet together, jumping jacks, and changing foot position back and forth. The fine motor section was complemented with tasks of bead lacing, cutting forms from paper with scissors, and finger-opposition test. The verbal and behavioral portions of the test were omitted, because these areas were more thoroughly examined with neuropsychologic testing. Hearing and vision had been screened in a well-child clinic. Thorough examination of the cranial nerves and assessment of muscle tone were added.

Imaging of the Brain

Either magnetic resonance imaging (MRI, Siemens Vision 1.5 T; Siemens, Erlangen, Germany) or computed tomographic scan (CT, GE Lightspeed 8; GE Medical Systems, Milwaukee, Wis) was performed on 20 children. CT was performed if MRI was impossible because of pacemaker wires or poor anesthesia tolerance. The images were analyzed by a single neuroradiologist (L.V.) blinded to cardiac diagnosis and developmental test results.

Cognitive Testing

The Wechsler Preschool and Primary Scale of Intelligence—Revised[15] served as a test of cognition. Three verbal and three performance subtests were administered, and verbal IQ (VIQ), performance IQ (PIQ), and FIQ were calculated according to the test manual. The IQ points of 1 moderately mentally handicapped child were counted as developmental age divided by calendar age times 100 because the tables did not score that low.

The neuropsychologic assessment was carried out with the Finnish Neuropsychologic Investigation of Children[16] (Table 4). Each subtest was scored and analyzed separately. The Visual Motor Integration Test—Revised[17] served as a specific measure of visuospatial functions.

Statistical Analysis

All data were analyzed with SPSS version 12.01 (SPSS Inc, Chicago, Ill). One-sample *t*-test was used to compare the mean IQ values with the average population mean of 100. Mann–Whitney tests allowed comparison of mean IQ values of different subgroups. IQ values were regarded as continuous values, as is usual in the medical literature. In the univariate risk factor analysis, the Pearson correlation coefficient served for normally distributed continuous variables and the Spearman correlation for categorical variables and continuous variables with skewed distribution to analyze correlation with the FIQ values, which were regarded as primary outcomes. Those continuous variables not normally distributed but with a significant Spearman correlation with FIQ were transformed with either log normal or exponent modification. If the transformed values were normally distributed, their Pearson correlation coefficient for FIQ was

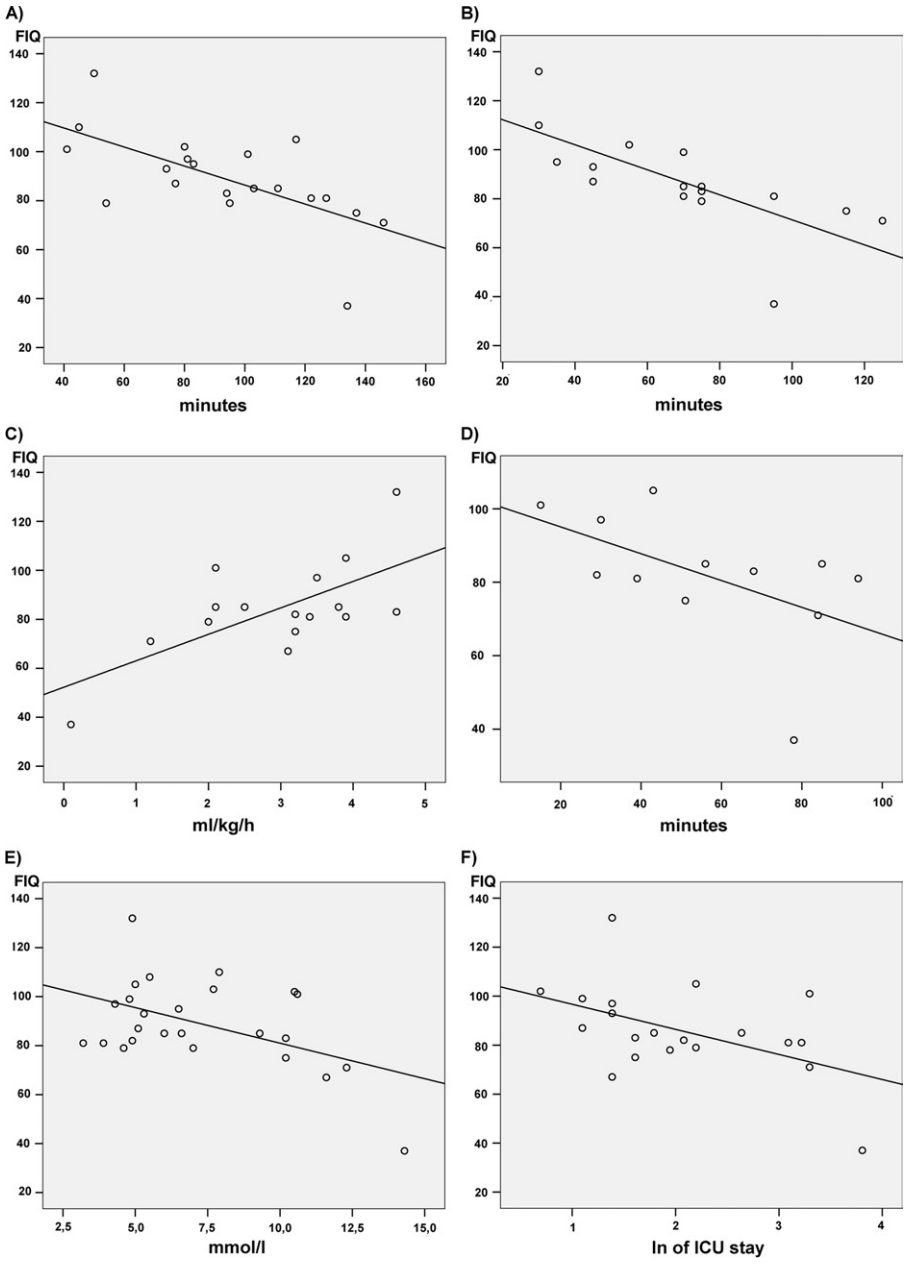

Figure 1. A, Correlations of full-scale IQ *(FIQ)* with perfusion time in Glenn operation (A), duration of hypothermia in Glenn operation (B), third postoperative day diuresis after primary operation (C), cumulative arrest time (D), highest blood glucose 0 to 6 hours after Glenn operation (E), and natural log of stay in intensive care unit *(ICU)* after primary operation (F).

calculated. Those binary and continuous factors for which association with FIQ approached significance at the level $P = .10$ were added to the linear regression model stepwise. To examine the association between binary factors, the Fisher exact test was used.

Results

Patient Characteristics

Of 32 eligible children, 27 underwent a neurologic examination and 26 took part in cognitive testing at the median age of 5.70 years (range 4.99-7.51 years). Two could not be reached, and the parents of 3 children refused. One of the latter group had already been followed up neurologically because of verbal dyspraxia and had received speech therapy. The others were not known to have any neurodevelopmental problems. All 27 patients examined had undergone total cavopulmonary connection (TCPC), and all 7 patients with HLHS and 2 with double-outlet right ventricle were operated on with the Norwood procedure during the neonatal period (Table 1). Norwood operations with DHCA and a modified Blalock–Taussig shunt were performed at our hospital from 1995 to 1999; since that time, we have used selective cerebral perfusion. Six patients underwent 1 additional operation, and 1 patient with

TABLE 1. Operations performed and median age

	Age (d)			
	Median	Range	Operation	N
Primary-phase operation	4.0	0–200	Norwood	9
			Blalock–Taussig shunt	7
			Damus–Kaye–Stansel plus shunt	1
			Aortic coarctation correction	1
			Pulmonary arterial banding	2
			TAPVD correction	2
			No operation	5
BDG operation	186.5	77–476		26
			No operation	1
TCPC operation	833.0	625–1917		27

TAPVD, Total anomalous pulmonary venous return; *BDG*, bidirectional Glenn; *TCPC*, total cavopulmonary connection.

HLHS underwent 3 additional operations before the study began. The median durations of DHCA and CPB are listed in Table 2. Twelve patients were subjected to DHCA, 4 for 1 period, 7 for 2 periods, and 1 for 3 periods.

Of the 20 children with other forms of UVH, 5 had double-outlet right ventricle, 5 had tricuspid atresia, 4 had double-inlet left ventricle, 2 had pulmonary atresia with intact ventricular septum, 3 had atrioventricular septal defect with isomerism, and 1 had ventricular septal defect with right ventricular hypoplasia. No child was known to have any specific genetic syndrome. Chromosome testing had been performed in 5 children with UVH and cardiac defect, abnormal facies, thymic hypoplasia, cleft palate, hypocalcemia; and chromosome 22q11 deletions (CATCH-22) diagnostics had been performed in 4 children (1 with HLHS), all with normal findings. One child had an anterior anus, 1 had aqueductal stenosis, 1 had Hirschsprung disease, and 1 had hemivertebra Th11. No other extracardiac malformations were found.

Neurologic Outcome

One patient in the UVH group had previously had diagnosed intellectual disability, and 3 had cerebral palsy, defined as disordered motor function as result of brain dysfunction evident in early infancy and characterized by changes in muscle tone, muscle weakness, involuntary movements, or ataxia. Two of these patients with cerebral palsy had mild hemiplegia, and 1 had spastic and ataxic features. The last-mentioned child, born prematurely at the 33rd gestational week, had hydrocephalus caused by aqueductal stenosis diagnosed at 9 months; there were no signs of intracerebral hemorrhage or ischemia on MRI, and the child underwent a ventriculoperitoneal shunt. All other chil-

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TABLE 2. Median support times

	Duration of CPB (min)			Duration of DHCA (min)		
	Median	Range	n	Median	Range	n
Primary-phase operation						
HLHS	106.0	96–264	7	40.0	30–47	7
UVH	105.0	95–146	5	29.0	15–58	5
Bidirectional Glenn shunt						
HLHS	117.0	81–137	7	21.0	16–23	3
UVH	81.5	41–146	14	32.0	27–56	3
Additional operation						
HLHS	140	94–186	2	—		
UVH	104	104	1	—		
TCPC						
HLHS	108	56–157	7	21	3–24	3
UVH	99.0	61–147	20	—		
Additional operation						
HLHS	114.0	90–319	3	—		
UVH	55	55	1	—		

CPB, Cardiopulmonary bypass; *DHCA*, deep hypothermic cardiac arrest; *HLHS*, hypoplastic left heart syndrome; *UVH*, other form of univentricular heart; *TCPC*, total cavopulmonary connection.

TABLE 3. Group Wechsler Preschool and Primary Scale of Intelligence—Revised scores for children with hypoplastic left heart syndrome and other forms of univentricular heart

	HLHS (n = 7)		Other UVH (n = 19)	
	Mean ± SD	*P* value	Mean ± SD	*P* value
Full-scale IQ	86.7 ± 10.5	.015	89.1 ± 20.0	.029
Verbal IQ	89.9 ± 12.5	.076	88.3 ± 18.6	.014
Performance IQ	89.6 ± 14.1	.098	94.2 ± 20.1	.222

One-sample *t* test served to compare group means with the population mean of 100. Values above 79 were considered normal. *HLHS,* Hypoplastic left heart syndrome; *UVH,* univentricular heart.

dren were term. One child with cerebral palsy was blind in one eye as a result of optic nerve atrophy. Cerebral palsy prevalences were 10.0% (2/20) in the UVH group and 14.3% (1/7) in the HLHS group. One patient with HLHS had a sensorineural hearing deficit and needed a hearing aid. Of all patients, 62.9% had been counseled by some therapist: 29.6% by a physiotherapist, 37.0% by a speech therapist, and 29.6% by an occupational therapist. One child received antiepileptic medication, and 3 others had received a postoperative anticonvulsant.

Mild hypotonia (62.9%) and difficulties in maintaining balance (76.0%) were common findings. Neurologic status was otherwise normal in 2 patients with HLHS (28.6%) and 10 with other forms of UVH (50.0%). Of the whole group, 34.6% had difficulties in gross motor function and 44.4% in fine motor function, the last-mentioned being more prevalent among children with HLHS (5/7) than among those with other forms of UVH (7/20). Three patients with other forms of UVH had mild abnormalities in cranial nerve function (squinting in 2 and ptosis in 1).

Cognitive Results

General intelligence. Mean FIQ, VIQ, and PIQ values (Table 3) did not significantly differ between the HLHS and UVH groups. As a prognostic factor, the Norwood operation seemed in this study population to be more important than the diagnosis itself, although it was not significant, with mean FIQs of 81.0 among those who had undergone the Norwood operation and 92.4 among those who had not (n = 17). The cognitive performance was at the level of intellectual disability in 2 children in the UVH group (FIQ <70). FIQ values of all patients in the HLHS group were above 70.

Unlike others, we found higher PIQ than VIQ scores in the whole group as well as in the UVH subgroup. For further analysis, we studied more carefully the results for 1 child with a hearing deficit (HLHS group), the 2 bilingual children (1 UVH group, 1 HLHS group), and 1 mainly Swedish-speaking child (UVH group). No significant difference emerged in PIQ and FIQ between these 4 children and the rest of the study population, but their mean VIQ was 75.0, compared with 91.2 for the other children ($P = .014$).

Neuropsychologic profile. Results of the Finnish Neuropsychologic Investigation of Children subtests and Visual Motor Integration Test—Revised for children with HLHS

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TABLE 4. Finnish Neuropsychologic Investigation of Children subtests and Visual Motor Integration Test—Revised (expected mean 10 ± 3) in hypoplastic left heart syndrome and other univentricular heart subgroups and the whole study population

	HLHS (n = 7)	Other UVH (n = 19)	All (n = 26)	*P* value*
Finnish Neuropsychologic Investigation of Children				
Attention and executive functions				
Auditory attention (part A)	6.0 ± 3.5	8.1 ± 3.4	7.5 ± 3.5	0.004
Visual attention	12.5 ± 2.6	11.8 ± 4.3	11.8 ± 3.8	0.042
Statue	8.6 ± 3.0	8.1 ± 3.4	8.3 ± 3.2	0.031
Language				
Phonologic segmentation	8.0 ± 1.4	8.5 ± 1.6	8.4 ± 1.6	<0.001
Comprehension of instruction	7.3 ± 2.7	8.6 ± 2.5	8.3 ± 2.5	0.003
Learning and memory				
Story memory	9.8 ± 3.9	10.4 ± 3.4	10.3 ± 3.5	0.715
Picture memory	6.8 ± 2.7	9.4 ± 3.2	8.8 ± 3.2	0.095
Sensorimotor functions				
Imitation of hand gesture	5.7 ± 4.6	6.6 ± 4.1	6.4 ± 4.2	0.001
Visuomotor accuracy	7.7 ± 2.5	8.9 ± 4.4	8.6 ± 3.9	0.116
Visuospatial functions				
Picture recognition	8.6 ± 1.5	11.3 ± 2.6	10.6 ± 2.6	0.291
Visual Motor Integration Test—Revised	6.8 ± 2.7	8.1 ± 3.1	7.7 ± 3.3	0.002

All values are mean ± SD. *HLHS,* Hypoplastic left heart syndrome; *UVH,* univentricular heart. **P* value reported for difference for the whole study population from the mean expected value of 10 (1-sample *t* test).

TABLE 5. Continuous and categorical variables found significantly correlated with full-scale IQ

	Pearson	Spearman	*P* value
Primary operation (n = 21)			
Postoperative laboratory values			
Lowest arterial blood pH 6–24 h	0.510		.018
Lowest arterial blood pH 48–72 h		−0.518	.019
Other postoperative factors			
Time spent on respirator		−0.491	.024
Time spent on respirator (natural log transform)	−0.503		.020
Time in intensive care unit		−0.441	.045
Time in intensive care unit (natural log transform)	−0.488		.025
Diuresis 48–72 h postoperatively	0.660		.005
Bidirectional Glenn shunt (n = 25)			
Duration of cardiopulmonary bypass (n = 20)	−0.652		.002
Aortic crossclamp time (n = 12)	−0.653		.011
Duration of hypothermia	−0.725		.001
Duration of cooling		−0.519	.040
Postoperative laboratory values			
Lowest venous blood oxyhemoglobin saturation	0.416		.043
Highest blood glucose level 0–6 h	−0.485		.014
Other postoperative factors			
Time spent in intensive care unit		−0.474	.017
No. of specific postoperative problems (0–3)		−0.483	.014
Duration of use of inotropic agents		−0.407	.044

Pearson correlation coefficient used for normally distributed continuous data; Spearman correlation coefficient for categorical data and for continuous data not normally distributed.

and those with other forms of UVH are presented in Table 4, along with the difference for the whole group relative to the expected population mean of 10. No significant differences existed between the HLHS and UVH groups on any of the subtests. A lower mean in the picture recognition test in children with HLHS approached significance ($P = .06$).

Signs of attention deficit hyperactivity disorder appeared in 57.1% of children with HLHS and in 52.6% of children with other forms of UVH. Occurrence of attention deficit hyperactivity disorder features correlated with neither any of the risk factors mentioned in Table 5 or the binary risk factors, nor was it associated with abnormal imaging findings.

Brain Imaging

Brain MRI or CT was available for 20 children and revealed old ischemic changes or infarcts, with cerebral atrophy in 1 patient. The main MRI abnormalities were mild ischemic changes, located predominantly in the watershed areas. Abnormal findings were more prevalent among patients who had undergone the Norwood procedure (5/8, 62.5%) than among other patients (2/12, 16.7%, $P = .062$). The difference was greater when only the CT findings were compared (3/4 vs 1/9, $P = .052$). Mean FIQ was significantly lower in the abnormal CT group than in the normal CT group (96.7 vs 68.5, $P = .045$). There was a similar difference in VIQ (98.1 vs 70.5, $P = .02$) but not PIQ.

Risk Factor Analysis

The results of those continuous and categorical factors that correlated significantly with the primary outcome FIQ at a level of $P = .05$ in the univariate analysis are presented in Table 5. Of the binary risk factor variables, only the occurrence of relevant atrioventricular valve regurgitation before the bidirectional Glenn (BDG) operation (FIQ 68.6 vs 93.2, $P = .015$) and postoperative complications afterward (FIQ 79.7 vs 98.8, $P = .008$) were significant. No variables concerning the TCPC operation were significantly correlated with FIQ values. Only 4 children had a fetal diagnosis, and their mean FIQ was similar to that of the remaining children. In multiple linear regression analysis, only the amount of diuresis on the third postoperative day after the primary-phase operation ($P = .008$) and the perfusion time in the BDG operation ($P = .019$) correlated significantly with FIQ.

Discussion

In our study, mean FIQ levels differed significantly from the population mean for the whole study population and for both HLHS and UVH subgroups, as did mean VIQ levels for the whole group and for the UVH subgroup. The mean FIQ value of our patients with HLHS was similar to values reported by other investigators, but at the lower end. The mean FIQ value in our UVH group was even lower than in earlier studies, but because of our relatively small study

group was greatly influenced by the results of a single moderately intellectually disabled child who had undergone resuscitation and sustained hypoxic-ischemic brain damage in connection with her Norwood operation. The fact that our study group included 2 bilingual children, 1 mainly Swedish-speaking child, and 1 child who used a hearing aid explains at least in part our lower VIQ than PIQ values, contrary to others' results.[5-7,10-11] These children's VIQ values also reduced the mean FIQ values to some extent. Surprisingly, socioeconomic status did not correlate significantly with FIQ, perhaps because of the limitations of our occupational scale and the presence of more potent factors that overwhelmed the effect of socioeconomic status. Unlike some earlier reports,[7,10] occurrence of clinically evident seizures during follow-up did not correlate significantly with FIQ, although a trend emerged toward lower FIQ in patients with clinically evident seizures.

The results for domain-specific neuropsychologic tests are for most part relative to the comparatively low overall intelligence level of the children with HLHS and other forms of UVH. In accordance with other studies,[18] however, certain neurocognitive deficits occurred in fine motor function and visuospatial skills. Deficiencies also appeared in visual memory and auditory attention, reflecting higher-order cognitive functioning. In adult studies, deficiencies in more complex cognitive functions have been associated with cerebral anoxia.[19] On the basis of these findings, we speculate that hypoxia may have more effect on the associative than on the primary areas.

Relative deficiencies were also evident in language functions, such as phonologic segmentation and comprehension of instructions. Difficulties in phonologic awareness have been associated with DHCA in children.[20]

One interesting finding in our study was a relationship between the neuroradiologic ischemic findings in CT and the FIQ and VIQ values. Because CT is less precise method than MRI, detecting only the more extensive lesions, it is logical that these lesions may have had more effect on general intelligence. In an earlier study, Goldberg and colleagues[7] found signs of previous ischemia or infarction on brain MRI in 13 of 29 (44.8%) children with HLHS or other forms of UVH. These signs were associated with a slightly lower mean FIQ, but the difference was not significant ($P = .21$). Neuroradiologic evidence of ischemic changes in patients with UVH has been described in few other studies. Kern and associates[9] found ischemic changes or infarcts in 3 of their 7 neuroradiologically examined patients with HLHS and cerebral atrophy in 1. Miller and colleagues[21] found abnormalities on brain MRI in 74% of 20 children after surgery with CPB or DHCA at a mean age of 66 months for various forms of congenital heart disease. In 1 case, the abnormality was a congenital structural anomaly, whereas in the others, there were ischemic changes. These findings suggested an association between abnormal results of brain MRI and abnormal results of neurologic examination, as well as lower IQ. Early postoperative—possibly reversible—periventricular leukomalacia changes have been reported in more than 50% of patients with congenital heart disease, especially in neonates.[22,23] The role of these early lesions in long-term functional outcome remains unknown, but these findings confirm that perioperative brain insult is common.

Our univariate risk factor analysis (Table 5) revealed that several factors related to the primary and BDG operations, but none related to the TCPC operation, correlated significantly with the primary outcome of FIQ. With respect to support times, the CPB time in the BDG operation correlated especially significantly with outcome in both univariate and multivariate analyses. The mechanisms by which CPB damages the brain are well known and include microembolic injury,[24] triggering of complex inflammatory microvasculopathy,[25] and disturbance of cerebral vascular autoregulation.[26] In our study population, DHCA was used in only 12 patients, among whom cumulative DHCA duration seemed to correlate clearly with outcome, although the correlation was not significant because of the small sample ($P = .07$). Some studies on neurodevelopmental outcome of patients with HLHS and other forms of UVH show a correlation between either use or duration of DHCA,[5-7,9,11] whereas others do not.[10] The significances of length of intensive care unit stay after the first and second operations and of postoperative complications after the BDG operation reflect the vulnerability in the acute postoperative period and probably capture several differing mechanisms of brain damage. The role of postoperative diuresis after the primary operation as a prognostic factor for neurodevelopmental outcome can be explained by the effect of postoperative cardiac output on vital organs such as the kidney and brain and serves as a simple indicator of hemodynamic state. In postoperative Norwood physiology, the balance between systemic and pulmonary circulation is of great importance, especially in the acute postoperative period. Normal blood pH is a prerequisite for this. According to our findings, arterial blood pH should be allowed to vary little in either direction from normal limits.

When the superior vena cava (SVC) is connected to the pulmonary artery in the BDG operation, the venous return from the brain changes as a result of the absence of the downstream pump (ie, right atrium and ventricle) and of the perfusion injury in the lungs. The longer the CPB time, the more extensive is the lung injury, leading to increased resistance of the pulmonary circulation and inhibition of the venous return from the brain. This may cause SVC syndrome—described in connection with BDG[27] and other pediatric cardiac surgery[28]—with possible neurologic manifestations and even a communicating hydrocephalus. Signs of SVC

syndrome were found in 3 patients after the BDG operation according to our retrospective analysis of patient records. Especially at times of lower blood pressure, the elevated SVC pressure and intracranial venous pressure may lead to low cerebral perfusion pressure and thus neurologic sequelae. We were unable retrospectively to trace SVC pressure changes reliably in our patients, but we speculate that this mechanism may at least partially explain the effect of BDG-related factors, such as CPB time, venous blood oxyhemoglobin saturation, and postoperative complications, on the neurodevelopmental outcome.

Evidence is growing regarding the deleterious effect of hyperglycemia on the prognosis of critically ill pediatric patients.[29] Among pediatric cardiac surgical patients in the prospective Boston circulatory arrest study, however, intraoperative and postoperative hyperglycemia was not associated with worse neurodevelopmental outcome.[30] Our findings, in contrast, suggest a correlation of higher blood glucose levels 0 to 6 hours after BDG operation with lower FIQ values, with a similar but not significant tendency 0 to 6 hours after the TCPC operation ($P = .058$).

The limitations of our study are its relatively small and heterogeneous study population, with various operations performed in the primary phase, and its retrospective nature. Neurologic events such as clinically detected seizures were only documented in medical records, and no routine postoperative electroencephalographic recording was performed to detect subclinical seizures. Thus it may be difficult to trace definitely the point and circumstances at which brain injury has occurred.

We conclude that intellectual and neurologic deficits are common findings in children with UVH. Neuroradiologic evidence of ischemia was frequent among patients who had undergone Norwood surgery and was associated with low FIQ and VIQ if only CT results were considered. On the basis of our risk factor analysis, we emphasize the role of acute postoperative hemodynamic stability after the primary and BDG operations in addition to the well-known neurodevelopmental risk factors related to support times and mechanisms.

We thank Professor Seppo Sarna for statistical advice and reviewing the statistical analysis of this study.

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