SURGERY FOR CONGENITAL HEART DISEASE

HYPOPLASTIC LEFT HEART SYNDROME: VALUING THE SURVIVAL

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Objective: To examine the survival, developmental status, quality of life, and direct medical costs of children with hypoplastic left heart syndrome who have undergone stage I, II, and III reconstructive surgery.

Methods: A total of 106 children underwent staged repair for classic hypoplastic left heart syndrome between February 1990 and March 1999 (stage I: 106; stage II: 49; stage III: 25; 4 converted to heart transplantation). Survival was analyzed by the Kaplan-Meier method. In a cross-sectional study, parents assessed quality of life by completing the Infant/Toddler Child Health Questionnaire or Child Health Questionnaire Parent Format-28; they assessed developmental progress by completing the Ages and Stages Questionnaire. The ratio-of-costs-to-charges method was used to derive hospital costs, and payments were used to capture physician time and wholesale pricing for outpatient medications.

Results: Institutional 1-year and 5-year actuarial survivals were 58% and 54%. Birth weight, the need for preoperative inotropic drugs, and surgical experience were predictors of survival. Norwood I patients achieved fewer developmental benchmarks than those who survived to subsequent stages. Child Health Questionnaire Parent Format-28 mean summary scores for physical and psychosocial health were 48.5 ± 6.3 and 42.8 ± 9.9 . The median inpatient costs for stage I, II, and III repairs were \$51,000, \$33,892, and \$52,183, respectively. Monthly outpatient and readmission costs were less than 10% of total costs.

Conclusion: A prospective, large-scale study of the comprehensive outcomes of staged repair and transplantation is needed. This study will need to address the longer-term developmental and quality-of-life outcomes, as well as the long-term cost effectiveness of these procedures. (*J Thorac Cardiovasc Surg* 2000;119:720-31)

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No one would deny the human or moral imperative to provide the best medical treatment for neonates with hypoplastic left heart syndrome (HLHS). The question, as usual, is how to define what is best. Before 1980, when no effective treatment was available, HLHS was uniformly fatal within the first month of life.^{1,2} The development of the Norwood procedure in 1980 and the first application of cardiac transplantation in 1986 have afforded new hope to the families of newborn infants with this lethal heart defect.³⁻⁷ Although the reconstructive approach requires a sequence of technically difficult procedures associated with a high operative mortality, actuarial 1-year and 5-year survivals of all treated patients (including those at high risk) approach 70% and 60% in experienced institutions.^{3,8} Actuarial 1-year

and 5-year survival curves for cardiac transplantation in infants with HLHS are 84% and 76% in experienced institutions.^{9,10} These survival figures, however, do not include the mortality of children on the waiting list, which according to the Pediatric Heart Transplantation Study Group is around 31%.¹¹

With these survival outcomes having been achieved, the focus of inquiry has expanded to include a broader set of issues. First, dimensions of health and well-being beyond survival have become increasingly important. Little is known, however, about the developmental status or quality of life of children with HLHS.^{12,13} In fact, our review of the literature disclosed only two articles concerning neurologic development and no articles concerning quality of life in patients with HLHS. Second, as with all new interventions, particularly the more dramatic and expensive approaches to saving lives, there are pressures to assess both their benefits and their costs. Here, too, little is known; our review of the literature disclosed only two economic analyses.^{14,15} This article, therefore, not only focuses on survival, but also examines the developmental status, quality-of-life, and cost outcomes associated with the staged repair of HLHS at our institution.

Methods

The overall study population includes all patients (n = 106) with HLHS and aortic atresia or near atresia who received surgical intervention at Columbia-Presbyterian Medical Center (CPMC) from February 1990 through March 1999. In view of the severe shortage of donor organs and the comparable survival outcomes of staged repairs and transplantation, our institution follows a staged repair protocol for all children who undergo surgery for the treatment of HLHS.

This study was initiated in January of 1998. All 106 patients were included in the analysis of survival. The outcome measures of quality of life and developmental status were obtained in a prospective fashion during the period from January 1998 through March 1999. Because patients were at various stages of surgical repair during this data collection period, the study design is cross-sectional and patients were not followed up longitudinally. The subgroup (n = 51) in which we measured developmental status and quality of life included all surviving patients older than 4 months of age for the Ages and Stages Questionnaire (ASQ) and 2 months of age for the Infant/Toddler Child Health Questionnaire (IT CHQ).

Our hospital financial information system underwent a fundamental change in 1993. The format of data collection was so different that we could not combine the data from the two time periods. The economic analysis, therefore, includes all patients operated on from January 1993 to January 1999 (stage I, 73; stage II, 36; stage III, 13). The research protocol was approved by the Institutional Review Board at CPMC.

We obtained informed consent from all participants completing the quality-of-life and developmental status assessments.

Surgical interventions

The Norwood procedure. The Norwood procedure was performed with deep hypothermia (18°C) and circulatory arrest. Up to April 1995, a patch of pulmonary allograft was used to reconstruct the native aorta to allow connection of the pulmonary trunk. After April 1995, no patch was used to augment the native aorta. Instead, the aortic isthmus, including the duct, was resected. The diminutive ascending aorta was transected at its junction with the innominate artery and the aortic arch was opened longitudinally. The descending aorta was mobilized distally, and a direct connection was then performed between the distal aortic arch and the descending aorta posteriorly. The pulmonary trunk was anastomosed directly to the reconstructed aorta. The ascending aorta, functioning as the main coronary artery, was then anastomosed to the right lateral sinus of the neo-aorta. A modified Blalock-Taussig shunt using a polytetrafluoroethylene graft* (3, 3.5, or 4 mm) between the base of the innominate artery and the right pulmonary artery was created in all patients. Three surgeons were operating at CPMC over the study period. Surgeon 1 performed 88 of the Norwood I procedures, surgeon 2 performed 12, and surgeon 3 performed 6 procedures.

Further procedures. Stage II procedures were either a bidirectional Glenn operation or a hemi-Fontan operation. In the majority of patients, enlargement of a central pulmonary artery stenosis (at the site of the previous duct) was performed during the same operation. The third stage of the repair completed the Fontan circulation by means of an intra-atrial polytetrafluoroethylene tunnel.

Developmental assessment

The ASQ (for children 4 to 48 months). The ASQ is designed to be completed by the infant or child's parent or primary caregiver. We analyzed 30 questions focusing on the infant or child's developmental repertoire. The 30 questions are equally divided into 5 domains: communication skills, gross motor function, fine motor function, problem solving, and personal-social skills. Questions relate to the child's ability to accomplish daily tasks, such as drawing circles, lining up blocks, and throwing balls. A questionnaire appropriate for the child's age can be administered at the following intervals: 4, 6, 8, 12, 16, 18, 20, 24, 30, 36, and 48 months of age.

Investigators administered the instruments between January 1998 and March 1999. Nine patients were interviewed after stage I, 10 patients after stage II, and 8 after stage III during this time period. Scores for each domain are compared with established norms. The normative ranges have been established in a reference population and vary by domain and age interval.¹⁶

The ASQ was designed as a screening instrument to identify those children who need extensive neurologic evaluation. The simplicity of its design facilitates the administration both

*Gore-Tex graft, registered trade name of W. L. Gore & Associates, Inc, Flagstaff, Ariz.

in person and by telephone and thus accommodates population studies. Its limitation is that it does not provide an in-depth picture of the neurologic deficits of the child, as would be provided by a trained neurologist. Nonetheless, it provides a "first cut" identification of those patients who are probably developmentally impaired. Rather than a multiple-day battery of neurologic testing, which would involve considerable time commitment of patients and their parents, we chose for ease of administration.^{17,18} The ASQ has been administered and validated in a variety of health and primary care settings, including children with heart defects and premature babies who spent their first days in the neonatal intensive care unit.¹⁹

Quality-of-life assessment. Quality-of-life assessment in children is notoriously difficult. Key aspects of quality of life, such as physical, emotional, and social functioning, rapidly evolve as the child ages.^{20,21} As a result, there is a need for age-adjusted normative values, which allow children with severe cardiac disease to be compared with healthy children of the same age. Moreover, in the case of young children, parents or primary caregivers need to be used as a proxy for direct patient-based responses. Despite these difficulties, a limited number of pediatric quality-of-life measures are currently being developed.²² To date, these measures have not yet been used in HLHS or validated in children with severe cardiovascular disease. We selected the Infant/Toddler Child Health Questionnaire (IT CHQ) and the Child Health Questionnaire PF-28 (CHQ PF-28). Despite the absence of validation in seriously ill children with cardiovascular disease, this instrument is easy to administer and has been used extensively in healthy populations and chronically ill patients. Parents provided information on the quality of life of their children by completing either the IT CHQ or the CHQ PF-28, depending on the child's age.

IT CHQ (for children between 2 months and 5 years). We analyzed the following 9 domains of the IT CHQ: physical abilities, growth and development, discomfort and bodily pain, temperament and moods, general behavior, behavioral interactions, general health perceptions, parental impact for emotion, and parental impact for time. The latter two items assess the health and well-being of the parent or family caregiver, such as their mental health, global health, the amount of anxiety or worry experienced, and limitations in time to meet personal needs. Each of the domains is uniformly scored on a 0 to 100 scale by the investigators, with 0 being the lowest and 100 the highest achievable scores. Nine patients were interviewed after stage I, 10 patients after stage II, and 8 patients after stage III between January 1998 and March 1999. The present study is the first application of this instrument to critically ill children, including those with life-threatening heart disease. Prior validation was conducted in a population of healthy children and children with otitis media (personal communication with Jeanne Landgraf). The results of this study will be used to further validate this instrument.

CHQ PF-28 (for children aged 5 years and older). The CHQ PF-28 addresses 14 health concepts (physical functioning, role/social-physical, general health perceptions, bodily pain, parental impact—time, parental impact—emotional, role/social emotional, role/social behavioral, self-esteem,

mental health, general behavior, family activities, family cohesion, and change in health) and provides a summary measure for the 2 broad domains of physical and psychosocial functioning. Each of the components is uniformly scored on a 0 to 100 scale. The CHQ has been extensively validated.²⁰

For both the ASQ and quality-of-life scales (CHQ and IT CHQ), a trained interviewer completed the questionnaire with the parent or caregiver. After stage III, quality of life was measured either by the IT CHQ or the CHQ dependent on the age of the child.

Cost measurement. Measuring health care costs is fraught with practical and conceptual difficulties. Although analyses have historically used the charges that providers bill as proxies for the costs of resources, charges may differ substantially from the resource costs of delivering care. In contrast to charges, payments relate to actual financial transactions, but these fixed reimbursements do not specify the actual amount of resources used among the various hospital services. Resource costs, the actual expenses paid to obtain the resources used to deliver care, are the most desirable conceptually, but standard methods are still under development. The ratio-of-cost-to-charges (RCC) method comes closest to approximating actual resource costs. This RCC is calculated by each hospital in the following manner: at the end of the year, a hospital compares its actual expenditures (costs) per resource category (eg, operating room, diagnostic tests, or bed days) to its charges.²³ The hospital develops an RCC for each resource category to reflect these actual expenditures. In light of this, we use the RCC method as the primary approach for measuring hospital cost, and we use payments for other providers' expenses. We have taken the "health care budget" perspective in this analysis, calculating the direct costs of all medical services associated with providing health care to patients with HLHS who are managed surgically, regardless of who bears the cost. This excludes the direct costs borne out of pocket by the families (such as travel and loss of productivity because of caretaking time). Indirect costs (ie, loss of productivity of patients) are not germane to this pediatric population.

We audited the hospital patient management system and gathered the line-item bills for hospital services and supplies for all patients with HLHS being analyzed. For each patient we captured the billable item, the date of the charge, and the amount of the charge. Inpatient routine charges included both intensive care unit and regular floor days. For ancillary services billed, each item was categorized into a departmental category (eg, chemistry, radiology) and each department category was then further categorized into use categories (eg, diagnostic tests). These categories included operating room, diagnostics, laboratory, blood products, drugs, therapeutic procedures, and rehabilitation. For each patient, we summed the total charges in each departmental category that were incurred in the period ranging from the day of hospitalization to the discharge date. For each departmental category, we multiplied the total charges by the corresponding RCC submitted by CPMC in its Health Care Financing Administration yearly institutional cost report. Another important component of the cost (to society) of initial hospitalization is the cost of

Fig 1. Flow chart.

the time spent and services provided by physicians. The difficulty with assessing such costs is that professional charges do not necessarily correspond to the actual cost of the services. The best solution to this problem is to report the actual financial expenditure: the payments made by third-party health care payers. Thus the actual dollars spent are captured. We used the departmental financial reimbursement records to account for all payments made to physicians, including cardiothoracic surgeons, anesthesiologists, cardiologists, and neonatologists.

Outpatient services include physician care, diagnostic tests, and medications related to cardiovascular care performed at CPMC; we imputed the number of physician visits, diagnostic tests, and use of out-of-hospital medications from a standard outpatient protocol used in our institution. We valued the costs of physicians' services by examining the reimbursements they received. All diagnostic tests were performed in the hospital and the associated charges were, again, converted to costs using hospital RCCs. We imputed the number of outpatient physician visits from the outpatient protocol. Outpatient diagnostic tests came from the clinical information system. Use of out-of-hospital medications was derived from outpatient medical records. Outpatient medications were based on the average wholesale price for each drug listed in the *Drug Topics Red Book*.²⁴ We identified all readmissions from the clinical information system and used the RCC method to assess their cost.

Baseline factors analyzed. The following potential predictors of outcome were considered: severely obstructed atrial septal defect, age at stage I operation, sex, gestational age, prematurity (<35 weeks), low birth weight (<2.5 kg), chromosomal abnormalities, Apgar score, preoperative ventilatory support, preoperative cardiac support with inotropic drugs (excluding dopamine, $2 \mu\text{g} \cdot \text{kg}^{-1} \cdot \text{min}$, for renal perfusion), surgeon, circulatory arrest time, and major extracardiac abnormalities.

Statistical analysis. The survival data were first examined univariately by means of standard contingency tables and the Kaplan-Meier product-limit estimate. Any variable with a P value less than .25 was explored as a potential risk factor in a multivariable analysis. The Cox proportional hazards model was used for the multivariable survival analysis of time to

death. Time zero was the date of the Norwood stage I repair. Four patients undergoing transplantation were censored at the date of transplantation. The model was checked for correlations to prevent multiple collinearity. The proportional hazards assumption was satisfied. We calculated the relative risk of death along with 95% confidence intervals (CIs).

Quality-of-life data were analyzed by the nonparametric analog to the analysis of variance (Kruskal-Wallis test) for the CHQ, and ASQ data were analyzed by the Fisher exact test for dichotomous outcomes. For the IT CHQ, we used the Dunnett multiple comparison procedure to compare group means to the reference populations. Because raw data were not available for the reference populations, we used an algorithm to compare the group means by calculating the test statistic L_r .²⁵ To determine significance, we then compared these values to a table of critical values for the Dunnett criterion using an independently estimated variance (see appendix).²⁶ A multiple, linear regression analysis was performed to examine which risk factors determined costs. All data were analyzed with SAS system software (SAS, Inc, Cary, NC). The results of all statistical analyses are presented without correction for multiple testing.

Results

Patient population. One hundred one of the 106 patients had classic HLHS, with aortic atresia in 91 patients and echocardiographic evidence of some antegrade flow from a diminutive left ventricle into the hypoplastic ascending aorta in 10 patients. In 5 patients, the ventricular anatomy was more complex. Two of these patients had aortic atresia, and ventricular contribution to antegrade flow in the ascending aorta was minimal in the other 3 patients. Patients undergoing the Norwood procedure for lesions with HLHS but with more significant antegrade ascending aortic flow were excluded from this study.

The median age at stage I surgery was 6 days (range 0-57 days), and the median weight was 3252 g (range 1160-3330 g). Seventy-two patients (68%) were boys and 34 (32%) were girls. The median age for the stage

Fig 2. Survival curve of the entire cohort (n = 106). The *squares* represent actual events, positioned along the horizontal axis at the time of the event and by the Kaplan-Meier method along the vertical axis. The *vertical bars* represent 95% confidence intervals. *Numbers in parentheses* represent patients remaining.

Table I. Cox proportional hazards model

Variable	Parameter estimate	SE	P > (χ^2)	Risk ratio	Lower 95% CL*	Upper 95% CL
Surgeon*	1.609965	0.34513	.0001	5.003	2.543	9.839
Weight	-0.000597	0.0002301	.0095	1.348†	1.076	1.689
Dopamine	0.898473	0.31278	.004	2.456	1.33	4.534

SE, Standard error; CL, confidence limit.

*Operating surgeon was other than surgeon number 1.

†For each 500-g decrease in birth weight.

II procedure was 9 months (range 6-18 months). Completion of the Fontan (stage III) circulation was undertaken at a median age of 34 months (range 1.5-5.9 years).

Survival. Fig 1 depicts the flow of patients through the staged repair process. One hundred six patients underwent the stage I Norwood procedure. The median circulatory arrest time was 51 minutes (25th percentile, 45 minutes; 75th percentile, 60 minutes). Seventy-two children (68%) survived the hospitalization. Four patients required conversion to cardiac transplantation, with 1 early postoperative death, and 12 patients are presently alive and await a stage II procedure. Forty-nine patients underwent stage II repair (bidirectional Glenn operation, 45 patients; hemi-Fontan operation, 4 patients). There were 2 early postoperative deaths, and 47 patients (96%) were discharged from the hospital. Of this group, 21 patients await a stage III procedure

and 26 children underwent stage III repair with 1 early postoperative death (96% survived hospitalization).

Fig 2 contains a Kaplan-Meier plot of overall survival for the entire group of 106 patients (the 4 heart transplant recipients were censored at the point of transplantation). The 1-year, 2-year, and 5-year survivals were 58% (95% CI: 48.4%, 67.8%), 57% (95% CI: 47.1%, 66.5%), and 54% (95% CI: 43.9%, 64.8%), respectively. Nearly all of the deaths (94%) occurred before the second stage of the repair. The 1-year survival after stage II repair was 94% (95% CI: 85.0%, 100%), and the 1-year survival after stage III repair was 96% (95% CI: 88.8%, 100%).

The multivariable model found significance for several factors (Table I). For every 500-g decrease in birth weight, the relative risk of dying was 1.35. The need for preoperative pressors increased the risk of dying by 2.5. Patients treated by surgeons 2 and 3 had

Fig 3. Survival curve stratified by surgeon. The *squares* and *triangles* represent actual events, positioned along the horizontal axis at the time of the event and by the Kaplan-Meier method along the vertical axis. The *vertical bars* represent 95% confidence intervals. *Numbers in parentheses* represent patients remaining.

Table II. *Ages and Stages Questionnaire (ASQ)*

Domain	Stage I (n = 9)	Stage II (n = 10)	Stage III (n = 8)	Fisher exact test (stage I vs II and III)
Communication	44%	80%	88%	$P = .07$
Gross motor	44%	30%	75%	$P = 1.0$
Fine motor	56%	60%	88%	$P = .4$
Problem solving	67%	70%	63%	$P = 1.0$
Personal and social	67%	80%	88%	$P = .2$
Meeting benchmarks in all domains	0%	40%	50%	$P = .06$

an increased mortality (relative risk: 3.9; 95% CI: 1.9, 7.8; Fig 3). The 1-year, 2-year, and 5-year survivals of patients operated on by the high-volume surgeon were 66% (95% CI: 55.7%, 75.8%), 64% (95% CI: 53.4%, 74.4%), and 60% (95% CI: 48.7%, 72.3%), respectively.

Developmental status. Twenty-seven of the 37 eligible parents (73%) completed the ASQ for their children. We were unable to locate 6 families, 2 families did not speak English, and 2 declined participation. Table II depicts the results of the ASQ testing by surgical stage. The first 5 rows show the percentage of patients without delayed development for the specified domain, and the 6th row shows the percentage of patients without any developmental delay in any domain. The last column shows the P values for the results in early (I) and late-stage (II and III) repair; the group of patients with stage I repair had more developmental delays than the groups

having stage II or III repair. None of the potential predictive factors correlated with developmental status, except circulatory arrest. Patients with higher circulatory arrest times are less likely to achieve normal problem-solving scores ($P < .06$).

Quality of life

IT CHQ. The ASQ and the IT CHQ are administered together. Seventy-three percent of parents completed the IT CHQ, and the reasons for noncompletion were the same as mentioned earlier. Table III depicts the scores for the various domains, as well as the mean and standard deviation for a healthy population of children from Australia.²² After stage I repair, HLHS children were not significantly different from the normal population. After stage II, however, HLHS children scored significantly worse on physical ability scale, on growth and development, on discomfort and pain, on temperament and mood scale, on the general health perception

Table III. Infant/Toddler Childhood Health Questionnaire (IT CHQ)

	Age (y)	PA	GD	BP	TM	GB	BE	GH	PE	PT
Stage I										
Mean (n = 8)	0.8	92.1	92.2	82.3	81.1	82.9	73.3	47.5	80.4	86.9
SD	0.5	7.5	6.7	12.9	8.6	15.8	10.8	13.8	11.9	18.3
Stage II										
Mean (n = 11)	1.9	75.5 [†]	76.8 [†]	62.9 [†]	69.8 [†]	77.2	68.5	42.0 [†]	78.9 [†]	77.9
SD	1.0	22.9	17.1	21.5	14.5	16.5	10.5	16.1	15.1	28.5
Stage III										
Mean (n = 8)	3.8	90.4	80.6	85.4 [‡]	80.4	76.3	73.3	54.2 [†]	83.0	85.7
SD	1.0	10.9	16.1	20.3	13.6	16.1	11.2	24.5	18.8	19.6
Normal*										
Mean (n = 958)		98.3	93.2	79.1	82.0	74.5	79.0	76.7	91.8	93.2
SD		28.9	16.4	5.0	12.2	12.0	14.6	8.5	12.6	18.6

PA, Physical abilities scale; GD, growth and development item; BP, discomfort and pain scale; TM, temperament and moods scale; GB, behavior overall scale; BE, getting along with others scale; GH, general health perceptions scale; PE, parental impact—emotional scale; PT, parental impact—time scale.

*Based on a normal population (see text).

[†]Significantly lower than the reference normal population.

[‡]Significantly higher than reference normal population.

Table IV. Childhood Health Questionnaire (CHQ)

	Age (y)	PF	RP	REB*	BP	BE*	MH	SE*	GH*	PE*	PT	FA*	FC	PHS	PSS*
HLHS (n = 11)															
Mean	7.3	85.9	93.9	66.7	90.9	59.3	72.0	74.2	42.6	63.6	78.8	64.8	64.1	48.5	42.8
SD	0.9	19.9	20.1	29.8	10.4	19.7	16.8	14.7	19.1	18.1	15.1	30.0	16.1	6.3	9.9
Normal population [†] (n = 83)															
	5-7														
Mean		96.7	93.2	94.5	84.4	71.5	80.3	87.3	96.3	81.2	88.8	89.2	76.9	53.7	52.1
SD		16.7	22.2	17.6	16.7	14.9	15.1	13.7	21.4	1.9	20.2	22.2	21.4	10.9	7.9

PF, Physical functioning scale; RP, role/social limitations due to physical health scale; REB, role/social limitations due to emotional or behavioral difficulty scale; BP, bodily pain scale; BE, behavior scale; MH, mental health scale; SE, self-esteem scale; GH, global health item scale; PE, parental impact—emotional scale; PT, parental impact—time scale; FA, family activities scale; FC, family cohesion item; PHS, physical summary score; PSS, psychosocial summary score.

*Subscales in which HLHS cohort differed significantly from normal population ($P < .05$).

[†]Based on a normal population (see text).

scale, and on the emotional parental impact scale. After stage III, HLHS patients were significantly better on the discomfort and pain scale than the reference population. They were significantly worse on only 1 scale: the general health perception scale. For all other scales, there was no significant difference from the reference population.

We correlated each of the baseline factors with the domains and found no single factor, or combination of factors, predictive of the outcomes in each of these domains except circulatory arrest time. Patients with lower circulatory arrest time (≤ 40 minutes) performed significantly better in the following domains: growth and development ($P < .02$), discomfort and pain ($P < .01$), temperament and moods ($P < .03$), and behavior overall ($P < .05$).

CHQ. Eleven of the 14 eligible parents (79%) completed the CHQ. The children of all of these parents had completed the HLHS staged repair process. We were unable to locate 3 families. Table IV shows the

scores for the various domains and 2 summary scores. The mean observed physical summary measure score was 48.5 ± 6.3 and the mean observed psychosocial summary measure score was 42.8 ± 9.9 . When compared with a normal population of 598 children aged 5 to 7 years* from Australia,²⁰ HLHS patients scored significantly lower in the following subscales: (1) role/social limitations due to emotional or behavioral difficulty; (2) behavioral; (3) self-esteem; (4) global health item; (5) parental impact—emotional; (6) family activities; and (7) psychosocial summary score. However, on the following subscales HLHS patients did not score significantly differently from the normal reference population: (1) physical function; (2) role/social limitations due to physical health; (3) bodily pain; (4) mental health; (5) parental impact—time;

*This reference population was, on average, slightly younger than our study group but was the closest group in age for which data were available.

Table V. Hospitalization costs for entire cohort

Resource category	Stage I procedure	Stage II procedure	Stage III procedure
	Median (25th percentile, 75th percentile) (n = 73)	Median (25th percentile, 75th percentile) (n = 36)	Median (25th percentile, 75th percentile) (n = 13)
Inpatient bed days	\$18,550 (9,275, 31,521)	\$13,086 (\$8,536, \$18,113)	\$15,232 (\$12,482, \$20,720)
Operating room	\$10,149 (\$9,031, \$15,715)	\$7,170 (\$2,834, \$16,359)	\$14,000 (\$8,843, \$2,659)
Diagnostics	\$2,864 (\$1,520, \$3,887)	\$1,098 (\$827, \$2,418)	\$1,345 (\$924, \$2,825)
Laboratory	\$2,055 (\$1,477, \$3,183)	\$1,059 (\$715, \$1,830)	\$1,384 (\$951, \$2,637)
Blood products	\$802 (\$712, \$1,072)	\$382 (\$244, \$728)	\$264 (\$256, \$946)
Drugs and supplies	\$4,310 (\$1,002, \$10,263)	\$743 (\$234, \$1,267)	\$1,603 (\$406, \$2,938)
Rehabilitation	\$750 (\$12, \$1,614)	\$202 (\$0, \$699)	\$28 (\$0, \$802)
Emergency department	\$0 (\$0, \$0)	\$0 (\$0, \$0)	\$0 (\$0, \$0)
Professional payments	\$5,063 (\$3,050, \$12,015)	\$6,711 (\$875, \$13,782)	\$17,147 (\$4,442, \$23,050)
Cost per patient	\$51,100 (\$41,044, \$70,374)	\$33,892 (\$24,527, \$52,943)	\$52,183 (\$47,781, \$69,836)

Table VI. Outpatient and readmission costs for entire cohort

	Stage I procedure	Stage II procedure	Stage III procedure
No. of readmissions	51 (29 patients)	15 (12 patients)	4 (1 patients)
Median cost of readmissions per month	\$38	\$24	\$63
25th and 75th percentiles	\$19, \$41	\$19, \$30	\$25, \$42
Monthly professional payments (per protocol)	\$155	\$27	\$38
Monthly cost laboratory tests and drugs (per protocol)	\$794	\$173	\$175
Median cost per patient per month (25th and 75% percentiles)	\$927 (\$908, \$930)	\$224 (\$219, \$300)	\$255 (\$238, \$276)

(6) family cohesion item; and (7) physical summary score.

Gestational age ($P < .01$, $R^2 = 0.8690$) and circulatory arrest time ($P < .01$) were predictive of the physical health summary score, with the former being positively correlated and the latter being negatively correlated. Neither gestational age nor circulatory arrest time correlated with the psychosocial summary score.

Cost. The median cost of the initial stage I-related hospitalization was \$51,100 (25th percentile, \$41,044; 75th percentile, \$70,374). The median costs of the hospitalizations for stage II and III repairs were \$33,892 (25th percentile, \$24,527; 75th percentile, \$52,943) and \$52,183 (25th percentile, \$47,781; 75th percentile, \$69,836), respectively. The cost breakdown by resource use categories is depicted in Table V.

Moving beyond hospitalization for the staged procedures, we examined outpatient costs and readmissions (Table VI). There were a total of 51 readmissions for 29 patients who had completed stage I repair, 15 readmissions for 12 patients who had completed stage II repair, and 4 readmissions for 1 patient after the stage III procedure (see Table VII for the breakdown of reasons for readmission). The median monthly outpatient and read-

Table VII. Readmissions by cause

Reason for readmission	Total No. = 70
Diagnostic catheterization	43
Upper respiratory tract infection	9
Viral syndrome	9
Pneumococcal septicemia	1
Pneumococcal pneumonia	1
Staphylococcal pneumonia/streptococcal septicemia	1
Urinary tract infection	1
Acute pericarditis	1
Pleural effusion	1
Hypovolemia	1
Gastritis with hemorrhage	1
Circumcision	1

mission cost of treating an HLHS patient was \$927 after stage I, \$224 after stage II, and \$255 after stage III. Baseline factors did not correlate with total costs.

Discussion

This article has begun to explore the more comprehensive outcomes of the staged repair approach for HLHS in our institution. The vast majority of these

patients had the extreme form of HLHS with aortic atresia. Despite the prevalence of this anatomic characteristic, our institutional 1-year and 5-year survivals were 58% and 54%. These levels are comparable with those of other centers that are dedicated to the staged repair of HLHS⁸ and are equivalent to expectations for cardiac transplantation given the scarcity of donor hearts. A further analysis of our survival by means of multivariable techniques delineated a few preoperative factors, including birth weight, surgical experience, and hemodynamic instability, which had a strong correlation with survival. Although much remains to be learned about the treatment of HLHS from rigorous survival studies, the primary focus for this article is to begin characterizing the quality of life and developmental progress achieved by patients undergoing the staged repair. As such, we present our survival experience to offer a context for interpreting the other outcomes.

Developmental status, as measured by the ASQ, was substantially delayed in our cohort. None of the patients assessed after stage I surgery met all of the benchmarks that are characteristic of normal development. Communication and gross motor skills were the areas in which fewest patients met the cutoffs for normal development. However, in this cross-sectional study, 40% of patients having completed stage II and 50% of patients having completed stage III showed normal developmental status on the ASQ.

There are, as mentioned, very few studies on neurodevelopmental status in HLHS patients, and these studies use different instruments, a fact which does not facilitate making comparisons. With that caveat in mind, we reviewed the literature on neurodevelopment in patients with HLHS in the context of our patients. Reporting on 7 patients after stage III surgery or modified Fontan repair, Rogers and colleagues¹² noted that the cognitive scores of 6 patients were in the mental retardation range (3 severely to profoundly retarded and 3 moderately retarded), based on a battery of cognitive assessment instruments (Clinical Adaptive Test–Clinical Linguistic Auditory Milestone Scale, Bayley Scales of Infant Development, and McCarthy Scales of Children's Abilities). Keeping in mind the differences in evaluative procedures, the cognitive development that we observed after stage III surgery was only moderately impaired. Communication norms were achieved in 88% of the 8 patients who completed stage III, and problem solving norms were completed in 63%. In our study, circulatory arrest times correlated negatively with problem-solving scores. This result corroborates earlier findings from this institution that pro-

longed circulatory arrest correlates negatively with IQ scores.¹³ Rogers and associates¹² found delayed motor function development in 3 of 7 patients, and 2 others had cerebral palsy. By comparison, we observed normal gross motor function in 75% of our patients after stage III and normal fine motor function in 88%. It is important to keep in mind that delays in developmental status in these very young children, who have not yet celebrated their 4th birthday, do not mean that they will not catch up to their peers over time. On the other hand, more subtle developmental delays may appear over time. These outstanding questions make the case for the need for long-term analysis of neurologic development.

Delayed developmental status does not necessarily indicate poor quality of life. For the younger HLHS children, parents' perception of quality of life after stage I was not significantly different from that in a reference population. This perception may reflect the modest expectation held by most parents for children in the first year of life. After stage II, however, HLHS children scored significantly lower in several domains than the reference population. These included their physical ability, growth and development, discomfort and pain, temperament and mood, general health perception, and impact on parents' emotions. After stage III, by contrast, only general health perceptions were significantly lower than those of the reference population, and patients did better on the discomfort and pain scale than the reference population. In general, it appears that quality of life of children after stage III repair is better than the quality of life of children after stage II repair.

Quality of life in older children, as measured by their summary psychosocial score, lags behind that of the reference population of healthy children. However, their physical summary score is not significantly different from that of the reference population. As was the case for younger children, circulatory arrest time was a factor in their quality of life.

This article provides a comprehensive look at the economics of the staged repair process. The median cost per patient of all 3 staged repair hospitalizations is \$137,175. This constitutes more than 90% of all the direct medical costs of caring for these patients (ie, readmissions and outpatient services and drugs amount to 8% of the costs of care for these patients). It is tempting to compare this figure with that of cardiac transplantation. Our review of the literature disclosed 2 economic analyses. One study, using the discharge database of the University Hospital Consortium, compared hospital charges of the Norwood procedure versus cardiac transplantation. In

636 patients admitted to 40 institutions between 1989 and 1993, median charges were \$57,418 for the Norwood procedure and \$126,695 for transplantation.²⁷ Another study compared selected hospital, physician, and outpatient charges between the Fontan operation and cardiac transplantation.²⁸ The total charges (surgery plus yearly follow-up) for the Fontan procedure were \$29,730 compared with \$96,475 for cardiac transplantation ($P < .001$).

These studies did not address actual resource use because they used charges, which may differ substantially from the actual costs of medical services. Moreover, these studies do not provide a comprehensive look at the costs of all stages of the reconstructive process. At the same time, the assessment of transplantation costs in these comparisons seriously underestimates the costs associated with long-term immunosuppression, rehospitalizations, and diagnostic testing. Moreover, these studies typically do not include the cost of caring for children who are being supported while awaiting transplantation, which would include temporizing procedures.

In summary, the lack of long-term data on survival, developmental status, quality of life, and costs has greatly contributed to the controversy and uncertainty regarding optimal treatment strategies. This article offers a "first cut" estimate of the quality of life and true costs associated with the staged repair of HLHS. Our findings corroborate that these patients have developmental setbacks that may be related in part to circulatory compromise during the procedures. In the area of quality of life, our patients achieve levels that are below standard normal populations, but the group of patients after stage III repair appears to be doing better than the group after stage II. Although expensive, the total cost of the staged repair is easily within the range of procedures currently funded by industrialized nations for life-threatening conditions. We believe that if the comprehensive approach to cost assessment taken here is used to cost cardiac transplantation, the total cost of transplantation will be considerably higher than that of staged repair.

At the same time, the research methods used here have limitations. We collected quality-of-life data during a 14-month period and were not able to interview the same patient at different stages of treatment. Thus we do not have a longitudinal data set to adequately explore time trends. Moreover, the small size of the resulting data set restricts more in-depth statistical analysis. Second, due to the absence of well-validated instruments for measuring quality of life in younger pediatric patients, we opted to use a quality-of-life questionnaire that had never been tested in a critically

ill patient population. Our study data will be used by the developer of the CHQ to validate its use in critically ill patients. Third, we captured the direct medical costs associated with treatment but did not look at the direct medical costs borne out of pocket by the families of these patients (specifically, the time out of work due to caregiving). Ultimately, if we want to capture the full economic burden of cardiac disease on society, these costs should be included.

What do the results of our study suggest for further research in this area? There needs to be a prospective, large-scale, possibly multicenter study of the comprehensive outcomes of staged repair and transplantation. This study will need to address the longer-term developmental and quality-of-life outcomes, as well as the long-term cost-effectiveness of these procedures. Insights into these dimensions of health and economic outcomes will be critical for all decision-makers facing the choice of how to treat a given patient with HLHS.

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Discussion

Dr John L. Myers (Hershey, Pa). The authors have taken on a monumental task, to tease out the developmental outcome, quality of life, and hospital costs in this group of patients. We are all aware of the basic principles of the Norwood operation, and all of us would believe that a perfect repair will result in a good outcome. However, seemingly minor technical problems can result in serious problems that may present themselves

acutely in the operating room, during the postoperative course, or later in follow-up. Neurologic injury and residual cardiovascular pathophysiology can result in developmental abnormalities and a decrease in the quality of life. The etiology of this neurologic morbidity is multifactorial and includes preoperative, intraoperative, and postoperative issues.

As has previously been stated, HLHS is an incurable form of congenital heart disease. Until Norwood's contribution nearly 20 years ago, this defect was uniformly fatal. All things considered, most programs with a dedicated interest in neonatal congenital heart surgery have achieved success with the Norwood operation. Many of us have cared for children who have received the Norwood-Fontan palliation protocol and are now entering their second decade, attending school, participating in activities, and enjoying life. There are certainly many children with other forms of serious congenital heart disease who are less fortunate in terms of their quality of life. Despite the abnormalities and developmental status that the authors are reporting, I believe that we are achieving good results, but we still have room for improvement.

My first question relates to developmental outcome. Have you applied your developmental outcome analysis and quality-of-life assessment studies in other children with other types of congenital heart disease?

Also, since other groups have reported that socioeconomic status seems to make a difference in developmental outcome, could you describe the socioeconomic mix of your patient group?

Your developmental assessments were performed in 23 of 37 eligible patients; however, 46 patients are alive. Thus only half of the survivors were actually assessed for developmental status. How might this affect the validity of your results?

You identified 4 risk factors—low-volume surgeon, preoperative pressors, nonwhite race, and low birth weight—as risk factors for survival. I can understand all of them except nonwhite race. Do you have an explanation for that?

My final comment and question relate to the summaries of the hospitalization costs that are shown in Tables V and VI. Approximately \$175,000 is the cost for hospitalization for the entire group averaged per patient. For those patients who are alive after all 3 procedures, the average cost is \$140,000. Therefore, the obvious way to reduce cost and improve survival is to reduce morbidity and develop strategies to reduce length of stay, particularly intensive care unit and hospital stay, as you have pointed out. In your detailed analysis of this group of patients and their hospital course, could you speculate on how you might reduce morbidity, mortality, and particularly hospital cost?

Dr Quaegebeur. This is an excellent question and points out one of the limitations in the study. These tests are screening tests; they are not extensive clinical tests. We have had previous experience using clinical assessment of patients, and it was very hard to get the cooperation from the patients. This is a first attempt. These tests are used by a trained interviewer with the parents. They have been used in critically ill patients, in trauma patients in the pediatric population in the neonatal intensive care unit, but not specifically for patients with congenital heart disease. We have been collaborating

Appendix Table I. Test statistics (L_i) for the Dunnett multiple comparisons procedure used in analyzing the IT CHQ data (Table III), which were then compared to the critical value of 2.51

Stage	N	L1	L2	L3	L4	
1	8	-0.60934	-0.17221	1.56363	-0.20755	
2	11	-2.62351	-3.30654	-9.26783	-3.29388	
3	8	-0.77642	-2.16981	3.07840	-0.36897	
		L5	L6	L7	L8	L9
		1.95224	-1.10582	-9.2673	-2.53275	-0.19089
		0.73468	-2.38493	-12.8936	-3.35548	-0.54276
		0.41834	-1.10582	-7.1409	-1.95510	-0.22725

with the developer of these tests, and I believe that she will use these results to validate them for the screening methods.

I do not have the answer for your second question about the socioeconomic impact. This relates also to the fact that non-white race came out as an independent risk factor. We certainly are going to further investigate that question, but it is not an easy question to answer.

The patients became eligible for these tests 2 or 3 months after the operation. Therefore a number of patients fell out for that reason. Ten families could not be traced at all, despite all of our efforts, and 2 families refused collaboration in this study.

With the present data set we were unable to find a specific risk factor influencing the costs. However, the patients who completed all 3 stages had lower initial costs. The inference from that is that if the patient does well, especially at stage I repair, the cost of these procedures can be reduced. I believe the best way to save money is to reduce the circulatory arrest time and improve cardiac performance after stage I.

I believe that the patients who died after stage I repair had much more severe ventricular dysfunction than other patients, with much longer crossclamp times. The reasons for that are unclear at present but may involve the coronary vessels, which are very tiny at the base of the small ascending aorta, and the postoperative relationship of those small coronary vessels to the large neoaorta. I believe technical improvements could lead to a substantial decrease in long-term costs.

Appendix

The Dunnett procedure is used when the sole comparisons of interest are of the several individual treatments against a control group.

This multiple comparison procedure was therefore employed to compare the IT CHQ data, that is, each group mean versus the reference population. The calculated test statistics (L_i) were compared to a table of critical values for Dunnett's criterion.

The critical value from the Dunnett table for 3, 198 degrees of freedom was 2.35. Because all sample sizes were not equal, this value was further adjusted, as recommended by Fleiss, by multiplying this value by

$$1 + 0.07(1 - ni/no)$$

where ni = treatment sample size and no = control sample size.

The adjusted critical value for all three treatments was 2.51. Therefore, all L_i were compared to 2.51.

Because raw data were not available, P values could not be generated; only whether the observable differences were significant or not by comparing the Dunnett test statistics to the critical value.

No additional adjustments (eg, Bonferroni) were made for the 9 outcome variables measured. For these tests, alpha was set at 0.05, 2-tailed.