Clinical Outcomes and Secondary Diagnoses for Infants Born With Hypoplastic Left Heart Syndrome

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ABSTRACT. ***Objective.*** **To explore clinical outcomes and secondary diagnoses present at discharge for infants born with hypoplastic left heart syndrome (HLHS), from a national perspective.**

Methods. **We examined hospitalizations for infants ≤30 days of age who were born with HLHS, using hospital discharge data from the 1997 Kids Inpatient Database. To explore treatment choices, clinical outcomes, and resource use, we used *International Classification of Diseases, 9th Revision, Clinical Modification* diagnostic and procedure codes to classify discharges according to type of surgical intervention versus no surgical intervention. To investigate outcomes in more detail, we identified secondary diagnoses noted at discharge, using *International Classification of Diseases, 9th Revision, Clinical Modification* codes, and stratified results according to type of surgical intervention.**

Results. **Of a total of 550 patients with HLHS, 234 underwent the Norwood procedure, 17 underwent orthotopic heart transplantation, and 106 died in the hospital with no reported surgical intervention. Although we found no demographic variables to be significantly associated with the type of treatment received, discharged patients who died without surgical intervention were significantly more likely to have received care in hospitals identified as small (odds ratio [OR]: 1.5; 95% confidence interval [CI]: 1.03–3.1) or not children's hospitals (OR: 2.02; 95% CI: 1.13–3.6). Secondary diagnoses of cardiac arrest (OR: 2.0; 95% CI: 1.1–3.4) and seizures (OR: 2.6; 95% CI: 1.2–5.5) occurred more frequently in orthotopic heart transplantation cases than in Norwood procedure cases.**

Conclusions. **These data from a national perspective reflect outcomes of infants with HLHS during a time when rates of initial survival after surgical intervention were considered to be improved. These findings may be useful to clinicians when they are considering and recommending initial medical and surgical strategies currently being proposed for the treatment of HLHS. *Pediatrics* 2004;114:e160–e165. URL: http://www.pediatrics.org/cgi/content/full/114/2/e160; *hypoplastic left heart syndrome, congenital heart disease, infants, Kids Inpatient Database, clinical outcomes, secondary diagnoses, resource use.***

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ABBREVIATIONS. HLHS, hypoplastic left heart syndrome; KID, Kids Inpatient Database; ICD-9-CM, *International Classification of Diseases, 9th Revision, Clinical Modification*; OHT, orthotopic heart transplantation; LOS, length of stay; THC, total hospital charges; OR, odds ratio; CI, confidence interval.

Hypoplastic left heart syndrome (HLHS) remains one of the most complex congenital heart defects to treat, both medically and surgically. Despite advances in treatment, HLHS continues to have the highest mortality rate, of all congenital heart defects, for infants <1 year of age.[1] HLHS is a combination of congenital cardiac anomalies involving hypoplasia of the ascending aorta, aortic valve atresia or stenosis, a small or absent left ventricle, and mitral atresia or hypoplasia.[2] Before 1980, HLHS was considered universally fatal in the newborn period, leaving the health care team with the sole option of providing compassionate care.[2–6] Currently, most infants diagnosed as having HLHS undergo a series of surgical palliations; a small percentage undergo orthotopic heart transplantation (OHT) as an initial surgical approach.[7–18]

As the rates of death after surgical intervention for HLHS have decreased, morbidities resulting from both surgical palliation and transplantation have been reported.[19–21] Neurologic complications have been noted to occur among infants with HLHS not only as a result of the surgical procedure but also during the preoperative and postoperative periods.[22–24] Researchers[20,23,25] have documented seizures, cerebral palsy, attention-deficit disorder, and decreased IQ scores for children with HLHS who have undergone either palliative surgery or OHT. Although most morbidities encountered after surgical intervention are neurologic, renal failure, complete heart block, respiratory failure, and sepsis have also been documented.[8,12,26–34]

Despite decreasing surgical mortality and morbidity rates in the past decade, there is no consensus regarding the best treatment. Physicians and parents must still consider the choice between surgical palliation, OHT, and compassionate care. The purpose of this investigation was to examine, from a national perspective, initial clinical outcomes and secondary diagnoses present at discharge for infants born with HLHS, to facilitate initial discussions of treatment choices between health care providers and parents.

METHODS

Data Source

A retrospective secondary analysis was performed by using the Health Care Cost and Utilization Project, Kids Inpatient Database (KID) 1997. The KID consists of a stratified random sample of 1 905 797 unweighted discharges (6 657 326 weighted discharges) from 2521 institutions in 22 states (Arizona, California, Colorado, Connecticut, Florida, Georgia, Hawaii, Iowa, Illinois, Kansas, Maryland, Massachusetts, Missouri, New Jersey, New York, Oregon, Pennsylvania, South Carolina, Tennessee, Utah, Washington, and Wisconsin). The sample includes 10% of uncomplicated in-hospital births from these institutions and 80% of other pediatric cases. To obtain information that is nationally representative, the sample is weighted to represent the population of pediatric discharges from all community nonrehabilitation hospitals in the United States that were open for any part of calendar year 1997. The KID 1997 used the American Hospital Association definition of hospitals to identify all nonfederal, short-term, general or specialty hospitals. Included among these hospitals are pediatric hospitals, academic medical centers, and specialty hospitals. To protect confidentiality, the KID did not contain specific patient or hospital identifiers.

Sample Selection

Data were abstracted for all hospital discharges of patients who were ≤30 days of age at admission and were diagnosed as having HLHS, ie, *International Classification of Diseases, 9th Revision, Clinical Modification* (ICD-9-CM) code 746.7. An assortment of procedure codes were used to identify stage I palliation (also known as the Norwood procedure), ie, cardiopulmonary bypass (code 39.61), surgical creation of an atrial septal defect (code 34.42), incision, excision, or occlusion of the aorta (code 38.14), and systemic to pulmonary shunt (code 39.0), because there is no specific ICD-9-CM procedure code for this intervention. ICD-9-CM code 37.5 was used to identify patients who underwent OHT. To determine the frequency of HLHS discharges of patients ≤30 days of age at admission for whom no surgical procedure during hospitalization was reported, the data element "disposition at discharge" was used to identify infants who died during hospitalization without undergoing a surgical intervention.

Secondary diagnoses for patients with HLHS who were ≤30 days of age at admission and who were identified as undergoing the Norwood procedure or OHT were determined by abstracting under the data element "diagnosis." Congenital heart anomalies other than HLHS and other congenital anomalies were excluded as secondary diagnoses, because children with congenital heart disease are commonly affected with other syndromes or malformations.

Statistical Methods

The HLHS discharge population was examined by using demographic data elements (gender, race, insurance status, median income, and geographic location) and hospital characteristics (hospital bed size, hospital ownership, location, teaching status, and children's hospital status). Descriptive statistics were used to describe the HLHS sample, surgical intervention, clinical outcome, and resource use reported for discharges. Resource use was examined by assessing length of stay (LOS) and total hospital charges (THC) accrued during hospitalization. χ^2 tests and Fisher's exact test were used to examine observed demographic and institutional differences between patients with reported surgical interventions and patients who died in the hospital with no reported surgical intervention. Demographic and hospital variables that were significant at $P \leq .05$ were used to construct a multivariate logistic regression model. Odds ratios (ORs) with confidence intervals (CIs) at a level of 95% were generated, with ORs of >1 and CIs not including 1 being considered significant. Fisher's exact test was also used to compare the frequency of secondary diagnoses according to the surgical intervention; ORs and 95% CIs were again calculated. All data were weighted by using the data element "discharge weight" and were analyzed by using SAS 8.2 (SAS Institute, Cary, NC) and Sudaan (Research Triangle Institute, Research Triangle Park, NC) statistical software.

RESULTS

Summary of HLHS Discharges

Table 1 presents demographic information for 550 patients with HLHS who were ≤30 days of age at admission. We found HLHS patients to have a male/female ratio of 2:1. Race was most frequently reported as white (43%), followed by Hispanic (10%). Race was not reported for 34% of the sample. Although HLHS patients were predominately privately insured (62%), there was no identifiable trend with respect to income. Analysis of hospital characteristics

TABLE 1. Demographic Characteristics for HLHS Patients ≤30 Days of Age at Admission

Demographic Characteristic	No. (%)				P Value*
	Overall HLHS (n = 550)	Surgical Intervention		No Surgery, Died (n = 106)	
		Norwood Procedure (n = 234)	OHT (n = 17)		
Gender					.03
Male	341 (62)	152 (65)	12 (68)	54 (51)	
Female	209 (38)	82 (35)	5 (32)	52 (49)	
Race					.005
White	238 (43)	103 (44)	7 (44)	43 (41)	
Black	36 (7)	16 (7)	0 (0)	6 (6)	
Hispanic	57 (10)	17 (7)	3 (17)	13 (12)	
Other	31 (6)	13 (5)	0 (0)	6 (6)	
Race missing	188 (34)	84 (36)	7 (39)	38 (35)	
Insurance					.35
Private	341 (62)	145 (62)	8 (46)	60 (57)	
Medicaid	149 (27)	63 (27)	5 (29)	29 (27)	
Other	60 (11)	26 (11)	4 (24)	17 (16)	
Median income					<.001
$0–25 000	143 (26)	52 (22)	5 (27)	33 (31)	
$25 001–30 000	97 (18)	42 (18)	2 (12)	10 (9)	
$30 001–35 000	91 (16)	35 (15)	3 (20)	22 (21)	
$35 001 or more	183 (33)	84 (36)	5 (28)	37 (35)	
Income missing	36 (7)	21 (9)	2 (13)	4 (4)	

* χ^2/Fisher's exact test.

revealed that most HLHS discharges occurred in hospitals that were medium to large (79%), private/not for profit (87%), located in urban areas (98%), and identified as teaching hospitals (74%), as well as a children's hospital or a hospital with a designated children's unit (70%) (Table 2).

Clinical Outcomes and Resource Use

Table 3 compares HLHS patients with a reported surgical intervention (Norwood procedure or OHT) and HLHS patients who died in the hospital with no reported surgical intervention. The Norwood procedure was reported for 234 patients, OHT was reported for 17 patients, and 106 patients died during hospitalization with no reported surgical intervention. Other nonsurgical HLHS discharges (193 of 550 cases) included the following dispositions: discharged home (44 cases), transferred to a short-term facility (127 cases), and transferred to another type of facility (22 cases).

Mortality rates were 32% for the Norwood procedure and 41% for OHT. We examined the LOS and THC for infants who received surgical intervention, stratified according to status at discharge as alive or dead. We also examined LOS and THC for patients who died with no reported surgical intervention. Mean and median LOS and THC for alive discharges after OHT exceeded those for the Norwood procedure by ~2:1. However, mean LOS and THC were similar for the 2 surgical groups of patients who died. HLHS patients who died with no reported surgical intervention were noted to have a median LOS of 4 days (range: 1–148 days).

Differences Among Patients With HLHS

We observed significant differences between HLHS patients with a reported surgical intervention ($n = 251$) and HLHS patients who died in the hospital with no reported surgical intervention ($n = 106$) with respect to the variables gender, race, median income, and geographic region (Tables 1 and 2). We performed multivariate logistic regression to examine in more detail the relationship of demographic variables for HLHS discharges with surgical intervention versus no surgical intervention. The demographic variables used in the logistic model were gender, race, income, and geographic region. We found no statistical difference between the groups when controlling for these demographic variables.

We examined the hospital profile for HLHS discharges by using the variables hospital bed size, hospital ownership, location/teaching status, and whether or not the facility was designated as a children's hospital (Table 2). χ^2 analysis demonstrated all institutional variables to be significant. Using the same variables, we performed multivariate logistic regression analysis to examine in more detail the relationship of hospital differences for HLHS discharges with surgical intervention versus no surgical intervention. Our regression model revealed that HLHS patients who were ≤30 days of age at admission were more likely to be discharged as dead with

TABLE 2. Hospital Characteristics for HLHS Patients ≤30 Days of Age at Admission

Hospital Characteristic	No. (%)				*P* Value*
	Overall HLHS ($n = 550$)	Surgical Intervention		No Surgery, Died ($n = 106$)	
		Norwood Procedure ($n = 234$)	OHT ($n = 17$)		
Hospital size (no. of beds)					.0035
Small (1–299)	115 (21)	52 (22)	3 (15)	24 (23)	
Medium (300–499)	176 (32)	95 (41)	8 (50)	22 (21)	
Large (≥500)	259 (47)	87 (37)	6 (34)	60 (56)	
Hospital ownership					.01
Government	55 (10)	22 (9)	0 (0)	7 (6)	
Private/not for profit	479 (87)	210 (89)	17 (100)	94 (89)	
Privately owned	16 (2)	2 ([lt]1)	0 (0)	5 (4)	
Hospital location					<.0001
Rural	11 (2)	0 (0)	0 (0)	1 (1)	
Urban	539 (98)	234 (100)	17 (100)	105 (99)	
Hospital teaching status					<.0001
Nonteaching	143 (26)	34 (15)	7 (39)	35 (33)	
Teaching	407 (74)	200 (85)	10 (61)	70 (66)	
Hospital location/teaching status					<.0001
Rural	11 (2)	0 (0)	0 (0)	1 (1)	
Urban nonteaching	132 (24)	34 (15)	7 (39)	35 (33)	
Urban teaching	407 (74)	200 (85)	10 (61)	70 (66)	
Children's hospital status					<.0001
Not children's hospital	170 (30)	33 (14)	4 (27)	38 (36)	
Children's unit in hospital	184 (34)	79 (34)	6 (34)	37 (35)	
Children's hospital	196 (36)	122 (52)	7 (39)	31 (29)	
Region					<.0001
Northeast	148 (27)	87 (37)	3 (20)	13 (12)	
Midwest	138 (25)	53 (23)	3 (16)	33 (31)	
South	83 (15)	29 (12)	4 (23)	18 (17)	
West	181 (33)	65 (28)	7 (41)	42 (40)	

* χ^2/Fisher's exact test.

TABLE 3. Outcomes and Resource Use for HLHS Patients ≤30 Days of Age at Admission

Outcomes/Resource Use	Surgical Intervention		No Surgery, Died (n = 106)
	Norwood Procedure (n = 234)	OHT (n = 17)	
Disposition at discharge, no. (%)			
Home	56 (49)	10 (57)	0 (0)
Short-term facility	12 (5)	0 (0)	0 (0)
Another type of facility	33 (14)	0 (0)	0 (0)
Died	75 (32)	7 (42)	106 (100)
LOS, days, alive			
Mean	25	4	0
Median	19	39	0
Minimum, maximum	1, 158	3, 119	0
LOS, days, died			
Mean	18	16	12
Median	7	7	4
Minimum, maximum	1, 158	3, 40	1, 148
THC, alive			
Mean	$168 611	$254 996	0
Median	$127 157	$252 169	0
Minimum, maximum	$2000, $995 428	$49 543, $558 188	0
THC, died			
Mean	$163 295	$137 072	$100 850
Median	$75 596	$85 897	$46 804
Minimum, maximum	$2000, $995 428	$49 543, $280 978	$729, $995 428

no reported surgical intervention in institutions reported as small (reference group: large; P = .02; OR: 1.5; 95% CI: 1.03–3.1) and institutions not identified as children's hospitals (reference group: children's hospitals; P = .001; OR: 2.02; 95% CI: 1.13–3.6).

Secondary Diagnoses at Discharge

We queried the database for secondary diagnoses for HLHS discharges with either the Norwood procedure or OHT. We also queried the database with the ICD-9-CM diagnostic codes for stroke, seizures, respiratory failure, feeding abnormalities, infection, and renal failure, because these comorbidities have been cited in the literature as postoperative complications for infants with HLHS. Table 4 summarizes secondary diagnoses for HLHS patients ≤30 days of age with a recorded surgical intervention.

Secondary diagnoses that were found to be significant ($P \leq .05$) with Fisher's exact test were examined for possible confounding or the presence of effect modification. For HLHS discharges, cardiac arrest (P = .01; adjusted OR: 2.02; 95% CI: 1.1–3.4) and seizures ($P < .0001$; adjusted OR: 2.6; 95% CI: 1.2–5.5) were found to be significant for OHT versus the Norwood procedure.

DISCUSSION

General Findings

The results of our secondary analysis of data for infants born with HLHS, using the KID 1997, reflects clinical outcomes, resource use, and secondary diagnoses from a national perspective, during a period of reported improved survival after surgical intervention. Use of the Norwood procedure as the initial surgical intervention for infants with HLHS is a trend that has been reported by individual institutions for the past 20 years. Reasons cited for this trend have been improvements in rates of survival after the Norwood procedure and a lack of neonatal hearts available for OHT.[35] Our study supported this trend, ie, 93% of surgically treated patients with HLHS underwent the Norwood procedure. The mortality rates were 32% for the Norwood procedure and 42% for OHT. These results are consistent with other available data and confirm the trend in improved immediate survival rates reported in the past 20 years by individual institutions.[15,17,36,37]

We are unsure whether discharges recorded as "died during hospitalization" (n = 106) represent patients who were waiting for surgical intervention or patients who were recommended for compassionate care. We observed the median LOS to be 4 days (range: 1–148 days). Jenkins et al[38] estimated that 1.7% of infants with HLHS died while waiting for the Norwood procedure and 24% of infants with HLHS died while waiting for OHT. Chang et al[39] attempted

TABLE 4. Secondary Diagnoses for HLHS Patients ≤30 Days of Age at Admission, According to Surgical Intervention

Diagnosis	No. (%)		Adjusted OR (95% CI)
	Norwood Procedure (n = 234)	OHT (n = 17)	
Cardiac arrest	37 (16)	5 (32)*	2.02 (1.1–3.4)
Congestive heart failure	30 (13)	1 (4)	
Pleural effusion	23 (10)	0 (0)	
Acidosis	23 (10)	0 (0)	
Hemorrhage	26 (11)	4 (16)	
Infection	16 (7)	4 (16)	
Seizure	19 (8)	5 (20)*	2.6 (1.2–5.5)
Stroke	5 (2)	2 (8)	
Respiratory failure	5 (2)	1 (4)	
Feeding abnormality	23 (10)	4 (15)	

* $P \leq .05$, Fisher's exact test.

to quantify the percentage of infants with HLHS from a large database who were discharged with the disposition "died in hospital." The researchers concluded that, of 637 infants who died in the hospital, 617 died as a result of planned compassionate care. The authors speculated that this was supported by the fact that more than one-half of the infants in the series died within an average of 3 days of hospitalization.[39] Our findings of a median LOS of 4 days are consistent with that study.

In our study, demographic variables were not found to influence the presence or absence of surgical intervention. However, we found that hospitals characterized as small and those not identified as children's hospitals were more likely to report HLHS death during hospitalization with no surgical intervention.

We observed that resource use varied according to the surgical intervention. For infants who survived surgery, the LOS and THC for OHT exceeded those for the Norwood procedure by ~2:1. However, the mean LOS and THC were similar for the 2 surgical groups of patients who died. Little published information is available on the cost of surgical care, and this should be an area of additional inquiry.

We noted that the secondary diagnoses for patients with HLHS who underwent surgical intervention varied in frequency according to the surgical intervention. Patients with HLHS who underwent OHT, compared with the Norwood procedure, were more likely to experience cardiac arrest and seizures. Our findings of seizures for 20% of the patients with HLHS who underwent OHT were similar to those of Raja et al,[40] who cited a 21% occurrence among a cohort of patients with HLHS who were monitored over time. The authors concluded that posttransplant seizures were associated with total cardiopulmonary bypass time and the presence of posttransplant complications.[40] Although we found this occurrence to be significant, additional studies are warranted, because of the small size of the OHT group.

Cardiac arrest in 17% of HLHS surgical cases is of interest and is another possible explanation for future developmental and intellectual delays. Previous studies reported that infants with HLHS are at risk for abnormal growth and development because of periods of acidosis, hypoxia, seizures, and use of cardiac bypass during the neonatal period.[20,41] For infants with HLHS, any of these diagnoses, depending on severity, could be devastating and greatly disabling, altering normal growth and development.[42]

Limitations

Although the KID 1997 is considered to provide a representative sample, discharge information originates from only 22 states. The KID did not contain unique patient identifiers or record linkage numbers, making it impossible to identify discharges as individual patients. In an effort to overcome this limitation, we identified an arbitrary age at admission of ≤30 days, to examine the initial hospitalizations for infants with HLHS. It is not known whether the HLHS discharges recorded as transferred to short-term facilities represent transfers to short-term facilities not included in the database or to other facilities included in the KID (thus being recounted in the total number of discharges with a surgical intervention). For this reason, we examined this sample of HLHS discharges under the assumption that an individual might incur multiple hospitalizations and could have >1 discharge record in the year 1997.

Missing data and coding errors are universal limitations in the use of large administrative databases. This was best indicated by the data element "race," which was reported as missing for 33% of the HLHS sample. We therefore could not conclude with certainty that race was not a factor in treatment choice or clinical outcome.

Compassionate care for this group of infants could not be identified with certainty, because there is no specific ICD-9-CM code available for this treatment option. We attempted to overcome this limitation by restricting the age at admission to ≤30 days, to identify the initial treatment and hospitalization period and to examine patients who died during hospitalization with no reported surgical intervention. It is also of note that some infants with HLHS might have been excluded from this database as a result of not being diagnosed during newborn admission and dying at home or possibly being misdiagnosed as experiencing sudden infant death syndrome.

At the beginning of our study, a limitation that was foreseen was the lack of clinical data, which is another limitation of all studies using administrative databases in outcomes research.[43] In this population, birth weight and organ function have been cited as predictors of initial clinical outcomes, as well as long-term growth and development.[44] Additional explanations of the severity of secondary diagnoses would have been useful for determination of the long-term health care services required. Conclusions regarding observed differences between surgical interventions according to secondary diagnoses should be investigated in more detail, because of the small sample of patients with HLHS who underwent OHT. This database was available only for the year 1997, limiting our ability to study trends in clinical outcomes and resource utilization with time. Additional studies should examine direct and indirect costs of care with time.

Implications

Although survival rates for infants after surgical intervention have improved in the past 20 years, there is still a great possibility that these infants will be at risk for residual mental and physical abnormalities. The initial consultations between health care providers and parents at the time of HLHS diagnosis are extensive, requiring discussion of various treatment options and outcomes, ie, not only survival rates but also descriptions of morbidities associated with treatment. Use of the only currently available national database of hospitalized children with disease allowed our research team to provide an overview of initial clinical outcomes for a relatively large number of patients with a rare and complex congenital heart defect.

CONCLUSION

Our results provide a comprehensive view of HLHS initial outcomes during a time of improved survival rates, allowing health care professionals and parents to weigh the risks and benefits of newer medical and surgical interventions currently being proposed for the treatment of infants born with HLHS.

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