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ORIGINAL ARTICLE

Heterotaxy Syndrome: Impact of Ventricular Morphology on Resource Utilization

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Abstract Patients with heterotaxy syndrome (HS) have significant cardiac and extracardiac anomalies that impact outcome. To improve the management of this complex patient population, we performed a comprehensive analysis of their anatomic and clinical features along with an evaluation of resource utilization data. The objectives were to describe anatomic and clinical features of patients with HS syndrome treated at a single center from 1992 to 2011 focusing on the impact of ventricular morphology (univentricular [UV] vs. biventricular [BV]) on clinical outcomes and resource utilization. Clinical and echocardiographic data from patients with HS were abstracted from medical records. Health care costs were indexed to inflation. Seventy-eight patients were identified with HS ranging in age from 1 day to 29 years old. UV morphology was present in 46 patients (59 %), most commonly with right-ventricular dominance (36 of 46). The presence of extra cardiac anomalies did not differ between the UV and BV groups (82 vs. 78 %) nor did morbidities, such as need for enteral tube feedings (47 vs. 25 %) or pacemaker placement (24 vs. 25 %). Mortality was 28 % in the entire cohort: 39 % in univentricuar patients versus 10.5 % in those with biventricular anatomy. Hospital length of stay for medical illnesses was similar in both groups, but length of stay after surgery was significantly longer in UV than BV patients. Among survivors, UV patients had greater median hospital costs ($200,634 vs. $67,732, $p < 0.001$), but when this was adjusted for mortality and variable follow-up, there were no differences in health care costs within the first year of life. Significant health care dollars are used to manage children with HS, the majority of which involve expenses related to surgical care. Although patients with biventricular morphology have better survival, morbidity and resource utilization are similar to those for UV patients especially within the first year of life.

Keywords Heterotaxy syndrome · Resource utilization · Univentricular · Biventricular

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Introduction

Heterotaxy syndrome (HS) includes a wide range of malformations including both cardiac and extracardiac manifestations. The Nomenclature Working Group, which belongs to the International Society for Nomenclature of Pediatric and Congenital Heart Disease, defines heterotaxy "as an abnormality where the internal thoracoabdominal organs demonstrate abnormal arrangement across the left–right axis of the body." They also state that "heterotaxy does not include patients with either the expected usual or normal arrangement of the internal organs along the left–right axis, also known as 'situs solitus,' or patients with complete mirror-imaged arrangement of the internal

organs along the left–right axis also known as 'situs inversus'" [6] .

Recent studies show improved current era surgical outcomes in patients with HS. Five-year survival rates have improved from approximately 50 % before 2003 to 80 % to 90 % [11]. However, morbidity due to complex cardiac and noncardiac illness persists. The presence of complex cardiac anatomy and other noncardiac anomalies have been identified as factors associated with increased resource use for congenital heart disease [4]. Within heterotaxy syndrome there is significant anatomic variation regarding both cardiac and noncardiac structures. Such anatomic variation often requires intensive surgical and medical care with some anomalies having a high degree of mortality. We sought to identify factors that most strongly impact resource use in an effort to identify areas for clinical improvement and provide families with accurate prognostic data.

Although the traditional syndromic classification of heterotaxy into right or left atrial isomerism and asplenia or polysplenia is useful in clustering anatomic variants, there is considerable overlap between the two forms of HS. Therefore, we favor a complete description of cardiac and thoracoabominal anatomy as suggested by the Nomenclature Working Group with a focus on ventricular anatomy and its impact on morbidity, mortality, and resource utilization.

Studies report excellent survival for patients with HS who undergo biventricular repair even for complex lesions, although some require cardiac reintervention and treatment for arrhythmias [10]. For univentricular patients, studies report improving outcomes in the current surgical era; however, neonatal surgery, long-standing palliation, total anomalous pulmonary vein return, and right-ventricular outflow tract obstruction are risk factors for mortality [1, 13].

This is the first study to evaluate resource use among this complex group of patients and assess the impact of ventricular morphology. Although patients with univentricular anatomy would seemingly have greater health care expenses, these costs may be mitigated by greater mortality. Likewise, noncardiac morbidity among patients with biventricular anatomy may be substantial. Hence, the current study was performed to analyze resource use among patients with HS with particular focus on the impact of ventricular anatomy.

Materials and Methods

Setting

The study was performed at Primary Children's Medical Center (PCMC), a 289-bed, freestanding, university-affiliated, tertiary children's hospital that serves a large geographic area in the Intermountain West. The hospital offers tertiary-level cardiac care to most children in a five state region including Utah (UT), Idaho (ID), Montana (MT), Wyoming (WY) and Nevada (NV). The study was reviewed and approved by the University of Utah Institutional Review Board, and need for informed permission/consent was waived.

Patients and Methods

The study was a retrospective review of all patients with HS identified through an echocardiography database at PCMC. The database was searched using key words "isomerism," "right-ventricle dominance," "left-ventricle dominance," "asplenia," "polysplenia," "dextrocardia," "heterotaxy," "interrupted IVC," and "unbalanced AV canal defect" to generate a list of patients with possible HS managed between January 1992 and June 2011. Echocardiograms and relevant clinical data were reviewed to confirm heterotaxy diagnoses. Diagnostic confirmation was based on the definition of heterotaxy given by The International Working Group for Mapping and Coding of Nomenclatures for Pediatric and Congenital Heart Disease, also known as the Nomenclature Working Group.

A detailed review of the electronic medical records and hospital charts of cases was performed and data collected in a preset information record sheet. The information included demographics, visceral and cardiac anatomy, extracardiac manifestations, clinical features, and details of hospitalization of each patient until the point of study. All available sources for a given case were used to determine visceral and cardiac anatomy. In most cases, cardiac anatomy was determined by the available echocardiograms; however, cardiac magnetic resonance imaging (MRI) and cardiac catheterization data were used, when available, to confirm or clarify the anatomy. Abdominal ultrasonography (US) was the most commonly available source for visceral anatomy, with few cases diagnosed by computed tomography (CT) of the abdomen. Data on resource use included days spent in the cardiac intensive care unit (CICU) and in the hospital, days of mechanical ventilation (referred to as ventilator days), and total costs of hospitalization. The total costs included the sum of all inpatient hospitalization costs as well as the aggregate costs from outpatient encounters that occurred within our health care system. No differentiation was made between cardiac and noncardiac inpatient costs because the majority of the noncardiac procedures occurred as a part of routine management under the cardiology service. The data on costs and total number of inpatient and outpatient hospital encounters for each HS patient were obtained from the hospital accounts and finance department. The finance department runs a quarterly process of costing

methodology structured on a transaction-based micro-accounting system that assigns costs to each individual charge code. Standard formulae are used to allocate supply, labor, overhead, and depreciation/capital expenses, and each charge code receives four categories of expense: total fixed, total variable, department fixed, and department variable. The total cost for an individual patient encounter is obtained by calculating the expenses for each charge code assigned. Physician fees were excluded because services were billed separately and were not a part of PCMC hospital accounts from which the financial data were derived.

For the purpose of the study, an encounter was defined as any patient contact with the hospital for medical, surgical, diagnostic, or laboratory service that incurred cost to the hospital. Admissions were defined as medical or surgical depending on the primary diagnosis listed in the medical record. Feeding problems were defined as the need for tube feeds (nasogastric, nasojejunal, or gastrostomy) at the time of any hospital discharge. The diagnosis of malrotation was based on results from upper gastrointestinal contrast studies or any other advanced imaging modality. Rhythm problems were reported as the need for pacemaker placement at any point of care. Extracardiac anomalies included all major and minor malformations identified by clinical examination and/or imaging of other organ systems. Because the ECHO database has only existed since 2003, no patients were identified who died before 2003. Therefore, mortality calculations were performed only for patients born after 2003.

Statistical Analysis

Data were analyzed by descriptive statistics using SPSS 18.0 (SPSS, Chicago, IL). All HS cases were described using summary statistics, and then we compared groups based on ventricular morphology: univentricular (UV) or biventricular (BV). Comparisons were made by Chi square test for categorical variables, whereas for nonparametric data, Mann–Whitney U-test or Student's t test were used depending on the mode of distribution.

Hospital costs were indexed to inflation and adjusted to 2011 US dollars by applying the Consumer Price Index inflation calculator available on the official website of the United States Department of Labor, Bureau of Labor Statistics (http://www.bls.gov/data/inflation_calculator.htm). These data represent changes in prices of all goods and services purchased for consumption by urban households. To account for mortality and variable follow-up time, time periods were developed a priori to correspond to the usual patient ages for univentricular disease surgical management (birth to 1 month, 1–6 months, 6–12 months, 1–5 years, 5–10 years, 10–20 years and >20 years of age). Cost data were transformed using the natural log, and the charges within each age duration were analyzed using multiple analysis of variance and adjusting for death. Because follow-up time periods were similar between the BV and UV group, total inflation-adjusted costs and medical resource consumption of survivors were compared between groups. Statistical significance was defined as $p < 0.05$.

Results

After review of echocardiograms and clinical records, 78 patients were confirmed as having HS. The detailed cardiac anatomy of the patient cohort is listed in the Table 1. Sixty percent ($n = 46$) had UV cardiac morphology. The cohort median patient age was 6.1 years (range 1 day to 29 years) at the end of the study. The patients were predominantly white (70 %) reflecting the racial composition of the geographical region. Nearly two-thirds of patients were girls (64 %).

Genetic testing was performed in 26 patients, and 5 patients were found to have a chromosomal anomaly. Two patients had chromosome 22q11 deletion, 2 had partial deletion of chromosome 8p23, and 1 had partial deletion of chromosome 2q13. The majority of patients (85 %) had an extracardiac manifestation, with gastrointestinal (GI) anomalies being the most common. Eleven patients had multisystem involvement with a combination of craniofacial, musculoskeletal, and genitourinary anomalies. Ten patients (13 %) had at least 1 midline defect. Among GI anomalies, malrotation was present in 34 of 53 (64 %) patients tested, with 8 patients (24 %) undergoing emergent abdominal surgery due to obstruction or perforation. The Ladd procedure was performed in 25 of 34 patients (74 %) and was elective in 17 patients. Among the 17 patients with prophylactic Ladd, 2 (12 %) had subsequent small-bowel obstruction secondary to adhesions and strictures. Feeding problems were found in 29 of 78 patients (37 %). Pacemaker placement was performed in 25 % of patients.

When comparing patients having UV morphology with those in the BV group (Table 2), the proportion of patients with extracardiac manifestations, feeding problems, and arrhythmias needing pacemaker were similar. The incidence of malrotation and decision for a Ladd procedure also did not differ between the two subgroups.

Details of survival and cardiac surgery data are listed in Table 3. There were 16 deaths among the 78 patients, with the majority of deaths (14 of 16) occurring among UV patients. The median age of the death was 76 days, with UV patients dying earlier than BV patients, but this was not statistically significant (46 vs. 210.5 days, $p = 0.47$).

Table 1 Detailed cardiac anatomy of children with HS (subgroups based on cardiac ventricular morphology)

Cardiac anatomy	Total patients ($n = 78$)	UV morphology ($n = 46$)	BV morphology ($n = 32$)
Visceral situs			
Solitus	16 (21 %)[a]	6 (13 %)	10 (31 %)
Inversus	25 (32 %)	18 (39 %)	7 (22 %)
Ambiguous	37 (47 %)	22 (48 %)	15 (47 %)
Cardiac position			
Dextrocardia	23 (30 %)	16 (35 %)	7 (22 %)
Levocardia	51 (65 %)	28 (61 %)	23 (72 %)
Mesocardia	4 (5 %)	2 (4 %)	2 (6 %)
Atrial situs			
Solitus	21 (27 %)	8 (17 %)	13 (41 %)
Inversus	18 (23 %)	14 (30 %)	4 (13 %)
Ambiguous	39 (50 %)	24 (52 %)	15 (47 %)
Ventricular anatomy			
Balanced	33 (42 %)	1 (2 %)	32 (100 %)
RV dominant	36 (46 %)	36 (78 %)	0 (0 %)
LV dominant	9 (12 %)	9 (20 %)	0 (0 %)
AV valve regurgitation			
Normal to mild	7 1 (91 %)	41 (89 %)	30 (94 %)
Moderate to severe	7 (9 %)	5 (11 %)	2 (6 %)
Ventricular loop (%)			
D-Loop	58 (74 %)	32 (70 %)	26 (81 %)
L-Loop	20 (26 %)	14 (30 %)	6 (19 %)
Great artery relation (%)			
Normal	33 (42 %)	10 (20 %)	23 (72 %)
Mirror image	7 (9 %)	3 (7 %)	4 (13 %)
D-TGA	25 (33 %)	21 (46 %)	4 (13 %)
L-TGA	9 (12 %)	8 (17 %)	1 (3 %)
Anterior malposition	4 (5 %)	4 (9 %)	0 (0 %)
VA communication			
Concordant	30 (39 %)	2 (4 %)[c]	28 (88 %)
Discordant	7 (9 %)	5 (11 %)	2 (6 %)
DORV	26 (33 %)	24 (52 %)	2 (6 %)
Pulmonary atresia	15 (19 %)	15 (33 %)	0 (0 %)
Aortic atresia	0 (0 %)	0 (0 %)	0 (0 %)
PVR			
Normal	36 (46 %)	13 (28 %)	23 (72 %)
Partial anomalous PVR	18 (23 %)	12 (27 %)	6 (19 %)
Total anomalous PVR[b]	24 (31 %)	21 (46 %)	3 (9 %)
Systemic venous return			
Normal IVC	38 (49 %)	31 (67)	7 (22)
Interrupted IVC	40 (51 %)	15 (33 %)	25 (78 %)
Normal SVC	18 (23 %)	10 (22 %)	8 (25 %)
Bilateral SVC	42 (54 %)	23 (50 %)	19 (59 %)
Left SVC	18 (23 %)	13 (28 %)	5 (16 %)
Aortic arch obstruction	15 (19 %)	10 (22 %)	5 (16 %)
PV obstruction	5 (6 %)	5 (6 %)	0 (0 %)

RV right ventricle, *LV* left ventricle, *AV* atrioventricular, D dextro, L levo, *TGA* transposition of great arteries, *DORV* double-outlet right ventricle, *VA* ventriculo-arterial, *PVR* pulmonary venous return, *IVC* inferior vena cava, *SVC* superior vena cava, *PV* pulmonary vein

[a] Percentages rounded to nearest whole number

[b] Only one patient had obstructed total anomalous PVR

[c] Patients initially thought to be favorable for biventricular repair but failed

Table 2 Select demographic and clinical features of children with HS

	Total patients ($n = 78$)	UV morphology ($n = 46$)	BV morphology ($n = 32$)	p
Age (year)[a]	6.1(2.1, 15.4)	5.8 (1.9, 16.1)	6.7 (2.6, 11.1)	0.324
Male	28 (36 %)	18 (39 %)	10 (31 %)	0.475
Female	50 (64 %)	28 (61 %)	22 (69 %)	0.631
Race				
White	55 (70 %)	33 (71 %)	22(69 %)	
Hispanic	12 (15 %)	8 (17 %)	4 (12 %)	
Black	1 (1 %)	0	1 (3 %)	
Unknown	10 (13 %)	5 (11 %)	5 (16 %)	
Chromosomal anomalies	5 (19 %)[b]	1 (2 %)	4 (13 %)	
Extracardiac anomalies	66 (84 %)	40 (82 %)	26 (78 %)	0.303
Asplenia[c]	27 (35 %)	25 (54)	2 (6)	<0.001
Polysplenia	27 (35 %)	10 (22)	17 (53)	0.007
Normal spleen	9 (12 %)	1 (2)	8 (25)	0.002
Right-sided spleen	11 (14 %)	6 (13)	5 (16)	0.752
Malrotation	34 (64 %)[d]	21 (46)	13 (41)	0.203
Ladd procedure	25 (74 %)[e]	18 (39)	7 (22)	0.108
Feeding problems	29 (37 %)	21 (45)	8 (25)	0.108
Pacemaker	19 (24 %)	11 (24)	8 (25)	0.912

[a] Median with interquartile range

[b] Only 26 patients were tested

[c] Four patients were not tested for splenic abnormality

[d] Fifty-three patients were tested for malrotation; hence, $n = 53$ was used for calculating percent

[e] Performed in 25 of 34 patients with malrotation

Mortality among patients born after 2003 was 28 % (13 of 47), with mortality in the UV being 39 % (11of 28). All five patients with chromosomal anomalies are alive at the time of the current study analysis. Death was most common in the first month (7 of 14) for the UV group, whereas all deaths ($n = 2$) in the BV group occurred before 1 year of age. Among the UV group, 3 died before any cardiac surgery. Seven patients with BV anatomy did not need any cardiac surgery, whereas the remaining 25 underwent definitive repair of a cardiac abnormality. Two patients in the UV group underwent heart transplantation after Fontan palliation. Indications for heart transplantation were refractory protein-losing enteropathy in one patient and early cirrhosis in the other. There was no mortality after cavopulmonary anastomosis at the time of this analysis.

Table 4 lists the inflation-adjusted median cost of care by age category. Health care costs were greatest in the first month of age for both cardiac morphology groups. Although costs were greater for the single-ventricle group, the median health care costs stratified by age categories did not significantly differ between ventricular morphology groups. Comparing the log-transformed costs of care across time periods adjusted for mortality, cardiac ventricular morphology groups did not differ significantly regarding health care costs over time ($p = 0.428$).

Resource use among surviving children are compared between the UV and BV groups in Table 5 for the entire study period. Both groups had frequent health care encounters, but this did not differ significantly with respect to the median number of outpatient encounters (29 vs. 19.5, $p = 0.06$). The median number of inpatient encounters was significantly greater (5 vs. 2, $p = 0.002$) in the UV group as were median cumulative hospital, CICU, and ventilator days. Medical admissions were less common than surgical admissions, but this did not differ significantly between The UV and BV groups (4 vs. 2.3, $p = 0.139$). Likewise, cumulative hospital length of stay (LOS), CICU LOS, and duration of tracheal intubation for medical admissions did not differ by group. Catheter-based interventions were significantly more frequent in the UV group (4 vs. 0.5, $p = 0.001$). The median inflation-adjusted total cost of hospitalization was significantly greater in the UV group ($200,634 vs. $67,732, $p < 0.001$).

A total of 235 medical admissions occurred in all patients with heterotaxy during the study period. The most common reason for nonsurgical admission was respiratory tract infection occurring in 63 of 235 admissions (27 %). Other reasons for medical admissions were rhythm issues 34(14 %), GI problems 15(6.3 %), admission in the newborn period for evaluation of congenital heart disease 11(4.6 %), fever without focus 10(4.2 %), acute heart failure 7(2.9 %), and septicemia 6(2.5 %). There were 6 hospitalizations for culture-proven bacterial sepsis occurring in 2 patients. The GI problems were related to feeding intolerance, vomiting, and abdominal distension of a nonsurgical nature. The cases requiring surgery for perforation and obstruction were not grouped under this category. The rhythm issues included management of atrial flutter, sinus node dysfunction, and pacemaker-related problems.

Table 3 Survival and cardiac surgical characteristics of children with HS

Variable	Total patients ($n = 78$)	UV morphology ($n = 46$)	BV morphology ($n = 32$)
Mortality (%)[h]	13 (28)	11 (39)	2 (11)
Age at death (days)[a]	76 (6, 400)	46 (5.5, 700)	210.5 (149)
Surgery			
Reparative	25 (32 %)	0 (0 %)	25 (78 %)
Palliative	43 (55 %)	43 (93 %)	5 (16 %)[f]
Death before surgery	3 (4 %)	3 (7)	0 (0 %)
No surgery need	7 (9 %)	0 (0 %)	7 (22 %)
Heart transplantation	2 (3 %)	2 (4 %)[g]	0
Primary palliation			
BT shunt[b]	19 (25 %)	18 (39 %)	1 (3 %)
PA band[c]	11 (14 %)	8 (17 %)	3 (9 %)
Norwood/DKS[d,e]	5 (6 %)	5 (11 %)	
Cavopulmonary anastomosis	8 (6 %)	8 (11 %)	
Central shunt	3 (4 %)	3 (7 %)	
Other	5 (6 %)	4 (9 %)	1 (3 %)
Survival to Glenn		32 (69 %)	
Age at Glenn (days)[a]		219 (141.5, 380)	
Awaiting Fontan		13 (28 %)	
Post-Fontan		19 (41 %)	
Age at Fontan (years)[a]		4.0 (2.6, 5.9)	

[a] Median with interquartile range

[b] Blalock–Taussig shunt

[c] Pulmonary artery band

[d] Damus-Kaye Stansel procedure

[e] Among the five patients, had BT shunt, and two had right ventricle–to–pulmonary artery conduit

[f] Had initial palliation followed by reparative surgery later

[g] Both patients were transplanted after undergoing Fontan procedure

[h] Mortality calculated for patients born after 2003 ($n = 47$ [UV = 28 and BV = 19])

Discussion

This article describes a single-center experience of children with HS during the last 20 years. Emphasis is placed on understanding the impact of ventricular morphology on clinical outcomes and resource use. We find that patients with HS require significant health care resources and that the health care burden is similar between univentricular and biventricular patients especially in the first few years of life. The morbidity and hospital resource use associated with cardiac surgery is high in the UV group compared with the BV group as manifest by increased hospital lengths of stay, CICU days, and ventilator days, but patients with BV anatomy have substantial and similar need for resources to care for GI, rhythm, and other medical issues.

We provide a detailed description of cardiac anatomy for patients with heterotaxy based on guidelines put forth by the Nomenclature Working Group. It should be noted that many studies lump the cardiac anatomy of HS into broad classifications, either asplenia/polysplenia or left/right isomerism. However, given the variability of cardiac morphology in HS, we advocate that a detailed and consistent anatomic description will facilitate more meaningful outcomes research in this population.

We found the incidence of extracardiac anomalies to be high (84 %) in our study cohort. GI anomalies were the most common extracardiac manifestation, which is consistent with previous reports [9, 17]. The largest study cataloguing extracardiac anomalies in patients with HS was performed by Ticho et al. [17] of Children's Hospital of Boston. They analyzed 160 autopsied cases of heterotaxy and found that 38 % of patients had at least 1 midline defect. Although we found a lower incidence of midline defects in our study population, our screening method was based on clinical examination and imaging rather than autopsy. It has been suggested that examination of autopsied specimens almost doubles the incidence of midline defects detected [17].

The overall mortality in UV patients with heterotaxy was similar to the mortality reported for patients with hypoplastic left heart syndrome. Jacobs et al. [7] reported 42 % total mortality through stage 3 palliation in their cohort of 199 patients with hypoplastic left heart syndrome and related malformations, including tricuspid atresia with transposition, double- inlet left ventricle with transposition, and severely unbalanced atrioventricular septal defect. Most deaths (almost 30 %) occurred before hospital discharge after stage 1 surgery in that population, and multivariable logistical regression analysis identified noncardiac abnormalities as a significant risk factor for hospital death. All of the deaths in our cohort were cardiac related, and the majority occurred immediately after or within the first 2 months of primary surgery. Although the mortality in this group of patients with heterotaxy and single-ventricle morphology is somewhat greater than early mortality

Table 4 Cost of care and mortality by ventricular groups

Age category	Inflation-adjusted mean costs	Deaths by age category	No. followed-up through age category	Median costs per age category (p)
0–1 (months)				0.131
BV ($N = 46$)	$61,741	0	32	
UV ($N = 32$)	$78,539	7	39	
1–6 (months)				0.656
BV	$16,302	1	31	
UV	$58,028	2	37	
6–12 (months)				0.958
BV	$23,086	1	30	
UV	$36,610	1	36	
1–5 (years)				0.305
BV	$31,794	0	16	
UV	$36,404	2	26	
5–10 (years)				0.109
BV	$4,425	0	8	
UV	$23,305	0	17	
10–20 (years)				0.145
BV	$27,100	0	2	
UV	$7,135	2	6	
Lifetime costs during study				0.027
BV	$175,807	2		
UV	$265,330	14		

reported by Jacobs et al., our patients would have been categorized as the subgroup at risk for increased mortality.

Malrotation is a common GI manifestation in children with heterotaxy that can lead to midgut volvulus and GI morbidity. Routine screening of asymptomatic children with HS for malrotation and management of those who have an asymptomatic rotational abnormality is controversial. The opinion among the scientific community is clearly divided with some investigators suggesting that routine screening may not be necessary as long as close follow-up can be assured [3]. Other investigators recommend evaluation and management of intestinal fixation and rotational abnormalities while the patient is asymptomatic in an attempt to prevent emergency abdominal surgery, which carries a substantial risk especially in patients with complex cardiovascular malformations [2, 19].

The study by Choi et al. [3] followed-up patients starting in 1968, a time when heterotaxy patients had high mortality, and some were offered only palliative care. In the current era, patient survival is significantly better, and there is greater need to address noncardiac malformations. Among those screened for malrotation, two-thirds had radiographic evidence of such, a rate similar to that in a recent study by Ferdman et al. [5]. Our institution favors routine screening of asymptomatic children and prophylactic Ladd procedure for those with malrotation. The Ladd procedure involves lysis of intra-abdominal bands and intestinal fixation such that the pedicle of mesentery is wider and hence less likely to twist. Recommendations for preventative Ladd procedures should be balanced by procedure-related complication risks. One study of preventative Ladd procedures for patients with heterotaxy and complex congenital heart disease noted that 14 % had postoperative bowel obstruction [16]. This compares to 12 % in our study cohort.

Most patients with HS are presumed to have splenic dysfunction. Routine antibiotic prophylaxis and pneumococcal vaccination are recommended to decrease the risk of bacterial sepsis with encapsulated organisms, such as pneumococcus and meningococcus. Prendiville et al. [12] reported 8 culture positive sepsis events among 29 patients, which was greater than reported in our study (6 events). However, these events are recorded only for medical admissions, and there might have been patients with culture positive sepsis in the postoperative period that were not captured. Even though we do not routinely evaluate immune function in HS patients, we assess splenic anatomy and provide prophylactic antibiotics for both polysplenia and asplenia.

Recent articles have highlighted respiratory complications among children with heterotaxy compared with other patients with congenital heart disease. Swisher et al. [14]

Table 5 Resource utilization among HS survivors

Characteristics	Total patients ($N = 62$)	UV morphology ($N = 32$)	BV morphology ($N = 30$)	p
Age of survivors[a]	7.0 (3.6, 17.1)	7.2 (4.2, 17.7)	7.0 (2.8, 12.7)	0.324
Total encounters	30 (14, 47.5)	35 (20, 70)	22.5 (12.7, 39.2)	0.043*
Inpatient encounters	3 (2, 7)	5 (3, 8)	2 (1, 2)	0.002*
Outpatient encounters	27 (13.7, 44)	29 (14.7, 62.5)	19.5 (11, 32)	0.060
Total hospital days	44.5 (17.2, 81.2)	60 (29, 107)	22 (9, 54.5)	<0.001*
Total ICU days	17.5 (6.2, 35.5)	29 (12, 43)	10 (5, 22)	0.004*
Total ventilator days	4 (1, 9.5)	7.5 (1, 13)	2 (0, 6.5)	0.019*
Total hospital costs (USD)[b]	$135,025 ($59,340, $33,0835)	$200,634 ($107,645, $392,844)	$67,732 ($31,600, $158,341)	<0.001*
Medical admissions[c]	3.2 (4.6)	4 (5.07)	2.3 (3.94)	0.139
Hospital days	6 (1, 20)	10 (1, 22)	4 (0, 18)	0.203
ICU days	0 (0, 5)	1 (0, 5.7)	0 (0, 5)	0.249
Ventilator days	0 (0, 0)	0 (0, 0)	2 (0, 6.5)	0.475
Noncardiac surgeries[d]	1.6 (2.05)	1.8 (2.08)	1.4 (2.04)	0.475
Cardiac catheterizations	2.5 (0.5)	4 (3, 6.7)	0.5 (0, 2)	<0.001*

[a] All continuous variables expressed as median with interquartile ranges unless specified otherwise

[b] Standardized costs adjusted for inflation to 2011 USD

[c,d] Statistical mean with SD is listed

* Significant p value at < 0.05

reported that 7 % of their heterotaxy cohort underwent tracheostomy for prolonged mechanical ventilation. In our series, there were no patients who required tracheostomy. The increased respiratory complications have been assumed to be due to bronchial ciliary defects because there is a reported association between heterotaxy and primary ciliary dyskinesia both in animal models and some clinical studies [8, 15]. Among our patient population, respiratory infections were the cause of most medical hospital admissions, but they were not usually severe as seen by the low number of ICU days for such admissions. None of our patients were tested for primary ciliary dyskinesia; therefore, it is difficult to comment on such an association.

Patients with HS often have extracardiac manifestations necessitating medical care. In our study, the incidence of noncardiac anomalies was similar between UV and BV patients. The median number of noncardiac surgeries and medical admissions was also similar between the two groups. This suggests that ventricular anatomy does not affect noncardiac morbidity in patients with HS.

Patients with single-ventricle anatomy have complex heart disease necessitating multiple staged cardiac procedures, which accounts for the increased surgical morbidity and resource use in this patient group [18]. In addition, when comparing hospital costs, patients who survived with univentricular disease had significantly greater median costs during the years of study. However, when adjusted for mortality and variable follow-up, there were no significant cost differences between subgroups. Infants in both groups used significant health care resources and had substantial morbidity as reflected by days in the CICU as well as frequent outpatient medical encounters. We would expect that with a larger study cohort and improved survival among the UV group that their hospital cost during a lifetime would be significantly greater compared with HS patients who have BV heart disease.

There are several limitations to our retrospective, single-center study. First, although the data were obtained and reviewed in detail by two of the investigators using both electronic medical records and paper charts under the guidance of a pediatric cardiologist, there may have been better data-capture methods. The determination of visceral anatomy was performed by the information available for each case (U/S or CT), and we acknowledge that the tests have different sensitivities. With respect to encounters and cost data, these were obtained from the hospital finance department, which maintains records in a consistent manner. Second, there is a possibility that some patients received medical care in other hospitals, thus making it difficult to determine true resource use. Patients might have been transferred to/from other centers, the details of which were not captured in this data. However, PCMC is the only tertiary care pediatric center and provides care for a five state region (UT, ID, MT, WY, and NV), so unless the patient relocated outside of the Intermountain West area, it

is likely that their cardiac and other subspecialty care primarily occurred in our facility. Cost comparison over time among patients with high mortality is complicated, but we corrected our cost analyses for inflation and adjusted for mortality and variability of follow-up. The other costs that should be considered in the management of patients with HS, which were not assessed in the present study, include quality-of-life costs, opportunity costs to the parents who miss workdays to support and be with their sick children, and overall costs to productivity to the society. Last, although prenatal diagnosis was made in 32 of 78 patients and the birth weight and gestational age recorded for those available, the impact of these factors was not assessed given the lack of complete data.

Our study is the first to evaluate resource use among patients with HS. The data indicate that children with HS consume significant health care resources with most of the care being related to surgeries. Patients with BV morphology have significantly better survival, but their morbidity and resource use is similar to those of UV patients especially in the first few years of life.

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