Impact of preoperative risk factors on outcomes after Norwood palliation for hypoplastic left heart syndrome

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Background: Infants with hypoplastic left heart syndrome (HLHS) are susceptible to pre-Norwood comorbidities (PCs) and complications. This study aimed to describe the effect of PCs on timing and survival of Norwood palliation (NP).

Methods: A single-center, retrospective review of infants with HLHS who underwent initial NP between 2003 and 2010 was performed. PCs included intact atrial septum, ≥ moderate atrioventricular regurgitation (AVVR), no antenatal diagnosis, mitral stenosis/aortic atresia subtype, genetic abnormality, and prematurity. Complications included pre-NP mechanical ventilation, inotropic support, infection, arrhythmia, and end-organ injury. The primary outcome measure was survival after NP.

Results: 113 patients were included with 78 (69%) patients having at least one PC and 61 (78%) of those patients having at least one complication. Patients with PCs underwent NP later than those without PCs (7 vs 6 days, $P = .036$) as well as when associated with a complication (8 vs 5 days, $P < .001$). Patients with PCs had similar post-Norwood hospital length of stay ($P = .116$) except when the PC occurred in conjunction with a complication (28 vs 21 days; $P = .015$). In-hospital mortality post-NP was 10% and interstage mortality was 15%. On multivariable analysis, ≥ moderate AVVR was associated with increased overall mortality (OR 2.8, 95% CI 1.3-6.2). Age at NP was not associated with mortality ($P = .638$).

Conclusions: Although PCs are common in infants with HLHS, only ≥ moderate AVVR was associated with increased mortality in this single-center experience. Older age at NP was not a significant risk factor for interstage mortality. (J Thorac Cardiovasc Surg 2014;147:897-901)

Infants born with hypoplastic left heart syndrome (HLHS) are vulnerable to significant comorbidities and complications during the preoperative period before Norwood palliation (NP).[1,2] These pre-Norwood comorbidities (PCs) and complications have been implicated in both survival and developmental outcomes in multiple single-center and multicenter reports.[1,3-8] Most recently, results from the Single Ventricle Reconstruction trial demonstrated several anatomic considerations, such as the degree of atrioventricular valve regurgitation (AVVR) and ascending aorta diameter, and patient considerations, such as prematurity and chromosomal abnormalities, that were associated with increased post-Norwood morbidity and mortality.[7,8] Fortunately, continued advancement in antenatal diagnosis of HLHS by fetal echocardiography has helped decrease the incidence of some PCs and complications.[9-11] However, the survival benefit from antenatal diagnosis remains unclear.[10,12,13]

Advancements in surgical technique and perioperative care have improved survival in this population.[14,15] Nevertheless, even the most recent reports demonstrate that early post-Norwood and interstage mortality continue to plague these infants.[16,17] The timing of NP, a potential modifiable risk factor, has been the topic of prior study and has yielded mixed results. Although several reports have demonstrated decreased survival in infants undergoing NP at older ages,[2,6,14,18] others have reported either no difference in mortality or even improved survival with older age at NP.[1,7,19] Ultimately, the age at NP is somewhat an institutionally dependent factor reliant on surgical availability and referral patterns.

The objective of this study was to assess how the presence of PCs and complications affect early and interstage mortality in infants with HLHS in a single, tertiary care pediatric cardiac center. Secondarily, we sought to examine the effect of PCs on the timing of surgery and implications on mortality.

METHODS

Patient Selection

A retrospective review of the pediatric cardiovascular surgery database was performed to identify all infants with HLHS who underwent NP at our institution between January 2003 and December 2010. All infants with HLHS who underwent NP as their initial surgical procedure during the study period were reviewed, including those who required atrial septal or other catheter-based interventions in the pre-Norwood period. Infants with variants of this condition such as double-outlet right ventricle with mitral atresia as well as patients requiring initial operations other than the

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Abbreviations and Acronyms

AVVR = atrioventricular valvular regurgitation
CI = confidence interval
HLHS = hypoplastic left heart syndrome
IQR = interquartile range
LOS = length of stay
NP = Norwood palliation
OR = odds ratio
PCs = pre-Norwood comorbidities

Norwood operation were excluded. Given the study objective, patients with HLHS who were not palliated surgically were not included. The cohort of patients was subsequently assigned into 2 groups on the basis of the presence of PCs.

All available medical records, laboratory and imaging results, and applicable surgical reports were reviewed. We recorded the presence of PCs (defined below), pre-Norwood complications (defined below), age at NP, post-Norwood length of stay (LOS), and mortality. Patient data were recorded through stage II palliation. The study was approved by the Baylor College of Medicine Institutional Review Board.

Definitions

PCs included intact atrial septum, ≥ moderate AVVR, the lack of antenatal diagnosis, mitral stenosis–aortic atresia HLHS subtype, genetic abnormality, and prematurity. Intact atrial septum was defined as the absence of any atrium-level communication. Genetic anomalies were determined by chromosomal microarray analysis, genetic consult, or presence of dysmorphisms. Prematurity was defined as gestational age <37 weeks. The patient cohort was divided into the group with ≥1 PC (PC group) and the group who had no-PC (no-PC group).

Preoperative complications included mechanical ventilation, inotropic support, arrhythmia, end-organ damage, and infection. Mechanical ventilation was defined as ventilation for ≥24 hours that was not associated with elective intubation for transport. End-organ damage included neurologic (preoperative seizure or brain injury documented by imaging), hepatic (defined as elevation of transaminase > twice normal values and either persistent coagulopathy or hyperbilirubinemia), or renal injury (defined as ≥ pRIFLE I* classification[20]). Infection was defined as documented preoperative bacterial infection based on identified organism or presumptive infection treated with intravenous antibiotics for ≥7 days.

Infancy was defined as age <12 months and the pre-Norwood period included the time from birth or transfer to our institution to the time of NP. Our study evaluated both the inpatient and interstage periods between Norwood and stage II palliation. The inpatient period was defined as either the time from NP to hospital discharge, from NP to stage II if the patient required continued hospitalization, or from NP to time of death if mortality occurred before hospital discharge. The interstage period was defined as the time after hospital discharge after the Norwood procedure but before stage II palliation.

Data Collection and Statistics

The data were not normally distributed. Descriptive statistics are reported using median and interquartile range for scale variables and proportions for categorical variables. Univariable analysis of categorical variables was performed by the Pearson χ^2 or Fisher exact test, whereas continuous variables were analyzed using the Mann-Whitney U test. Univariable and multivariable Cox regression analyses were used to determine risk factors for mortality and are expressed as hazard ratios and 95% confidence intervals (CIs). Univariable factors found to be associated with mortality with a P value < .100 were included in the multivariable analysis. Survival functions were estimated using Kaplan-Meier analysis with log rank test of significance. Two-tailed test of significance was used in all statistical analyses. Statistics were performed using SPSS version 19.0 (IBM Corp, Armonk, NY).

* RIFLE = Risk, Injury, Failure, Loss, and End-stage kidney disease.

RESULTS

Patient Population

Of 117 patients identified with HLHS, 113 patients met inclusion criteria and were included in the data analysis. Four patients with HLHS did not undergo initial NP and were excluded from data analysis. These patients included 1 patient who underwent initial bilateral pulmonary artery banding who died in the interstage period, 2 patients with intact atrial septum who received comfort care, and 1 patient who underwent hybrid palliation as a bridge to successful cardiac transplantation owing to coronary artery–left ventricle fistulas.

A total of 78 (69%) patients had at least 1 PC. Patient demographics and frequency of PCs are listed in Table 1. Among patients with PCs, 36 (46.1%) patients had 1 PC, 36 (46.1%) had 2 PCs, 5 (6.4%) had 3 PCs, and 1 (1.3%) had 4 PCs. Of the 78 patients with a PC, 61 (78.2%) had a pre-Norwood complication. Patients with PCs had more frequent preoperative complications than those without PCs as demonstrated by higher rates of inotropic support (57.7% vs 28.6%; $P = .004$), mechanical ventilation (44.9% vs 22.9%; $P = .026$), and infection (11.5% vs 0%; $P = .036$). There was no significant intergroup difference in the rate of arrhythmia (1.3% vs 8.6%; $P = .053$). The presence of pre-Norwood complications by PC is listed in Table 2.

Despite similar rates of antenatal diagnosis in nonwhite versus white patients (62.3% vs 48.3%; $P = .138$), nonwhite patients were more likely to be born outside of our institution (odds ratio [OR], 3.0; 95% CI, 1.4-6.6). However, the frequency of PC did not differ between nonwhite versus white patients (55.1% vs 48.6%; $P = .518$). With regard to pre-Norwood complications, patients with no antenatal diagnosis were more likely to have a complication than those with antenatal diagnosis (OR, 8.3; 95% CI, 3.6-19.3). The use of a modified Blalock-Taussig shunt versus a Sano conduit was similar between the PC and no-PC groups (76.9% vs 88.6%; $P = .148$).

The overall survival to stage II palliation for the cohort was 75.2% (85 patients). Among the 28 patients who died, 11 (9.7%) patients died during the inpatient period and 17 (15.1%) died during the interstage period. On univariable analysis of PCs, intact atrial septum and ≥ moderate AVVR were associated with increased overall mortality (Table 3). Likewise, mechanical ventilation before the NP was found to be associated with increased mortality ($P = .010$). On multivariable analysis, only ≥ moderate