Stage I palliation for hypoplastic left heart syndrome in low birth weight neonates: can we justify it?

Christian Pizarro, Deborah A. Davis, Mark E. Galantowicz, Hamish Munro, Samuel S. Gidding, William I. Norwood

Objective: Although the outcome of cardiac surgery in neonates with low birth weight (LBW) has improved, LBW remains a risk factor for surgical palliation. Few surgical series of LBW patients include those with hypoplastic left heart syndrome (HLHS). To identify variables associated with poor outcome in this group, we reviewed our experience with patients with HLHS and LBW who underwent Stage I Norwood palliation.

Methods: Between January 1998 and December 2000, 20 consecutive LBW (<2500 g) neonates with HLHS (n = 13) or HLHS variant (n = 7) underwent surgical palliation. Retrospective review of all patient data and analysis to identify risk factors was performed.

Results: Mean age at surgery was 5.1 ± 4.6 days (range 1–17), mean weight was 1.98 ± 0.44 kg (range 1.1–2.5), including nine patients under 2 kg. Ten patients were born at <35 weeks gestation. Anatomic diagnosis included HLHS in 13 patients (10 with aortic atresia), unbalanced atioventricular canal defect in two, double outlet right ventricle in two and other variants in three. Mean ascending aortic size was 4.0 ± 1.8 mm (range 1.5–8). Associated cardiac defects were present in three patients, and a genetic syndrome and/or congenital anomaly was present in four of them. Mean circulatory arrest time was 60 ± 10 min. Extracorporeal support was used perioperatively in 10 patients. Early mortality was 9/20 (45%). At a mean follow up at 22 ± 10 months (range 8–38), six patients underwent stage II, and are awaiting stage III; four patients have completed their Fontan. Anatomic variant, ascending aortic size, prematurity, age at surgery, weight, duration of circulatory arrest, cardiopulmonary bypass time and associated non-cardiac anomalies were not risk factors for poor outcome whereas restrictive pulmonary venous drainage and coronary artery anomalies were associated with decreased survival.

Conclusion: LBW newborns with HLHS and physiologic variants have an increased early surgical risk but have acceptable intermediate survival rates for subsequent palliation including Fontan. LBW and prematurity should not be contraindications to early surgical palliation.

Keywords: Hypoplastic left heart syndrome; Norwood procedure; Congenital; Pediatric; Cardiac surgery; Single ventricle

1. Introduction

Hypoplastic left heart syndrome (HLHS) is one of the most common forms of congenital heart disease characterized by a single ventricle and is universally lethal if left untreated. The overall survival after the first stage surgical reconstruction for HLHS has improved continuously since its original successful introduction by Norwood et al. almost two decades ago [1]. In the current era, the Norwood procedure has emerged as the preferred management strategy for patients with HLHS and many other complex forms of congenital heart disease with compromised systemic blood flow. Currently, survival rates approach 80% in several different centers [2–6]. In light of these encouraging reports, the natural evolution of this surgical management strategy has resulted in the gradual extension to a subgroup of patients considered high risk, namely those with ventricular dysfunction, some degree of AV valve regurgitation, and associated non-cardiac anomalies.

Increasingly, neonatal surgery has been extended to infants with low birth weight (LBW) and prematurity. This is critical because many serious congenital heart defects including HLHS are associated with diminished birth weight [7]. Reasonable success has been reported in studies that include patients with tetralogy of Fallot, transposition of the great arteries, and truncus arteriosus [8–10].
However, few studies have included patients with HLHS or single ventricle complexes which result in a ductus-dependent systemic circulation [11].

The objective of this report is to (1) describe our experience with the reconstructive surgical strategy for LBW neonates with HLHS and/or other conditions resulting in a single ventricle and a ductus-dependent systemic circulation and (2) identify potential risk factors for poor outcome.

2. Material and methods

We reviewed all patients who underwent the Stage I Norwood procedure at our institution between January 1998 and December 2000. A total of 85 patients were identified. Of these, 20 had a birth weight of ≤2500 g (LBW) and constitute the focus of this report. Patient data were obtained by review of clinical records, including operative reports, perfusion data and preoperative imaging.

The anatomic diagnosis of HLHS or HLHS variant was based on two-dimensional echocardiography and required the presence of a small ascending aorta, aortic atresia or hypoplasia and a hypoplastic left ventricle and/or a single ventricle complex with a ductus-dependent systemic circulation. Any cardiac anomaly not considered a basic feature of HLHS or HLHS variant was labeled as an associated cardiac defect.

Stage I surgical reconstruction included atrial septectomy, association of the aorta and main pulmonary artery, aortic arch augmentation with cryopreserved homograft and creation of a systemic to pulmonary artery shunt between the innominate artery and right pulmonary artery. Shunt size was determined according to the innominate artery and right pulmonary artery. Shunt size was determined according to the innominate artery and right pulmonary artery. Shunt size creation of a systemic to pulmonary artery shunt between the aortic arch and main pulmonary artery, association of the aorta and main pulmonary artery, hypoplasia and a hypoplastic left ventricle and/or a single ventricle complex with a ductus-dependent systemic circulation. Any cardiac anomaly not considered a basic feature of HLHS or HLHS variant was labeled as an associated cardiac defect.

Stage I surgical reconstruction included atrial septectomy, association of the aorta and main pulmonary artery, aortic arch augmentation with cryopreserved homograft and creation of a systemic to pulmonary artery shunt between the innominate artery and right pulmonary artery. Shunt size ranged between 3 and 4 mm, and was determined according to the innominate artery and right pulmonary artery. Shunt size was determined according to the innominate artery and right pulmonary artery. Shunt size was determined according to the innominate artery and right pulmonary artery. Shunt size was determined according to the innominate artery and right pulmonary artery. Shunt size was determined according to the innominate artery and right pulmonary artery.

The second stage was performed at about 6 months, mostly by creation of a hemi-Fontan type connection, and the Fontan was completed by 12 months of age.

Risk factors examined for their potential influence on operative mortality included age, birth weight, weight at surgery, gestational age, multiple pregnancy, prenatal diagnosis, lowest preoperative pH, HLHS or HLHS variant, aortic atresia, and additional cardiac or non-cardiac diagnosis. Echocardiographic risk factors included assessment of ventricular function, AV valve regurgitation and restriction of pulmonary venous return. A flow velocity ≥2 m/s by color flow interrogations of interatrial septal communication or anomalous pulmonary venous connection was defined as restrictive pulmonary venous drainage. Surgical variables included cardiopulmonary bypass and circulatory arrest times, use of extracorporeal circulatory support, shunt size, and need for additional surgery.

Operative mortality was defined as mortality within 30 days or prior to hospital discharge. Significant morbidity was defined as dysfunction of at least one organ system, which resulted in prolonged hospital course and/or required specific therapeutic intervention.

Follow-up data was obtained from all 11 survivors (100%). This information was obtained directly from the family and/or the patient’s cardiologists during a 2-month period ending July 31, 2001. We examined Stage I mortality and survival to second and/or third stage when appropriate.

3. Results

There were 11 males and nine females. The mean patient weight was 1.98 ± 0.44 kg (range 1.1–2.5), and nine patients were under 2.0 kg. The mean age at the time of surgery was 5.1 ± 4.6 days (range 1–17), and ten patients were born at ≥35 weeks gestation. There was no appreciable weight change between birth weight and weight at surgery. Five patients were the products of multiple pregnancy. Genetic syndromes were identified in four patients, two with Turner’s, one with CHARGE association and one with partial chromosome 18 translocation.

Distribution of anatomic subtypes was as follows: six had aortic atresia with mitral atresia (aa,ma), five had aortic atresia with mitral stenosis/hypoplasia (aa,ms) and two had aortic stenosis with mitral stenosis/hypoplasia (as,ms). Seven patients had other variants, including two patients with unbalanced complete common AV canal and two patients with double outlet right ventricle and mitral hypoplasia or atresia (ma).

The ascending aorta diameters had a broad range of distribution. Eleven patients had a diameter between 1.5 and 4 mm (including two patients with diameters under 2 mm) and nine patients had a diameter >4 mm. Ascending aorta diameters tended to be larger in patients with aortic stenosis rather than atresia (Fig. 1).

Preoperative ventricular function was preserved in 16 patients, and three had impaired ventricular function. There were no patients with significant AV valve regurgitation. Five patients had some form of restriction of pulmonary venous return, one of them with total anomalous pulmonary venous drainage. Three patients had a significant associated cardiac diagnoses. Coronary anomaly was present in two patients, one with a coronary cameral fistula and one with a high take off of the right coronary artery above the sinotubular junction (Table 1).

The mean duration of deep hypothermic circulatory arrest
was 60 ± 10 min. Nine patients received extracorporeal circulatory support in the postoperative period due to cardiac [9] and/or respiratory [1] failure. Support was initiated in the operating room in five patients (two survivors), and in the intensive care unit in nine patients (one survivor), respectively.

The median hospital stay for hospital survivors was 16.5 days, with a range of 8–85 days, and 3 days, with a range of 1–8 for non-survivors. The median hospital stay for all patients was 9 days, with a range of 1–85 days.

Significant morbidity was present in all but two patients. Cardiac dysfunction was present in 12 patients, renal dysfunction in nine, respiratory failure including periodic breathing and/or apnea in eight patients, feeding intolerance and poor weight gain in six, seizures in four and infection in four.

Early mortality was 9/20 (45%). Hospital mortality was due to cardiac causes in eight patients with two of these from coronary insufficiency documented by direct operative or angiographic inspection. Three patients developed multi-system organ dysfunction, and one had necrotizing enterocolitis as the terminal event. One patient died of respiratory complications.

Among the patients with coronary perfusion problems, one was a 1500 g 33-week premie, product of a twin pregnancy whose diagnosis was HLHS (aa,ma) and a 1.5 mm ascending aorta; the other was a 2400 g term newborn with HLHS (as,ma) and a 4 mm ascending aorta, associated with a high origin of the right coronary artery noted during the surgical procedure. Both patients had intraoperative signs of low cardiac output and were temporarily placed on extracorporeal support. The death due to respiratory failure occurred in a 17-day old 1400 g triplet with HLHS (aa,ms) and moderate ventricular dysfunction, after extubation on the first postoperative day.

Continuous variables examined as potential risk factors for mortality are shown in Table 2. There was a tendency towards worse outcome at earlier gestational age (34.2 vs. 36.2 weeks), but this difference did not reach statistical significance. Median cardiopulmonary bypass time was 89 min in non-survivors and 96 min in survivors; only four patients had bypass time >2 h, in each group.

Among the categorical variables analyzed, the presence of restrictive pulmonary venous drainage (4/9 vs. 1/11, \( P = 0.058 \)) was associated with early mortality. Due to the fact that all patients had adequate AV valve function, and only three had significant ventricular function impairment, no significant comparison could be made for these two variables. However, two of three patients with ventricular dysfunction died. At least one of the above mentioned variables was present in six of nine non-survivors. Use of a shunt <4 mm and need for extracorporeal circulatory support (ECCS) in the perioperative period demonstrated a tendency towards increased mortality independently, however, they did not reach significance \( (P < 0.10) \). Prenatal diagnosis, lowest preoperative pH, anatomic variant, ascending aortic size, additional cardiac and non-cardiac diagnosis, and multiple pregnancy did not have an impact on outcome.

At a mean follow-up of 22 ± 10 months (range 8–38), there was one late death of a 4-month-old patient with HLHS (aa,ma) after Stage I palliation, from recurrent RSV bronchiolitis. Among 10 late survivors, four patients completed all three stages and six have completed a second stage (bi-directional Glenn or Hemifontan) and are awaiting their Fontan completion. Among the four patients with specific genetic syndromes, three survived after hospital

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**Table 1**

<table>
<thead>
<tr>
<th>Additional cardiac and non-cardiac diagnoses</th>
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<tbody>
<tr>
<td>Number</td>
</tr>
<tr>
<td>---------------------------------------------</td>
</tr>
<tr>
<td>LSVC(^a)</td>
</tr>
<tr>
<td>Left atrial membrane</td>
</tr>
<tr>
<td>Coronary-cameral fistula</td>
</tr>
<tr>
<td>High coronary origin</td>
</tr>
<tr>
<td>TAPVD(^b)</td>
</tr>
<tr>
<td>Turner syndrome</td>
</tr>
<tr>
<td>CHARGE association</td>
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<tr>
<td>Partial chromosome 18 translocation</td>
</tr>
</tbody>
</table>

\(^a\) LSVC, left superior vena cava.
\(^b\) TAPVD, total anomalous pulmonary venous drainage.

**Table 2**

Comparison between continuous variables\(^a\)

<table>
<thead>
<tr>
<th>Variable (mean value)</th>
<th>Survivors/non-survivors</th>
<th>( P )</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age at surgery (days)</td>
<td>4/6</td>
<td>NS</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>2.0/1.9</td>
<td>NS</td>
</tr>
<tr>
<td>Gestational age (weeks)</td>
<td>36.2/34.2</td>
<td>NS</td>
</tr>
<tr>
<td>Shunt size (mm)</td>
<td>3.7/3.5</td>
<td>NS</td>
</tr>
<tr>
<td>CPB time (min)</td>
<td>111/131</td>
<td>NS</td>
</tr>
<tr>
<td>Circulatory arrest time (min)</td>
<td>60.4/60.3</td>
<td>NS</td>
</tr>
</tbody>
</table>

\(^a\) CPB = cardiopulmonary bypass, NS = not significant.
discharge and have completed the second stage with two awaiting the Fontan completion.

4. Discussion

Despite the remarkable progress made in achieving successful repair of congenital heart defects in the neonatal period, this approach has only been recently applied in LBW neonates, due to the perception that LBW would add a significant risk for early mortality [12]. The reasons for the increased risk in this group of patients are most likely multiple. They include technical aspects of the surgical reconstruction, decreased cardiac compliance of the immature heart, underdeveloped pulmonary vasculature, increased incidence of hyaline membrane disease and necrotizing enterocolitis, immature kidney and liver function, defective calcium and glucose homeostasis, immature germinal matrix and poor tolerance of the deleterious effects of cardiopulmonary bypass.

LBW is common in infants with congenital heart disease [7]. In fact, it was present in over 20% of our patients who were candidates for staged surgical reconstruction for HLHS. Recent studies suggest that complete repair in LBW infants with a variety of lesions, including tetralogy of Fallot, transposition of the great arteries, truncus arteriosus and aortic arch obstruction with ventricular septal defect can be successfully accomplished with low mortality [8–10,14].

After two decades of continuous experience, Norwood’s first stage surgical reconstruction for HLHS has reached widespread acceptance as the management strategy for this lethal form of congenital heart disease. The current success with this approach is well documented in the literature worldwide [2–6,13]. However, LBW is still considered a risk factor for palliation of single ventricle complexes with a ductus-dependent systemic circulation. This may be due to the increased demands and potential imbalance of the systemic and pulmonary flow ratios, resulting in a labile physiology, which is more evident in the LBW neonate. Bove et al. [2] and Forbes et al. [16] have reported their experience to support the notion of increased mortality in a group of patients under 3.0 kg who underwent Stage I palliation. In our study that includes only LBW infants, mortality was higher than the reported risk for staged surgical reconstruction for normal birth weight infants.

A number of other potential risk factors for early mortality after Stage I Norwood palliation have been reported in the literature including the presence of aortic atresia, mitral atresia, diagnosis other than HLHS, preoperative organ dysfunction, pulmonary venous obstruction/intact atrial septum, prolonged cardiopulmonary bypass, among others [2,3,6,13,15–17]. Our results revealed that coronary artery anomalies, preoperative ventricular dysfunction and/or restrictive pulmonary venous drainage had a negative impact on early survival.

In order to reduce the operative risk of staged surgical reconstruction, other forms of treatment for HLHS have been sought, including cardiac transplantation. Experience has been gained with cardiac transplantation for HLHS and its application has also included LBW patients. However, the Congenital Heart Surgery Study showed LBW to be an incremental risk factor for mortality in both the staged surgical reconstruction and the cardiac replacement protocols [3]. Moreover, recent experience from the Pediatric Heart Transplant Study Group suggested that the proportion of LBW neonates transplanted has increased significantly, but their overall risk after listing, including pre- and post-operative mortality, remain as high as 57% [18]. Based on this data, it would seem reasonable to use the surgical reconstruction strategy even for LBW patients with HLHS in order to leave the limited donor pool to the patients who do not have any other surgical alternative of treatment.

Another effort to reduce the morbidity and mortality after staged surgical reconstruction includes the use of ECCS in the perioperative period. Nearly half of the patients in this cohort received ECCS, mostly due to cardiac/pulmonary dysfunction, but only three patients survived after hospital discharge. The limited success with ECCS is perhaps related to the high number of premature newborns in this group and their decreased ability to tolerate the side effects of ECCS. This observation agrees with the overall experience with ECCS for neonates with single ventricle physiology after Norwood palliation reported by our institution and others [19,20].

In our study, there was one late mortality after completion of Stage I Norwood. All other patients have followed the normal staging process with good results and no mortality during the follow-up. With reference to neurological outcome, two patients have evidence of developmental delay on clinical examination, however, a true impact of LBW on neurological outcome after Stage I surgical palliation is difficult to ascertain without a formal neurodevelopment assessment in a larger cohort of patients. Our observations in this group of patients lead us to the conclusion that once the perinatal and perioperative issues have been resolved, the overall outcome of these patients seems no different from their normal size peers.

We conclude that staged surgical reconstruction for LBW neonates with HLHS carries an increased initial surgical risk, but provides a good and reproducible management strategy with reasonable survival rates for this subgroup of patients. Further staged palliation can be carried out with results similar to larger infants. LBW and prematurity should not be regarded as a contraindication to staged surgical reconstruction for HLHS.

5. Limitations

The main limitation of this review is the retrospective data acquisition and the reduced number of patients.
These factors need to be considered with reference to the potential lack of power for statistical analysis. The lack of a randomization process and the lack of a group for comparison also make the analysis difficult and susceptible to error. Due to the inclusion criteria, it was not possible to identify patients who were not referred for surgery because of low weight or patients who died before surgery, making the population studied subjected to bias.

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References
