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ORIGINAL ARTICLE

Clinical Course and Interstage Monitoring After the Norwood and Hybrid Procedures for Hypoplastic Left Heart Syndrome

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Abstract Infants with hypoplastic left heart syndrome (HLHS) are at risk for interstage morbidity and mortality, especially between the first and second surgical stages after the Norwood and hybrid procedures. This study compared the morbidity and mortality of patients treated by either the Norwood or the hybrid procedure for HLHS between the first and second stages who were undergoing interstage monitoring. Between October 2008 and December 2011, 26 infants (14 boys) with HLHS ($n = 16$) and other univentricular heart malformations with aortic arch anomaly ($n = 10$) were scheduled for interstage monitoring after Norwood I ($n = 12$) and hybrid ($n = 14$) procedures. Three infants (11.5 %) died after first-stage palliation (one hybrid patient and two Norwood patients), and three infants (11.5 %) died after second-stage palliation (two hybrid patients and one Norwood patient) ($p = 0.83$), all after early second-stage surgery (<90 days). The Norwood I and hybrid procedures did not differ in terms of overall mortality (23 %) (three hybrid and three Norwood patients; $p = 1.00$). Seven infants (26.9 %) could not be discharged from the hospital due to hemodynamic instability and were referred for early second-stage surgery (<90 days). After the first stage, the invasive reevaluation rate before discharge was high (53.8 %), with cardiac catheterizations for 8 of 14 patients after the hybrid procedure and for 6 of 12 patients after the Norwood procedure ($p = 0.69$). A total of 11 reinterventions were performed (eight by catheter and three by surgery). Of the eight catheter reinterventions, five were performed for hybrid patients ($p = 0.22$). For 14 infants, 89 days (range 10–177 days) of interstage monitoring were scheduled. One infant (3.9 %) died during the interstage monitoring. The findings showed a breach of the physiologic criteria for interstage monitoring in seven infants (50 %) after 10 days (range 4–68 days) (five hybrid and two Norwood patients), leading to rehospitalization and catheterization for six patients (four hybrid and two Norwood patients), requiring interventions for two patients (patent arterial duct stent dilation, and atrial septal defect stenting, all for hybrid patients). Overall, three of the seven patients with red flag events of interstage monitoring were candidates for early second-stage surgery. In conclusion, morbidity among infants treated for HLHS remains high, either before or after hospital discharge, emphasizing the need of interstage monitoring programs. Despite retrograde aortic flow in infants with HLHS after the hybrid procedure, the mortality rate was comparable between the two groups. Mortality occurs after early second-stage surgery (<90 days).

Keywords Hypoplastic left heart syndrome · Interstage morbidity and mortality · Norwood procedure · Hybrid procedure

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Introduction

Hypoplastic left heart syndrome (HLHS) is one of the most complex types of congenital heart disease. The last decade has seen continuous efforts to optimize treatment for

patients with HLHS. The Norwood procedure has been the classical surgical treatment for HLHS, but meanwhile, the hybrid procedure has been used as an alternative approach, with comparable results [1, 11].

The hybrid procedure combines cardiac surgery (bilateral pulmonary branch artery banding) and catheter intervention with stenting of the patent arterial duct (PDA) and balloon dilation of the atrial septal defect (ASD) [1, 11]. Nevertheless, patients after first-stage palliation with either the Norwood or the hybrid procedure remain at risk for interstage morbidity and mortality [4, 10, 17, 24]. Therefore, interstage monitoring has proved to be effective in reducing interstage mortality and for that reason has been introduced in many centers to optimize the patient's safety in the ambulant setting [12].

In the past decade, studies have compared both treatment options [3, 19, 22], but to date, prospectively collected data on interstage morbidity and mortality of infants after the Norwood and hybrid procedures are limited. We reviewed the clinical course, the outcomes, and the characteristics of the subjects enrolled in the interstage monitoring program. Outcome was defined as mortality and morbidity, including rehospitalization and need for reinterventions.

Patients and Methods

Study Design

We conducted a longitudinal observational study of the clinical courses and outcomes of patients undergoing the interstage home monitoring program after the Norwood I and hybrid procedure for infants with variants of HLHS.

Study Population

Since October 2008 and December 2011, all infants with HLHS and other univentricular heart malformations with aortic arch anomaly have been scheduled to undergo interstage monitoring after the Norwood I and hybrid procedures.

Interstage Monitoring

Our standardized program of interstage home monitoring was adopted from former published protocols [12, 13, 15]. Parents were taught by specialized nurses to recognize symptoms of deterioration such as poor feeding, increased sweating, dyspnea, tachypnea, edema, and irritability. Furthermore, the parents were taught to detect failure to thrive and deterioration of systemic oxygenation and to perform daily measurements of body weight and transcutaneous oxygen saturation ($tcSO_2$). Measurement of body weight was recommended once per day at the same time point before feeding (at about noontime).

For measurement of $tcSO_2$, we used a small handheld pulse oximeter (Rad-5; Masimo Co., Irvine, CA, USA). Measurements were performed three times per day at comparable time points in the morning, at noon, and in the evening. The sensor was placed around the same hand, and $tcSO_2$ values were noted when the infant was calm and signal intensity was good. The values of body weight and $tcSO_2$ were noted in a protocol given to the parents after detailed instructions before discharge of the infants from the hospital. The red flags of interstage monitoring were defined as (1) loss of body weight exceeding 50 g within 2 days or gain in body weight less than 20 g or more than 150 g for two consecutive days, and (3) $tcSO_2$ values lower than 70 % or higher than 85 % or those otherwise predefined individually by the pediatric cardiologist before the infant's discharge from the hospital.

Parents were instructed to contact the staff pediatric cardiologist of our hospital immediately for rehospitalization aimed at an urgent diagnostic workup in case of red flags during interstage monitoring. Clinical visits were routinely performed every 2 weeks either by the staff pediatric cardiologist of our hospital or by the individual outpatient pediatric cardiologist.

Clinical Course

Morbidity was defined as the need for rehospitalization and reintervention and included cases of red flags during interstage monitoring. Cardiac diagnoses were made by an experienced cardiologist based on findings in echocardiography, cardiac catheterization, and cardiac magnetic resonance imaging.

Ethics

Ethical approval for the study and data collection was obtained according to the guidelines of the local ethics committee.

Statistical Analysis

For descriptive statistics, values are shown as median with range. Differences between the treatment groups were tested using Fisher's exact test for categorical variables and an exact Mann–Whitney U test for quantitative variables.

Results

Patients

Between June 2008 and December 2011, 26 infants (14 boys) with classical HLHS ($n = 16$) and its variants

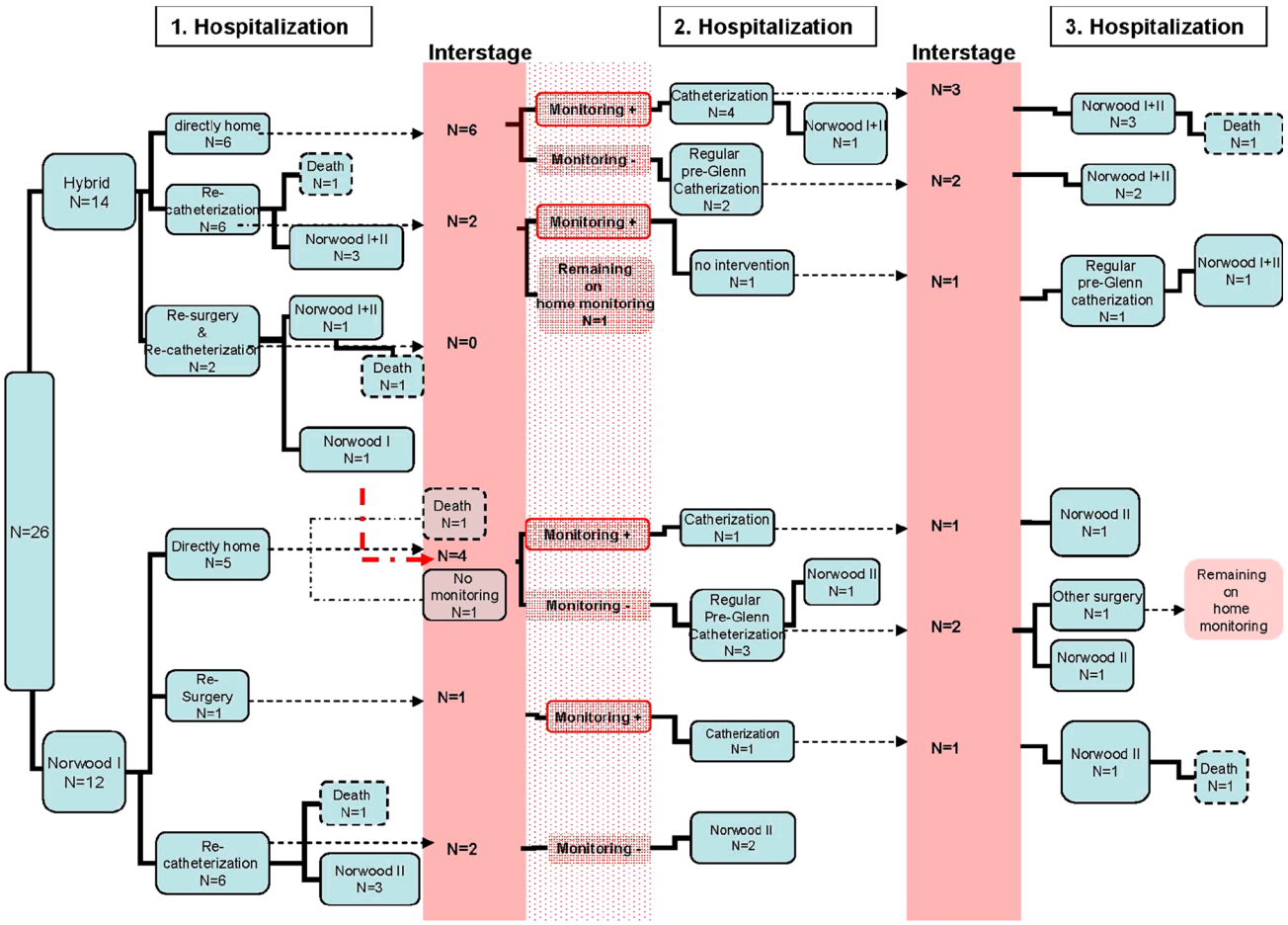

Fig. 1 Overview of the clinical course and interstage monitoring of infants with hypoplastic left heart syndrome treated by the hybrid and Norwood procedures

(functional hypoplastic left heart complex), including univentricular heart malformations with aortic arch anomaly ($n = 10$), were scheduled for interstage monitoring. The cardiac diagnoses of the patients with variants of hypoplastic left heart included double-outlet right ventricle ($n = 4$), double-inlet left ventricle ($n = 2$), dysbalanced atrioventricular septal defect ($n = 2$), and borderline hypoplastic left heart with left ventricular outflow tract obstruction ($n = 2$). Of the 26 infants, 12 were treated by the Norwood I procedure and 14 by the hybrid procedure. The infants treated by the Norwood I procedure received the modified Blalock–Taussig (BT) shunt ($n = 7$) or the right ventricle-to pulmonary artery (Sano) shunt ($n = 5$).

The median age at first-stage palliation was 8 days (range 1–36 days). The infants undergoing the hybrid procedure were younger at first-stage palliation (age, 4 days; range 1–17) than those undergoing the Norwood procedure (age, 9 days; range 3–36 days) ($p = 0.02$). The median day at second-stage palliation, if performed, was 99 days (range 48–190 days). These values did not differ between the Norwood and hybrid procedures ($p = 0.44$). The clinical course after first-stage palliation, with either the hybrid or Norwood procedure, is depicted in Fig. 1.

Mortality

Three infants (11.5 %) died after first-stage palliation. One patient died after the hybrid procedure at the hospital before discharge (at age 44 days), and two patients died after the Norwood I procedure, either before discharge at the hospital (at age 90 days) or after discharge at home (at age 33 days; Fig. 1).

Three infants (11.5 %) died after second-stage palliation. Two patients in the hybrid group died after comprehensive stage 1 or 2 palliation at the hospital before discharge, one early (at age 124 days) and one late (at age 10.4 months). One patient in the Norwood group died early after Norwood II (at age 106 days). Whether infants died after first- or second-stage palliation or survived did not differ between the treatment groups ($p = 0.83$).

All the patients in the Norwood group who died were treated primarily with a BT shunt. For all the patients who died after second-stage palliation, the time until the second

stage was less than 90 days. The Norwood I and hybrid procedures did not differ in terms of mortality rate (23 %; $p = 1.00$).

Morbidity

Seven infants (26.9 %) could not be discharged from the hospital due to hemodynamic instability and were referred for early second-stage palliation (<90 days) (Fig. 1). After first-stage palliation, the invasive reevaluation rate before discharge was high, with cardiac catheterizations needed for 14 patients (53.8 %; eight hybrid and six Norwood patients; $p = 0.69$).

Catheter reinterventions became necessary for eight infants (30.7 %; five hybrid and three Norwood patients; $p = 0.22$). These eight reinterventions included stenting of the left pulmonary artery ($n = 1$), residual aortic coarctation ($n = 1$), and stenosis of the Sano shunt ($n = 1$) in infants after the Norwood procedure, as well as balloon dilation of pulmonary artery banding ($n = 3$) and balloon dilation and/or stenting of atrial septal defect ($n = 2$) in infants after the hybrid procedure.

Surgical reinterventions were necessary for three infants (11.5 %) including enlargement of residual aortic coarctation ($n = 1$; after the Norwood procedure) and rebanding of pulmonary artery side branches ($n = 2$; after the hybrid procedure) ($p = 1.00$).

Interstage Monitoring

Only 14 of the 26 infants could be discharged from the hospital and received interstage monitoring for a period of 89 days (range 10–177 days) (Fig. 1). One of the two additional infants scheduled for interstage monitoring received home monitoring until the end of the study period (to date, without red flags), and the family of the other infant did not perform interstage monitoring (Fig. 1).

One infant (3.9 %) died during interstage monitoring after the Norwood procedure. We found a breach of the physiologic criteria for interstage monitoring in 50 % of the infants ($n = 7$, comprising five hybrid and two Norwood patients) after 10 days (range 4–68 days).

The red flags for interstage monitoring included lower oxygen saturation ($n = 6$); clinical signs of congestive heart failure including poor feeding, sweating, dyspnea, tachypnea, and sudden malaise with episodes of irritability ($n = 4$); and excessive body weight gain ($n = 1$). All the red flag events of interstage monitoring led to rehospitalization within 48 h and cardiac catheterization for six infants (four hybrid and two Norwood infants; $p = 0.39$), requiring interventions for two infants (PDA stent dilation or ASD stenting, all for hybrid patients). Three of the seven patients with red flag events of interstage monitoring were candidates for an early second-stage surgery.

Discussion

Infants with HLHS and its functional variants are at risk for a complicated clinical course including severe morbidity, or even interstage mortality, after first-stage palliation by the Norwood or hybrid procedure. Reinterventions either by cardiac catheterization or by cardiac surgery were common in both treatment groups. Remarkably, only 3 of the 26 patients (two after the hybrid procedure and one after the Norwood procedure) experienced a completely uneventful clinical course without the need for reintervention, leading to successful second-stage palliation with a fairly good outcome.

In our cohort, the number of patients not discharged after first-stage palliation was relatively high (26.9 %), leading to earlier timing of second-stage palliation. Nevertheless, the Norwood and hybrid procedures did not differ in overall mortality. Previous studies have described early second-stage palliation as associated with risk factors for interstage mortality including reduced pulmonary artery growth, elevated pulmonary vascular resistance, and reduced myocardial function associated with atrioventricular valve regurgitation [2, 14]. On the other hand, the early timing of second-stage palliation may reflect a sicker phenotype of HLHS interacting with a higher rate of perioperative complications.

Before the first discharge from the hospital, an invasive reevaluation with cardiac catheterization became necessary for more than half of the patients (53.8 %). Catheter reinterventions were indicated for both the hybrid and Norwood procedures (30.7 %). Surgical reinterventions became necessary less frequently but also were comparable between the two treatment groups (11.5 %).

As described by previous publications, the complications in the current study included vascular stenosis of the left pulmonary artery, residual aortic coarctation, and stenosis of the right ventricle-to-pulmonary artery (Sano) shunt. Also as described previously [5, 7, 9], we were able to treat these complications successfully by endovascular stent implantation. Suboptimal banding of the pulmonary branch artery was treated by surgical revision.

Even if discharge from hospital is reasonable, the risk of adverse events remains high but can be sufficiently detected by interstage monitoring. If a breach of physiologic criteria for interstage monitoring occurs, we prefer invasive reevaluation with cardiac catheterization. Otherwise, we could find no other conclusive explanation. This led to a considerable number of catheter reinterventions.

Additionally, monitoring data serve as part of the clinical decision-making process together with hemodynamic findings obtained by cardiac catheterization. To date, no significant difference has been detectable between patients treated by the Norwood procedure and those treated by the hybrid procedure, only a trend toward more red flag interstage monitoring events and more reinterventions for patients after the hybrid procedure. Further multicenter studies are necessary to determine whether this difference, which may be attributable to the circumstance of ongoing retrograde aortic flow in patients after the hybrid procedure, can be confirmed.

One single patient of our cohort died despite red flag events of interstage monitoring at home after the Norwood procedure with a BT shunt at the age of 33 days. After red flag events of interstage monitoring, this patient was transferred immediately to the local children's hospital, where sudden hemodynamic collapse with impossibility of successful resuscitation occurred directly after arrival. Due to the geographic distance to the primary treating cardiac center, no further support, including options of assist devices, was available. The exact cause of death remained unexplained, but as described in the literature, BT shunt might have been a risk factor for this patient [14, 20].

The overall interstage mortality at home in our cohort was 7.1 %. This number is well within the range of interstage mortality (0–22 %) described in the literature [12, 15, 21].

The high number of red flag interstage events in our cohort shows clearly that interstage home monitoring is a valuable and substantial part of the treatment program for patients with HLHS. Interstage monitoring for patients with HLHS provides a sensitive surveillance of physiologic instability and facilitates early recognition of signs denoting clinical deterioration.

Although the risk factors for interstage mortality remain multifactorial and are most often not modifiable, the goal of interstage monitoring is effective detection of potentially harmful constellations such as a simple intercurrent illness, fever, or dehydration, which might destabilize the patient at risk. This also includes detailed extensive parental education long before discharge to teach parents about signs and symptoms to be monitored, written guidelines, when to contact our hospital, and clear detailed guidelines for the outpatient cardiologist and pediatrician to ensure emergent admission in case of red flag interstage monitoring events.

Further approaches for interstage monitoring have recently been described in the literature including weekly telephone contact by high-risk cardiac nurse practitioners and use of telemedicine devices or smartphone apps [6, 8, 18]. Future research is needed to determine the psychosocial impact of interstage monitoring on the family itself, affecting family stress and quality of life [16, 23].

Study Limitations

Of course, the overall number of patients in this study was small, limiting further statistical analysis, especially for those patients being discharged from hospital. Furthermore, the study period was part of a learning curve regarding technical aspects of optimizing interventional and surgical therapy such as grading of pulmonary artery banding after the hybrid procedure and stenosis of the left pulmonary artery after the Norwood procedure.

Conclusions

Morbidity among infants after first-stage surgery before discharge is characterized by a high reintervention rate (30.7 %) independent of the surgical approach. Despite retrograde aortic flow in infants with HLHS after the hybrid procedure, the mortality rates were comparable between the two groups. Mortality after second-stage surgery occurred with an early age at second-stage palliation (<90 days). After discharge, we found a breach of physiologic criteria for interstage monitoring in 50 % of the patients, indicating the need for catheter treatment for 29 % of the patients. This highlights the importance of interstage monitoring in both treatment groups.

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