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Introduction to a Norwood Program in an Emerging Economy: Learning Curve of a Single Center

Murat Başaran,[1] Eylem Tunçer,[1] Füsun Güzelmeriç,[2] Nihat Çine,[1] Naci Öner,[3] Ayşe Yıldırım,[3] Ömer Şavluk,[2] Behzat Tüzün,[1] Hakan Ceyran[1]

Departments of [1]Pediatric Cardiac Surgery, [2]Anesthesiology and Reanimation, and [3]Pediatric Cardiology, Kosuyolu Heart Center, Istanbul, Turkey

ABSTRACT

Background: There has been a notable improvement in the outcome of stage 1 palliation for hypoplastic left heart syndrome (HLHS) in recent years. Nevertheless, developing a new Norwood program requires a steep learning curve, especially in emerging economies where rapid population growth brings a high volume of patients but, on the other hand, resources are limited. In this paper we aimed to summarize the initial results of a single center.

Methods: Hospital records of 21 patients were reviewed for all patients having a stage 1 palliation procedure for HLHS between May 2011 and May 2013. There were 13 male (62%) and 8 female (38%) patients. Median age was 14 days (range, 4-74 days) and median weight was 3030 g (2600-3900 g). HLHS was defined as mitral or aortic stenosis or atresia (or both) in the presence of normally related great vessels and a hypoplastic left ventricle. Transthoracic echocardiography was the diagnostic modality used in all patients. All procedures but one were performed using an antegrade selective cerebral perfusion method and moderate hypothermia. Cerebral perfusion was monitored with cerebral oximetry in all patients. Modified ultrafiltration was routinely used in all patients.

Results: Overall hospital mortality was 47.6% (n = 10). Mortality rates considerably decreased from the first year to second year (69% and 12.5% respectively). No risk factors were identified for mortality.

Conclusions: Surgical palliation of neonates with hypoplastic left heart syndrome continues to be a challenge. To decrease the overall mortality nationwide and improve outcomes, a referral center with a dedicated team is necessary in emerging economies.

INTRODUCTION

Hypoplastic left heart syndrome (HLHS) refers to the group of congenital cardiac abnormalities characterized by severe stenosis or atresia of the mitral and aortic valves, diminutive ascending aorta, and left ventricular hypoplasia, which substantially decreases the ability of the left ventricle to support the systemic circulation, which must be maintained by the right ventricle through a patent ductus arteriosus. The first successful surgical palliation of HLHS was reported by Norwood et al more than 3 decades ago [Norwood 1980]. Today surgical palliation of neonates with hypoplastic left heart syndrome continues to be a challenge. The mortality rate in earlier eras was 40% to 60% and more recently is reported to be as low as 10% in select patients [Azakie 2001]. This decrease in mortality has been attributed to modifications in surgical techniques and perioperative medical care, together with a better understanding of postoperative physiology.

There have been large series from various centers in the developed nations with improving early outcomes [Azakie 2001; Hornik 2012]. Yet in developing countries there is a lack of large series, owing to the relatively high mortality associated with this surgery, high resource utilization, need for dedicated intensive care support, and social and economic inadequacy of families in terms of understanding and accepting the concept of staged palliation. In the setting of emerging economies, pediatric cardiac centers must have the resources and willingness to initiate intensive therapeutic programs, even when the initial period of such a program may involve setbacks and disappointments. We reviewed the clinical details and early postoperative outcomes of the first 21 neonates who underwent stage 1 palliation at our institute.

METHODS

The study was conducted in a tertiary cardiac care center. Permission to perform the health record review was obtained from the ethics board of the institute. Hospital records were reviewed for all patients having a stage 1 Norwood operation between May 2011 to May 2013. HLHS was defined as mitral or aortic stenosis or atresia (or both) in the presence of normally related great vessels and a hypoplastic left ventricle. Transthoracic echocardiography was the diagnostic modality used in all patients.

Demographic data and intraoperative variables included age, weight, sex, cardiopulmonary bypass (CPB) time, aortic

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Correspondence: Eylem Tunçer, Cardiovascular Surgery Department, Kosuyolu Heart Center, Istanbul, Turkey; 05053854857; fax: 02164596321 (e-mail: eylemkvc@yahoo.com).

cross-clamp time, and hypothermia. Postoperative outcomes studied included mortality, maximum inotrope score, duration of mechanical ventilation, need for tracheostomy, acute renal failure, need for peritoneal dialysis, intensive care unit stay, hospital stay, and bloodstream infections. The inotropic scores were obtained after CPB by using a modification of the calculation described by Wernovsky and colleagues: dopamine (μg/kg per minute) + dobutamine (μg/kg per minute) + ([epinephrine(μg/kg per minute) + norepinephrine(μg/kg per minute)] × 100) [Wernovsky 1995].

Patients

The study population consisted of 21 patients who underwent an operation for HLHS. There were 13 male (62%) and 8 female (38%) patients. Median age was 14 days (range, 4-74 days) and median weight was 3030 g (2600-3900 g). Eight patients needed mechanical ventilation support before surgery. Two patients were underwent surgery on an urgent basis due to a preshock state. The distribution of typical HLHS malformations included the following: aortic stenosis and mitral stenosis in 8, aortic atresia with mitral atresia in 8, and aortic atresia with mitral stenosis in 5 patients. Median ascending aorta diameter was 4 mm (range 2-7.2 mm). Three patients had coexisting anomalies. One had interrupted aorta, 1 had cor triatriatum sinister, and 1 had a mass on the tricuspid valve. One patient had previous atrial septal defect closure surgery as a newborn. This patient showed severe congestive heart failure symptoms following birth and was diagnosed with total anomalous return of pulmonary veins. During surgery the pulmonary venous return was detected to be normal. Instead there was very large atrial-septal defect causing the return from pulmonary veins to be directed back to the right atrium, resembling total anomalous return of the pulmonary veins. This patient was operated on and discharged uneventfully. But after a month, congestive heart failure manifested again, along with severe pulmonary hypertension. After full examinations and echocardiographic assessment, a borderline left heart system was diagnosed i this patient and she underwent a Norwood operation was carried out.

Operative Technique

All procedures but one were performed using an antegrade selective cerebral perfusion (ASSP) method and moderate hypothermia. Patients with an interrupted aorta were operated on under total circulatory arrest. Cerebral perfusion was monitored with cerebral oximetry in all patients. Arterial cannulation sites were the main pulmonary artery or innominate artery (via the distal ascending aorta or a 3.5-mm–sized Gore-Tex graft) Single right atrial venous cannulation was used. Myocardial protection was achieved by antegrade cold blood cardioplegia. Median CPB time was 183 minutes. Median duration of aortic cross-clamping was 65 minutes. Pulmonary blood flow was established with a right modified Blalock-Taussing shunt (MBTS) in 11 (52%) of patients, and right ventricle–to–pulmonary artery (RV-PA) conduit in 10 (48%). The right MBTS was formed by anastomosing a polytetrafluoroethylene (PTFE) tube conduit between the innominate artery and the upper border of the right pulmonary artery. The size of the graft was 3.5 mm for patients above 3000 g and 3 mm for patients under 3000 g. The RV-PA conduit consisted of a PTFE tube conduit that passed to the left of the neoaorta. The size of the RV-PA conduit was 5 mm for all patients.

Arch reconstruction was accomplished with an autologous pericardial patch in 14 (66%), or with a modification as described by Ishino and colleagues [Ishino 1999] or by Fraser and Mee [Fraser 1995] in 7 (34%) patients. Modified ultrafiltration was routinely used in all patients.

Delayed sternal closure was used in 5 (23%). Inotropic support was commenced at the time of weaning from CPB. The most common inotropic agents used were dobutamine 10 μg/kg per minute, dopamine 3 μg/kg per minute, and epinephrine 0.003-0.01 μg/kg per minute.

Postoperative Management

Perioperative ventilatory and hemodynamic management targeted a pulmonary-to-systemic blood flow (Qp/Qs) of 1-1.5, arterial oxygen saturation of 75%-85%, central venous oxygen saturation of 50% or more. Mechanical ventilation with pressure-regulated neonatal ventilators was adjusted to an arterial carbon dioxide tension of 35–45 mmHg. Every effort to maintain a diastolic blood pressure equal to or higher than 40 mmHg, especially for those who received MBTS, was carried out either with ventilatory maneuvers or by reducing the size of the shunt surgically by simply clipping.

Statistical Analysis

All statistical analyses were performed using SPSS (SPSS version 16.0 Inc.; Chicago, IL. USA) packaged software. Visual histograms and analytical methods (Kolmogorov-Simirnov/Shapiro-Wilk's test) were used for determination of normal distributions. Continuous parameters were represented as mean ± standard deviations or median and maximum minus minimum values. Categorical data were represented as number (percentage), and proportions were compared using the Chi-square or Fisher's exact test. Comparison of means between 2 groups was done using an independent sample t test for parametric variables and using a Mann–Whitney U test for nonparametric variables. $P < 0.05$ was considered as the level of statistical significance.

RESULTS

Overall hospital mortality was 47.6% (10 patients out of 21). Mortality rates considerably decreased from the first year to the second year (69%, 9 patients of 13, and 12.5%, 1 patient of 8, respectively). The cause of death was low cardiac output syndrome in 8 (38%) and sepsis in 2 (9.5%). Table 1 shows characteristics of those who did not survive. Two of 5 patients whose sternum was left open died on the day of the operation, and in the latter 3 the sternum was closed on the third, sixth, and seventh days. The mean time

Table 1. Characteristics of Nonsurvivors

Variable	Sex	Age, days	Weight, g	Time Oo*	Type oS	Preoperative Ventilator Support	PoMIS	Total Perfusion Time	Cross-Clamp Time	Cause of Death	Time of Death, postoperative days
1	F	8	3500	1st year	RV-PA	–	25	140	38	Lco	1
2	M	28	3300	1st year	RV-PA	–	50	169	100	Sepsis	30
3	M	8	3250	1st year	RV-PA	+	45	157	37	Lco	1
4	F	8	2750	1st year	MBTS	–	60	171	59	Lco + sepsis	17
5	M	4	2900	1st year	RV-PA	+	30	133	114	Lco	1
6	M	15	3000	1st year	RV-PA	–	50	174	65	Lco	1
7	M	7	3060	1st year	RV-PA	+	35	223	77	Lco	3
8	F	16	3000	1st year	MBTS	–	40	184	63	Lco	1
9	M	6	2600	1st year	MBTS	+	46	207	70	Lco	8
10	M	45	3000	2nd year	RV-PA	–	70	183	66	Lco	1

*Time Oo indicates time of operation; Type Os, type of shunt; PoMIS, postoperative maximum inotrope score; Lco, low cardiac output.

Table 2. Comparison of Baseline and Operative Parameters between Survivors and Nonsurvivors

Variable	Survivors(n = 11, 52.4%)	Nonsurvivors (n = 10, 47.6%)	*P*
Male sex	7 (63.6%)	6 (60%)	0.86
Weight, g	3354.54 ± 469.81	3011.00 ± 278.86	0.10
Mechanical ventilation	4 (36.4%)	4 (40.0%)	0.86
Time of cross-clamping, min	67.80 ± 19.73	69.55 ± 25.39	0.86
Time of CPB, min	204.30 ± 43.63	173.00 ± 28.98	0.08
Hypothermia, °C	21.20 ± 2.82	24.66 ± 4.33	0.05
Maximal inotrope score	35.36 ± 13.03	44.60 ± 13.84	0.13
Ascending aorta diameter, mm	4.15 ± 1.58	4.67 ± 1.78	0.51
MBTS	8 (72.7%)	3 (30%)	0.08
RV-PA shunt	3 (27.3%)	6 (60.0%)	0.20

for the first attempt at extubation was the sixth day. Eight patients of 11 survivors were re-intubated following the first attempt. Two of these patients required tracheostomy on the following days but were able to wean from ventilatory support and were decannulated at the 22th and 29th days. Three (14%) patients required peritoneal dialysis for postoperative renal failure.

Both MBTS and RV-PA options were used for the pulmonary blood supply (52 % and 48%, respectively). During the first year of the program the RV-PA shunt was preferred (9 of 13 patients; 69%, versus 4 MBTS patients, 31%). The second year there were 7 MBTS patients of 8; 87.5%, versus 1 RV-PA patient, 12.5%. Comparison of baseline and operative parameters between survivors and nonsurvivors did not reveal out any prognostic factors (Table 2).

DISCUSSION

The management of HLHS continues to present one of the greatest challenges in congenital heart surgery. Since the introduction of staged surgical palliation for hypoplastic left heart syndrome by Norwood et al [Norwood 1983] in 1983, results have improved rapidly during the last 3 decades. Mortality rates, which have been reported to be as high as 40% to 50% [Jacobs 1998; Mahle 2000], improved to a survival rate of 70% to 90% [Jacobs 1998; Mahle 2000; Azakie 2001]. In the literature, risk factors for in-hospital mortality are earlier era of operation, older age at operation, lower weight at operation, anatomic subtype, diagnosis of HLHS versus that of another single-ventricle physiology, prematurity, ascending aortic diameter, preoperative condition, associated noncardiac anomalies, pulmonary venous obstruction or restrictive interatrial communication, and an aberrant right subclavian artery [Azakie 2001].

Many authors have observed improvement in outcome over time in their series [Mahle 2000; Gaynor 2002; McGuirk 2006]. Several reasons have been postulated to explain this "era effect," including increasing antenatal diagnosis, improved perioperative medical management, and modifications in surgical technique. The learning curve is of utmost importance in HLHS compared to other pathologies because it requires not only surgical skills but also a profound knowledge of preoperative assessment and postoperative physiology. Our mortality rate has decreased to 12.5% from 69% in 2 years. This decrease should be mostly attributed to the experience of both the surgical and intensive care unit teams and the better preoperative condition of selected patients. In our series patients who needed mechanical ventilatory support and underwent surgery on an urgent basis showed significantly poor outcomes. Median age at operation was high in our series compared to that of other series [Ishino 1999; Azakie 2001; Gaynor 2002; Tweddell 2002; McGuirk 2006]. Age is defined as a risk factor both for in-hospital mortality and interstage mortality and also has adverse effects on future cavapulmonary connection owing to the development of progressive pulmonary vascular disease and volume load effects on the systemic ventricle and atrioventricular valve [Mahle 2000; Checchia 2004; Hehir 2008; Alsoufi 2011]. In our country we are seeking to reduce the median age in the future with increasing number of antenatal diagnoses and prompt management and transport of patients after the diagnosis is made.

Our adopted operative approach to first-stage reconstruction involves the avoidance of circulatory arrest by using antegrade selective cerebral perfusion techniques, monitoring cerebral oxygenation, and use of modified ultrafiltration in the period after CPB. The arch is reconstructed by using either an autologous pericardial patch or one of the modified techniques previously described by Ishino and colleagues [Ishino 1999] and by Fraser and Mee [Fraser 1995]. The use of any exogenous material or homograft for arch repair has possible consequences, such as neoaorta obstruction due to lack of growth, degeneration, and calcification. Homograft availability is another matter of concern, especially in developing countries. The method of reconstruction of the arch without patch supplementation has been developed to avoid such complications. We tend to prefer modified arch reconstruction techniques as long as the aorta is not extremely hypoplastic. After all the ductal tissue is resected, primary autogenous tissue–tissue anastomoses between the back walls of the descending aorta, the arch, and the main pulmonary artery are performed. We did not observe any neoaortic obstruction on follow-up with either of these techniques.

There are several studies on the ideal blood supply for pulmonary arteries in stage 1 palliation. We have been using both the MBTS and RV-PA options since the introduction of the program. The preference of the shunt type shifted to MBTS from the RV-PA shunt in the second year. The main reasons for this shift were unsatisfactory results of the first year but more likely concerns about the effect of the right ventriculotomy required with RV-PA shunt on ventricular function along with volume overload secondary to diastolic flow reversal, which would possibly accelerate ventricular dysfunction. MBTS, which avoids a ventriculotomy in a univentricular heart, is frequently reported to confer a significant risk of myocardial ischemia due to diastolic hypotension and coronary insufficiency. This problem can be overcome with close follow-up and strict control of diastolic runoff during the immediate postoperative period. Recently we have preferred not to close the chest before adequate balance is provided between the 2 circulations by adjusting the shunt size with clipping if necessary.

Advantages of the use of an RV-PA shunt are better coronary perfusion due to higher postoperative diastolic blood pressure and a more favorable balance between the pulmonary and systemic circulation, resulting in improved systemic perfusion, a more stable postoperative course, and better immediate survival. Furthermore, the modified Norwood procedure has a significantly lower interstage mortality compared with the classic Norwood procedure [Cua 2005]. However, universal acceptance of the RV-PA shunt has been hindered by concerns regarding the adverse effects of ventriculotomy on myocardial systolic and diastolic function, the atrioventricular valve function, and the

incidence of ventricular arrhythmias [Raja 2010]. Graham and colleagues [Graham 2010] reported that despite the survival advantage offered by the RV-PA shunt, it results in impaired late ventricular function that may result in an increased need for cardiac transplantation in the long term. Comparisons of pulmonary artery growth with both techniques have also been carried out. According to Caspi and colleagues [Caspi 2008], hemodynamic changes after an RV-PA shunt provide better conditions for a bidirectional Glenn shunt because the Nakata index in patients with RV-PA is higher than in patients with MBTS. MBTS also has a recognized incidence of acute shunt occlusion, which is perhaps less common with the larger RV-PA conduit 20. In addition, the RV-PA shunt requires early stage 2 palliation due to the previously mentioned volume overload and has a higher re-intervention rate for treatment of both conduit and PA stenosis [Tabbutt 2005; Rüffer 2011].

Other mechanisms underlying the potential benefits of one shunt over another have been extensively hypothesized but incompletely validated. We think that the final choice between the Norwood operation and modifications depends on the preferences of the surgeon or clinic.

Although our institute is one of the oldest tertiary cardiac surgery centers in Turkey, the congenital cardiac surgery division is relatively young. Considering that the rapid growth of the population results in a high volume of patients, especially in emerging economies, a notable accumulation of experience with this group of patients is expected within a few years. Hornik and colleagues in their study showed that both center and surgeon volumes appear to influence Norwood outcomes [Hornik 2012]. However, while surgeon volume does appear to play a role, the magnitude of this effect (relative to that associated with center volume) was smaller compared with what has been reported previously in adult cardiac surgery. In the report of their study, Karamlou et al state that it has been hypothesized that for the Norwood operation, center- level variables impacting the ability to care for these complex infants both in regard to their preoperative and postoperative cardiovascular physiology, as well as other common noncardiac issues, may have an important impact on outcome in addition to technical issues pertaining to the surgery itself [Karamlou 2010].

In conclusion, initiation of a successful Norwood program requires high resource utilization along with a dedicated heart team, including surgeons, cardiologists, and intensivists. The learning curve is steep and involves optimization of center-level variables and gained experience not only on a surgical basis but also thorough the procedures from preoperative assessment to postoperative care. Even larger series, with satisfying midterm and long-term results, are necessary for the establishment of an ingrained program to successfully address HLHS.

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