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Profile of patients with hypoplastic left heart syndrome submitted to the first surgical stage

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Abstract

Background: Hypoplastic Left Heart Syndrome (HLHS) is responsible for 23% of deaths of cardiac origin during the first week of life and 15% of deaths by the same cause by the end of the first month. The initial surgery strategy has a prognostic impact on morbidity and mortality predominantly in the first two palliative stages and its choice is still controversial. This study aims to evaluate the morbidity and mortality of patients diagnosed with HLHS who underwent the Hybrid procedure or Norwood Surgery and its evolution to the second stage (Glenn's surgery) and the third stage (Fontan's surgery).

Methods and findings: A study was conducted based on the analysis of medical records of patients diagnosed with HLHS who underwent the hybrid procedure or Norwood Surgery between January 1995 and December 2018. It was analyzed: gender, twinness, birth weight, prematurity, prenatal diagnosis of congenital heart disease and other comorbidities, presence of preoperative organ dysfunction, type of surgery, age and weight in surgery, length of stay in the Intensive Care Unit, length of hospital stay, chance of survival and discharge from the ICU.

The sample had 172 patients, 15 Hybrid procedures (9%), 97 Norwood-Sano surgeries (56%), and 60 classic Norwood surgeries (35%). 39 patients (23%) were discharged from the ICU after the surgical procedure and, of these, 34 were discharged from the hospital. Patients discharged from the ICU were concentrated in 2008 and has increased since 2016. The chance of discharge from the ICU was lower in patients with low birth weight (p = 0.059) and in the last years of the study (p<0,0001). Once it is a retrospective study through the analysis of medical records, the work is subject to incomplete data, making it impossible to analyze some variables in detail.

Conclusions: The evolution in the treatment of HLHS in our service is evidenced by the decrease in in-hospital mortality in the last years, but survival is still far from that described in developed countries. New strategies must be implemented to reduce morbidity and mortality between the first and second stages.

Abstract:

Hypoplastic Left Heart Syndrome (HLHS) consists of a group of congenital heart diseases characterized by varying degrees of underdevelopment of the left ventricular cavity, and biventricular surgical correction is not possible. This syndrome is present in 1.4% to 3.8% of all congenital heart diseases, which corresponds to 0.016 to 0.036% of live births. Despite low incidence, the HLHS is responsible for 23% of deaths of cardiac origin during the first week of life and 15% of deaths by the same cause by the end of the first month [1].

Norwood surgery was first described in 1981 and consists on the first of a 3-step phase for a palliative cardiac approach based on the right ventricle as a single cardiac pump [2]. Despite the improvement in the survival of these patients, the first stage is still associated with a high length of hospital stay, a high rate of complications and a high mortality rate [2,3].

Some comorbidities, such as prematurity, low weight, or associated malformations increase the risk for Norwood's surgery, increasing its morbidity and mortality. In these cases, the hybrid procedure emerged as an alternative in the last 20 years because it is less invasive, offering a lower risk to patients [4-6]. Despite the decrease in early mortality with this surgical strategy, the patients still maintained a high mortality level after the 2nd stage, with late survival comparable to Norwood Surgery [7-8]. In the United States, only 13% of cardiac surgery services have high hybrid procedure rates and 50% opt for Norwood Surgeries in all cases of HLHS [9].

Treatment for HLHS by Norwood surgery or hybrid procedure is evolving in the last 30 years and today achieves a survival at the first surgical procedure of up to 90% [7]. This evolution translates the preparation of patients, the evolution of intensive care, and especially the individualization of the choice of the first surgical stage.

The initial surgery strategy has a prognostic impact on morbidity and mortality predominantly in the first two palliative stages [11], and its choice is still controversial and should only be performed after the analysis of the anatomy of the patient and risk factors present at birth such as low birth weight, associated genetic anomalies, prematurity and preoperative dysfunction organs [10-11]. Promoting a developed pulmonary vascular bed and protecting the function of the single ventricle represent the most important objectives of the initial palliative procedures, and should be taken into account in the choice between the hybrid procedure and the Norwood surgery and its subtypes, that is, shunt between the right ventricle and the pulmonary artery (Norwood-Sano) versus the modified Blalock-Taussig shunt (Classic Norwood) [11].

The experience of the service also brings a great variability of results, making the retrospective analysis of cases essential for the creation of protocols on this topic.It is important to improve not only longevity but also the quality of life of patients [8]. This study aims to evaluate the morbidity and mortality of patients diagnosed with HLHS who underwent the Hybrid procedure or Norwood Surgery and its evolution to the second stage (Glenn's surgery) and the third stage (Fontan's surgery).

Methods:

A descriptive, retrospective and cross-sectional study was conducted in the analysis of medical records of patients diagnosed with HLHS who underwent Hybrid procedure or Norwood surgery between January 1995 andDecember 2018 at the Pequeno Príncipe Children´s Hospital, located in the city of Curitiba - PR, Brazil, totaling 194 patients. 22 patients with incomplete medical records were excluded from the study (n = 172).

The criterion for choosing the type of surgical procedure was analyzed individually through clinical meetings held with pediatric cardiologists and experienced pediatric cardiac surgeons after a complete analysis of the patient's anatomy and the presence of risk factors.

The preoperative variables that were analyzed were gender, twinness, birth weight, prematurity, prenatal diagnosis of congenital heart disease, prenatal diagnosis of other comorbidities the diagnosis of genetic syndromes, the presence of preoperative organ dysfunction, the highest lactate and the lowest pH before the procedure. The variables related to the surgical procedure were the type of surgery, the age in the surgical procedure and the weight in the surgery, while the postoperative variables were the length of stay in the Intensive Care Unit, the length of hospital admission and the age at the time of death.

The assessment of survival and subsequent surgical procedures of patients who were discharged from the hospital and were followed up at this service was performed by reviewing medical records. To update the data of patients who were transferred to another service or who did not attend the last scheduled appointments, attempts were made to contact the number registered at the hospital. Patients who missed follow-up after hospital discharge were excluded from the survival analysis [12], and then the survival assessment of 160 patients was performed.

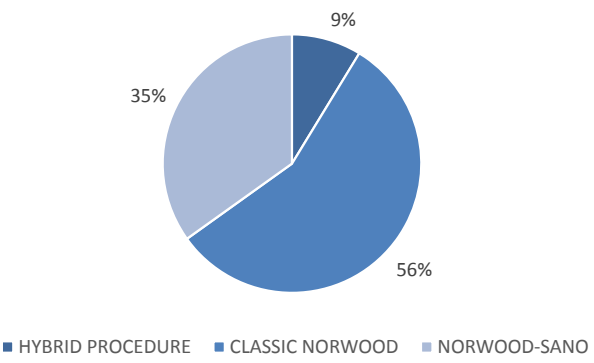
Categorical variables were analyzed through frequencies and percentages while non-categorical variables were analyzed through means (symmetric variables) and medians (asymmetric variables). The chi-square test was performed to assess the chance of discharge from the ICU, as well as logistic regression for multivariate analysis. For the survival analysis, the Kaplan-Meier test was used. In all cases, a p below 0.05 was considered statistically significant.

This study was approved by the Ethics and Research Committee of the Pequeno Príncipe Children's Hospital (opinion number: 2.997.021).

Results:

From January 1995 to December 2018, 172 newborns went the first surgical stage for HLHS, being 15 Hybrid procedures (9%), 97 Norwood-Sano surgeries (56%) and 60 Classic Norwood surgeries (35%), shown in GRAPH 1. The distraction of surgeries performed was homogeneous in the years of study.

GRAPH 1. TYPES OF SURGERIES PERFORMED



There were 105 male newborns (61%), of which7 were born by twin birth (4%) and 84 had the prenatal diagnosis of HLHS, corresponding to 52% of the patients. Birth weight averaged was 3025 ± 474g, and 22 patients were born with low birth weight (below 2500g), representing 13% of the sample. The mean gestational age was 38 ± 1.9 weeks, and 14 patients were born premature (below 37 weeks), totaling 12% of the sample. The characteristics of the sample are described in TABLE 1.At the time of surgery, the mean weight was 3019 ±463g, while the median age was 5 (1-121) days. Only 33 patients had preoperative lactate measurement, of which 26 (79%) showed a significant increase in lactate, and of the 163 patients who underwent preoperative blood gas analysis, 138 (85%) had acidemia suggesting an important prevalence of preoperative organ dysfunction (TABLE 2).

TABLE 1. PREOPERATIVE DEMOGRAPHIC CHARACTERISTICS

Features		
Male		105 (61%)
Twinning		7 (4%)
Prenatal Diagnosis		84 (52%)
Birth weight	Average (grams)	3025 ±474
	Low birth weight (<2500g)	22 (13%)
Gestational Age	Average (weeks)	38 ±1.9
	Preterm infants (<37 weeks)	14 (12%)

SOURCE: The author, 2020

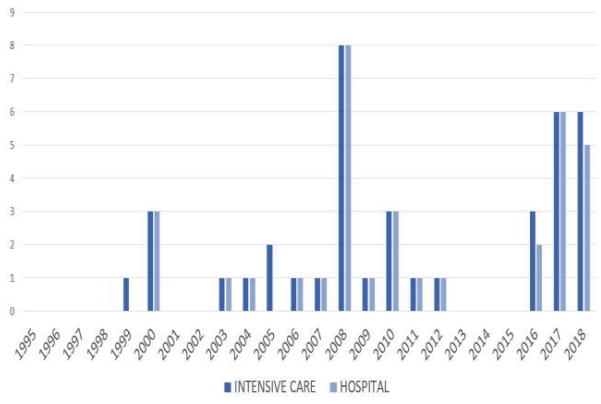
TABLE 2. SAMPLE CHARACTERISTICS IN SURGICAL TIME

Features	
Weight in surgery (grams)	3019 ±463
Age in surgery (days)	5 (1-121)
Higher lactate >2	26 (79%)
Lowest pH <7.35	138 (85%)

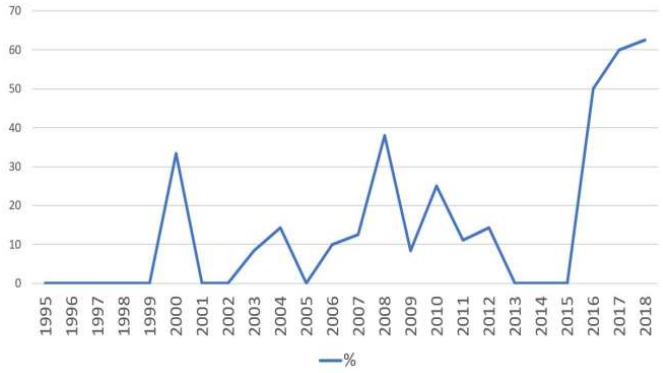
Of the 172 patients, 39 (23%) were discharged from the ICU after the surgical procedure and, of these, 34 were discharged from the hospital. The median length of stay in the ICU of these patients was 24 (11-135) days, and the median length of hospital stay was 40 (11-161) days. The other 133 patients died postoperatively in the ICU, with a median time of permanence in the ICU of 2 (1-327) days.

ICU discharges have not been consistent over the years. As observed in GRAPH 2 and GRAPH 3, patients discharged from the ICU were concentrated in 2008 and has increased since 2016. Even with a large number of discharges in 2008, this number corresponds to only 38% of procedures performed this year, while discharges represent 75% of procedures performed in 2016, 60% of procedures performed in 2017, and 75% of procedures performed in 2018. The evolution of the median age at the time of death is shown in GRAPH 4.

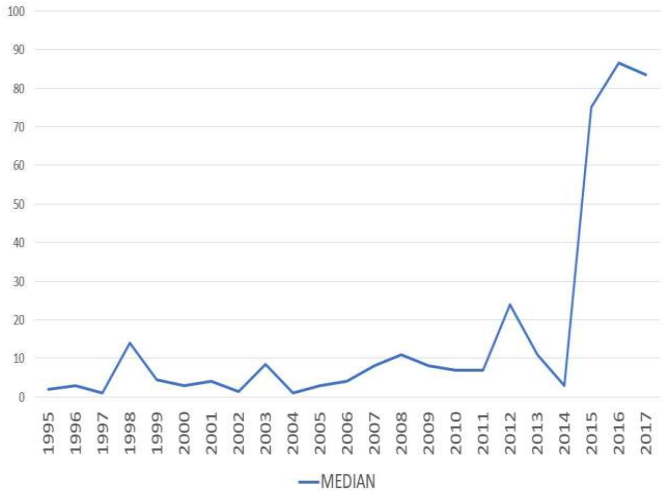
GRAPH 2. DISCHARGES FROM THE ICU AND HOSPITAL PER YEAR OF STUDY



GRAPH 3. PERCENTAGE OF PATIENTS THAT WERE DISCHARGED FROM THE HOSPITAL PER YEAR OF STUDY



GRAPH 4. MEDIAN AGE AT THE TIME OF DEATH PER YEAR OF STUDY



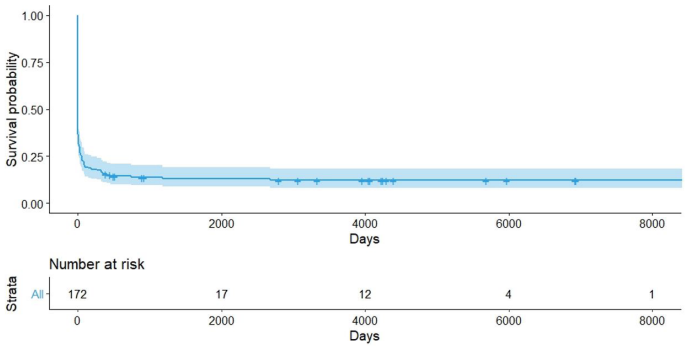
When performing logistic regression to determine the chance of discharge from the ICU, all variables with p below 0.2 were included in the multivariate analysis. The variable low birth weight (below 2500g) was not significant in the univariate analysis but had a borderline p-value in the multivariate analysis (p = 0.059), while the year in which the surgery was performed was statistically significant in both analyzes. The p-values of all the variables analyzed are shown in TABLE 3.

TABLE 3. LOGISTIC REGRESSION FOR THE CHANCE OF DISCHARGE FROM THE ICU

UNIVARIATE ANALYSIS		
	OR	p-value
Gender	1,00 (0,48 – 2,13)	0,95
Type of surgery	1,13 (0,65 – 1,92)	0,65
Low birth weight (<2500g)	0,28 (0,04 – 1,02)	0,096
Prematurity (<37 weeks)	0,55 (0,12 – 1,82)	0,37
Higher lactate >2	1,85 (0,31 – 15)	0,51
Lowest pH<7,35	1,16 (0,42 – 3,71)	0,78
Twinness	0,59 (0,03 – 3,63)	0,63
Prenatal diagnosis of congenital heart disease	0,74 (0,35 – 1,56)	0,44
Preoperative organ dysfunction	0,90 (0,39 – 1,95)	0,80
Year of surgery	2,46 (1,59 – 3,91)	<0,0001
MULTIVARIATE ANALYSIS		
Low birth weight (<2500g)	0,22 (0,034 – 0,86)	0,059
Year of surgery	2,67 (1,71 – 4,35)	<0,0001

12 patients lost their follow up, 1 of whom underwent Glenn's surgery and 2 underwent Glenn and Fontan's surgery before losing contact, making it impossible to assess the survival of these patients. Currently, 2 patients await Glenn's surgery, 4 patients have undergone Glenn's surgery and await Fontan's surgery, 3 patients have undergone Fontan's surgery and are alive, while the other 151 patients (93%) have died. GRAPH 5 shows the overall survival curve of the studied patients.

GRAPH 5. OVERAL SURVIVAL OF PATIENTS SUBMITED TO SURGERY



Discussion:

The risk factors that increase the mortality of patients with HLHS are already well established and are determinant in the choice of the surgical procedure to be realized. In our sample, 13% of the patients had low birth weight, 12% were premature, 79% had an increase in lactate and 85% had preoperative acidemia. The presence of these risk factors associated with structural alterations such as aortic atresia, restrictive inter-atrial septum, or severe dysfunction of atrioventricular valves considerably increase the mortality rate intra-hospital and interstage [7].

Even with the presence of risk factors, studies report a longer survival than that found. Pizarro et al [10] reported survival of 48.5% up to the moment of the 2nd stage, while Hansen et al [3] described a hospital and interstage survival of 65%, and Dibiardino et al [7], a survival of 78% for the hybrid procedure and 56% for Norwood surgery in 5 years. Our total mortality rate of 93% is still far from these values.

However, it was possible to observe a progressive evolution in the treatment of HLHS in our service. The proportion of patients discharged from the ICU in 2016 and 2018 shows an important drop in in-hospital mortality, a consequence of the improvement in the quality of patient preparation, surgical procedures and intensive care after surgery. The year in which the surgery was performed was statistically significant for the chance of discharge from the ICU in both univariate and multivariate analysis ($p < 0.0001$) proving the evolution of the results over time. Another evidence is that even the patients who died in these years had a median age at the time of death higher than that of previous years, surviving longer after the surgical procedure. As reported by Marrone [11], the surgeon's experience in performing the Norwood procedure, as well as the number performed annually, contribute to greater survival.

Of the 34 patients who were discharged from the hospital, less than half reached the second stage, reflecting the great current challenge, which is mortality between the first and second surgical stages. Several services have already managed to reduce this mortality through the development of programs that include home monitoring, education of those responsible for warning signs, periodic consultations, and well-defined surgical times [14].

Once it is a retrospective study through the analysis of medical records, the work is subject to incomplete data, making it impossible to analyze some variables in detail. The echocardiographic description of the anatomy of several patients was incomplete, making it impossible to analyze these data. This study did not present any conflicts of interest of the researchers.The evolution in the treatment of HLHS in our service is evidenced by the decrease in in-hospital mortality in the last years, but survival is still far from that described in developed countries. New strategies must be implemented to reduce morbidity and mortality between the first and second stages.

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