Survival benefits of the wait-and-grow approach in small babies (≤2000 g) requiring heart surgery

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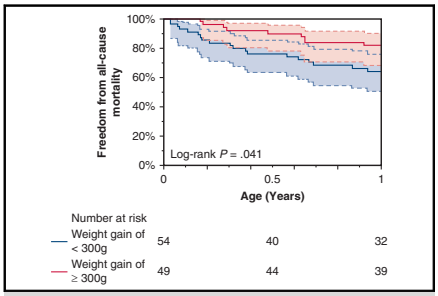
ABSTRACT

Objective: The best approach to minimize the observed higher mortality of newborn infants with low birth weight who require congenital heart surgery is unclear. This retrospective study was designed to review outcomes of newborn infants weighing <2000 g who have undergone cardiovascular surgery to identify patient parameters and clinical strategies for care associated with higher survival.

Methods: A retrospective chart review of 103 patients who underwent cardiovascular surgery from 2010 to 2021 who were identified as having low birth weight (≤2000 g). Patients who underwent only patent ductus arteriosus ligation or weighing >3500 g at surgery were excluded.

Results: Median age was 24 days and weight at the time of surgery was 1920 g. Twenty-six (25%) operative mortalities were recorded. Median follow-up period was 2.7 years. The 1- and 3-year overall Kaplan-Meier survival estimate was 72.4% ± 4.5% and 69.1% ± 4.6%. The 1-year survival of patients who had a weight increase >300 g from birth to surgery was far superior to the survival of those who did not achieve such a weight gain (81.4% ± 5.6% vs 64.0% ± 6.7%; log-rank $P = .04$). By multivariable Cox-hazard regression analysis, the independent predictor of 1-year mortality was genetic syndrome (hazard ratio, 3.54; 95% CI, 1.67-7.82; $P < .001$), whereas following a strategy of increasing weight from birth to surgery resulted in lower mortality (hazard ratio, 0.49; 95% CI, 0.24-0.90; $P = .02$).

Conclusions: A strategy of wait and grow for newborn infants with very low birth weight requiring heart surgery results in better survival than immediate surgery provided that the patient's condition allows for this waiting period. (JTCVS Open 2024;18:156-66)



Kaplan-Meier curves for freedom from all-cause 1-year mortality.

CENTRAL MESSAGE

A strategy of wait and grow in newborn infants with congenital heart disease with low birth weight who require heart surgery provides better survival than immediate surgery.

PERSPECTIVE

It might be reasonable to consider that very-low-birth-weight patients who are able to achieve growth to ≥300 g from birth to surgical intervention have increased survival.

Low birth weight and prematurity remain as strong predictors of increased mortality and morbidity in surgery for congenital heart disease (CHD).[1,2] The data suggest that experienced surgeons are capable of performing complex operation even in such small babies, although the question remains as to whether this results in better outcomes. We previously reported that delayed surgery provides better outcomes in infants with extremely low birth weight (≤1500 g) with complex lesion, but mortality rate was still high.[3] For these high-risk neonates, the clinical dilemma of whether or not to pursue higher-risk palliative or corrective surgery or to delay for growth and maturation before proceeding. There are some data demonstrating that waiting for surgery may lead to unfavorable outcomes.[4,5]

Given the ongoing controversy, we retrospectively reviewed the outcomes of newborn infants weighing <2000 g undergoing cardiac surgery in our institution, comparing patients undergoing rapid surgery to the group where surgery was delayed such that weight gain of at least 300 g

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Abbreviations and Acronyms
CHD = congenital heart disease
CPB = cardiopulmonary bypass
VSD = ventricular septal defect

from birth to surgery was documented. Our hypothesis is that patients with lower weight at the time of surgery are at greater risk than those in whom surgery is delayed for growth and maturation.

PATIENTS AND METHODS

Patient Population and Definition

This study was approved by the Institutional Review Board at Children's National Hospital on March 7, 2021 (#00015689). Informed consent was obtained from each patient to include their information in this publication. We conducted a retrospective review of surgical outcomes for all newborn infants weighing <2000 g who required cardiac surgery in our institution. We excluded patients who only underwent patent ductus arteriosus ligation or weighed >3500 g at the time of surgery. A total of 103 patients met the criteria. Because there are no previous reports that have determined a specific cutoff value resulting in survival risk in low birth weight neonates based on weight gain from birth to surgery, we established a minimum weight gain of 300 g, which was determined based on the median weight change of 287 g observed in this cohort.

There were a total of 49 neonates and infants with congenital cardiac anomalies who underwent surgical palliation or repair and had a weight increase ≥300 g from birth to surgical intervention. These patients were compared with a group of 54 infants whose weight increased by <300 g from birth to immediate surgical intervention.

Prematurity was defined as babies born alive before 37 weeks of pregnancy are completed. Operative mortality was defined as all deaths, regardless of cause, occurring during the same hospitalization in which the operation was performed, and within 30 days postoperatively. Postoperative major complications included requiring mechanical circulatory support, cerebral infarction or bleeding, re-exploration for bleeding, tracheostomy, necrotizing enterocolitis, renal failure requiring dialysis, and spinal cord injury. Follow-up data were obtained by clinical visit, e-mail, or written correspondence. The closing date of follow-up for this study was February 28, 2022. We defined and categorized the various congenital heart disease into 3 subtypes (Table E1). Single-ventricle CHD, including hypoplastic left heart syndrome, double-outlet right ventricle with remote ventricular septal defect (VSD), pulmonary atresia with intact ventricular septum, tricuspid atresia, double-inlet left ventricle, completed atrioventricular septal defect with unbalanced atrioventricular valve and hypoplastic ventricle, and congenitally corrected transposition of the great arteries with VSD. Simple CHD with a biventricular circulation included atrial septal defect, VSD, and coarctation of the aorta. Complex biventricular CHD included coarctation of the aorta with additional defect (ie, VSD, mitral stenosis, and atrioventricular septal defect), tetralogy of Fallot with pulmonary stenosis or atresia, truncus arteriosus, completed atrioventricular septal defect, transposition of the great arteries, double-outlet right ventricle with subaortic or subpulmonary VSD, pulmonary atresia with VSD, mitral regurgitation, and infective endocarditis.

Statistical Analysis

There were no missing data. Age, weight, length of hospital stay, and follow-up period was expressed as median with interquartile range (IQR). Categorical variables were expressed as the number (percent) of patients. A comparison of the clinical characteristics between 2 groups was performed using the χ^2 test for categorical variables and the unpaired *t* test for continuous variables. Assumption of normality of continuous data was tested with visual diagnostics. If the assumption of normality was met, continuous variables were compared using the analysis of variance. The values of 1-year and midterm survival were computed using the Kaplan-Meier methods and are expressed as the rate ± SE. Overall survival was calculated from the date of birth to the date of a death or to the date of data censoring. The log-rank test was used to compare survival across each group. The multivariable Cox-proportional hazards model yielding hazard ratio (HR) and 95% CI was used to determine variables that are independently associated with 1-year survival. Variables selection was based on preoperative factors, which included genetic syndrome, gender, birth weight, gestational age at surgery, amount of weight change from birth to surgery, preoperative mechanical ventilation, and preoperative shock. These predictors were entered into bivariable analysis, and any variable with P values < .05 was entered into the multivariable mode. Two- sided P values <.05 were considered to indicate statistically significant differences. Data analyses were performed with JMP 11.0 software (SAS Institute Inc).

RESULTS

Patient Characteristics

The characteristics of the 103 patients displayed in Table 1. Age at surgery was significantly older in patients whose weight increase ≥300 g from birth to surgery (weight gain ≥300 g group) than in those undergoing operation with a weight gain by <300 g (weight gain <300 g group) (68 days vs 10 days; $P < .001$). Birth weight was significantly lower in the weight gain ≥300 g group than those in the weight gain <300 g group (1.48 vs 1.76 kg; $P < .001$). Preoperative mechanical ventilation (n = 9 [19%] vs n = 22 [42%]; $P = .01$) and shock (n = 1 [2%] vs n = 9 [17%]; $P = .01$) were more frequent in the weight gain of <300 g group than in the weight gain ≥30 g group.

Intraoperative Details

Table 2 summarizes the intraoperative patient data. Operation with cardiopulmonary bypass (CPB) was performed in 61 patients (59%). Among them, surgery with CPB was performed more often in the weight gain ≥300 g group compared with the weight gain <300 g group (n = 39 [80%] vs n = 22 [41%]; $P < .001$).

Early Outcomes

Early outcomes are summarized in Table 3. There were 26 (25%) recorded operative mortalities, with 10 out of 49 (20%) in the weight gain ≥300 g group and 16 out of 54 (30%) in the weight gain <300 g group ($P = .28$). The cause of death was considered to be cardiac in 15 cases, pulmonary in 7, neurological in 2, hepatic in 1, and necrotizing enterocolitis in 1. The median survival period for the 26 patients who died was 138 days (IQR, 62-238 days). Major complications were observed in 16 cases in the weight gain ≥300 g group (33%) and 28 cases in the weight gain <300 g group (52%), with a significantly higher incidence in the weight gain <300 g group compared with the weight

TABLE 1. Preoperative characteristics of patients

Variable	All patients (N = 103)	Weight gain ≥300 g (n = 49)	Weight gain <300 g (n = 54)	*P* value
Gestational age (mo)	33 (32-35)	34 (32-36)	33 (31-35)	.49
Prematurity	83 (81)	43 (88)	40 (74)	.11
<32 wk	26 (25)	17 (35)	9 (17)	.04*
Age at surgery (d)	24 (10-66)	68 (46-91)	10 (6-16)	<.001*
Male sex	44 (43)	15 (31)	29 (54)	.85
Birth weight	1.67 (1.32-1.82)	1.48 (1.17-1.75)	1.76 (1.53-1.93)	<.001*
<1.0 kg	6 (6)	5 (10)	1 (2)	.06
Weight at surgery	1.92 (1.70-2.52)	2.53 (2.30-3.00)	1.73 (1.60-1.84)	.004*
Weight gain from birth to surgery	0.29 (0-1.07)	1.13 (0.75-1.56)	0 (−0.02-0.10)	<.001*
Genetic syndrome	36 (35)	18 (37)	18 (33)	.72
Mechanical ventilation	31 (31)	9 (19)	22 (42)	.01*
Shock	10 (10)	1 (2)	9 (17)	.01*

Values are presented as median (interquartile range) or n (%). *$P < .05$.

gain ≥300 g group ($P = .048$). A total of 26 patients required extracorporeal membrane oxygenation initiation postoperatively. Their median weight was 1.9 kg (IQR, 1.7-2.1 kg). Nineteen patients died postoperatively.

1-Year and Midterm Outcomes

Median follow-up period was 2.7 years (IQR, 0.6-5.8 years). The 1- and 3-year overall Kaplan-Meier survival estimate was 72.4% ± 4.5% and 69.1% ± 4.6% (Figure 1). Besides the 26 with in-hospital mortality, 8 patients died during the follow-up period. The cause of death was cardiac in 3 patients, pulmonary in 2, and unknown in 2. The 1-year survival of patients in the weight gain ≥300 g group was superior to the survival of those in the weight gain <300 g group (81.4% ± 5.6% vs 64.0% ± 6.7%; log-rank $P = .041$) (Figure 2).

The only independent risk factor for 1-year mortality (multivariable Cox-hazard regression analysis) was associated genetic syndrome (HR, 3.54; 95% CI, 1.67-7.82; $P < .001$) whereas following a strategy of increasing weight from birth to surgery resulted in lower mortality (HR, 0.49; 95% CI, 0.24-0.90; $P = .02$) (Table 4).

Surgical Pathway

The diagnosis of CHD is summarized in Table E1. All patients underwent 1 of 3 surgical pathways: staged single ventricular repair (19 patients [18]), primary biventricular full repair (73 patients [71%]), or staged biventricular repair (11 patients [11%]). Surgical strategy significantly differed between the weight gain <300 g group and the weight gain ≥300 g group ($P = .005$).

Of the 19 patients in whom single ventricular palliation with Norwood, shunt, or pulmonary artery banding was undertaken, 10 (53%) died before reaching age 1 year. One additional patient in this group later died at age 3 years after a Glenn procedure. The 1-year overall Kaplan-Meier survival estimate in patients who underwent single ventricle palliation was 43.8% ± 12.4% in the weight gain <300 g group and 66.7% ± 27.2% in the weight gain ≥300 g group (log-rank $P = .37$). In addition, among the 8 survivors of initial single ventricular palliation, 6 have proceeded with subsequent staged palliation and currently are candidates for the Fontan procedure (32%); 2 (66%) in the weight gain ≥300 g group and 4 (25%) in the weight gain <300 g group (Table E2).

Eighty-four patients (82%) received a biventricular repair; 33 (40%) had a simple biventricular CHD, and 51 (60%) had complex biventricular CHD (Table E1). Of 84 patients, 18 patients (35%) died before age 1 year. The 1-year overall Kaplan-Meier survival estimate for patients with a simple versus complex biventricular CHD did not show a significant difference in survival (84.6% ± 6.3% in a simple biventricular CHD vs 74.2% ± 6.2% in a complex biventricular CHD; log-rank $P = .26$) (Figure E1). Out of 84 patients with biventricular repair, primary complete repair was performed in 73 patients (87%) and palliative procedure was performed in 11 patients (13%) (Table 2). The 1-year overall Kaplan-Meier survival estimate was significantly higher in the patients who underwent primary full repair than those who underwent palliative procedure (81.9% ± 4.6% in a full repair vs 54.6% ± 15.0% in a staged repair; log-rank $P = .017$).

Sixty-one (59%) of the 103 overall patients received primary operation with CPB (Table 2). More patients in the weight gain ≥300 g group than in the weight gain <300 g group underwent surgery using CPB (39 out of 49 [80%] vs 22 out of 54 [41%]; $P < .001$). The 1-year overall Kaplan-Meier survival estimate in patients who underwent

TABLE 2. Operative data

Variable	All patients (N = 103)	Weight gain ≥300 g (n = 49)	Weight gain <300 g (n = 54)	*P* value
Operation with CPB	61 (59)	39 (80)	22 (41)	<.001*
TOF repair	12 (12)	8 (16)	4 (7)	
ASD + VSD closure	11 (11)	11 (22)	0 (0)	
VSD closure	7 (7)	7 (14)	0 (0)	
Aortic arch repair with VSD closure	7 (7)	1 (2)	6 (11)	
Truncus arteriosus repair	4 (4)	1 (2)	3 (6)	
Complete AVSD repair	3 (3)	3 (6)	0 (0)	
Aortic arch repair	2 (2)	0 (0)	2 (4)	
PA reconstruction + systemic-to-pulmonary shunt	3 (3)	3 (6)	0 (0)	
Arterial switch procedure	2 (2)	0 (0)	2 (4)	
ASD closure	2 (2)	2 (4)	0 (0)	
DORV repair	1 (1)	1 (2)	0 (0)	
Mitral valve repair	1 (1)	1 (2)	0 (0)	
PA/VSD repair	1 (1)	1 (2)	0 (0)	
Aortic arch repair and PA banding	1 (1)	0 (0)	1 (2)	
ALCAPA repair and systemic-to-pulmonary shunt	1 (1)	0 (0)	1 (2)	
Cardiac tumor resection	1 (1)	0 (0)	1 (2)	
Norwood procedure	1 (1)	0 (0)	1 (2)	
Rastelli procedure	1 (1)	0 (0)	1 (2)	
Operation without CPB	42 (41)	10 (20)	32 (59)	<.001*
Aortic arch repair	20 (19)	5 (10)	15 (28)	
PA banding	15 (15)	4 (8)	11 (20)	
Aortic arch repair and PA banding	2 (2)	0 (0)	2 (4)	
Systemic-to-pulmonary shunt	2 (2)	1 (2)	1 (2)	
PDA stenting	2 (2)	0 (0)	2 (4)	
PDA stenting and PA banding	1 (1)	0 (0)	1 (2)	
Surgical pathway				.005*
Staged single ventricle repair	19 (18)	3 (6)	16 (30)	
Primary biventricular full repair	73 (71)	41 (84)	32 (59)	
Staged biventricular repair	11 (11)	5 (10)	6 (11)	

Values are presented as median (interquartile range) or n (%). *CPB*, Cardiopulmonary bypass; *TOF*, tetralogy of Fallot; *ASD*, atrial septal defect; *VSD*, ventricular septal defect; *AVSD*, atrioventricular septal defect; *PA*, pulmonary artery; *DORV*, double outlet right ventricle; *PA/VSD*, pulmonary atresia with ventricular septal defect; *ALCAPA*, anomalous left coronary artery from the pulmonary artery; *PDA*, patent ductus arteriosus. *$P < .05$.

surgery with CPB was significantly higher in the weight gain ≥300 g group than those of in the weight gain <300 g group (86.4% ± 5.7% in the weight gain ≥300 g group vs 48.4% ± 10.1% in the weight gain <300 g group; log-rank $P = .001$) (Figure E2).

DISCUSSION

Patients with low birth weight and congenital heart defects are difficult to manage and have high mortality despite significant advancements in care. The small size of the baby and of the heart not only increases the technical difficulty of surgery, but also exposure of the immature organs to CPB puts the baby at significant risk.[3,4,6,7] In the past several decades, significant advances in surgical techniques and conduct of CPB have resulted improved survival for even such small babies. However, deciding the optimal timing of intervention is such small neonates remains a topic of controversy due to limited data. Previous reported have shown good outcomes in low-birth-weight infants, including those weighing <2500 g,[4,8,9] <2000 g,[10,11] and <1500 g.[3,12] Concomitantly, Chang and colleagues[4] found that delayed surgical intervention actually increased morbidity and mortality, without additional benefit in a study of 100 neonates with birth weights <2500 g. Similarly, in a single center report by Reddy and colleagues,[8] in 102 infants weighing <2500 g it was found that delayed intervention conferred higher preoperative morbidity, including ventilator dependency, poor weight gain, sepsis, necrotizing enterocolitis, chronic pulmonary disease, and renal failure. Finally, Haas and colleagues[9] reported good midterm outcomes after primary complete repair in 21 newborn infants whose mean weight at surgery was 2310 g, including 12 patients who weighed <2500 g. However, it is important to note that these reports did not include cases of single-ventricle CHD, and the majority of patients had biventricular CHD with most requiring relatively

TABLE 3. Early outcomes

Variable	All patients (N = 103)	Weight gain ≥300 g (n = 49)	Weight gain <300 g (n = 54)	*P* value
Operative mortality	26 (25)	10 (20)	16 (30)	.28
Cause of death				
Cardiac	15 (15)	6 (12)	9 (17)	
Pulmonary	7 (7)	3 (6)	4 (7)	
Neurological	2 (2)	0 (0)	2 (4)	
Hepatic	1 (1)	1 (2)	0 (0)	
NEC	1 (1)	0 (0)	1 (2)	
Length of hospital stay (d)	63 (29-139)	70 (28-146)	63 (30-125)	.87
Major complications	44 (43)	16 (33)	28 (52)	.048*
Detail of major complications				
Mechanical circulatory support	26 (25)	9 (18)	17 (31)	
Cerebral	14 (14)	4 (8)	10 (19)	
Re-exploration for bleeding	11 (11)	4 (8)	7 (13)	
Tracheostomy	8 (8)	5 (10)	3 (6)	
Necrotizing enterocolitis	5 (5)	3 (6)	2 (4)	
Renal failure required dialysis	3 (3)	1 (2)	2 (4)	
Spinal cord injury	1 (1)	0 (0)	1 (1)	

Values are presented as median (interquartile range) or n (%). *NEC*, Necrotizing enterocolitis. *$P < .05$.

simple repair. In contrast, in a recent report from our group, we found that waiting for growth in patients with extremely low birth weight, specifically those weighing <1500 g, to slightly improved long-term outcomes.[3] Similarly, in another series of small newborn infants weighing <2000 g, Hickey and colleagues[10] demonstrated that delay in surgical intervention did not compromise survival. In practice, despite multiple single center small reports of good outcomes after early surgery, it is difficult to estimate true survival benefit given that it is impossible to determine whether or not all centers follow a plan that includes early surgery or whether a case-by-case approach to determine whether the wait-and-grow approach is still utilized. Like many other centers, we have had a mixed practice and hence undertook this analysis of our outcomes to better identify best practice.

To our knowledge, there are no data available to determine how long to wait and how much growth should occur before surgery in newborn infants weighing <2000 g. We choose the weight estimate of ≥300 g to base on our current historical patient data given the median weight gain of our cohort. With this analysis, we have found that a strategy of waiting for at least ≥300 g weight gain as long as there is clinical stability in newborn infants weighing <2000 g before heart surgery is performed provided a far better survival than moving forward with surgery soon after birth.

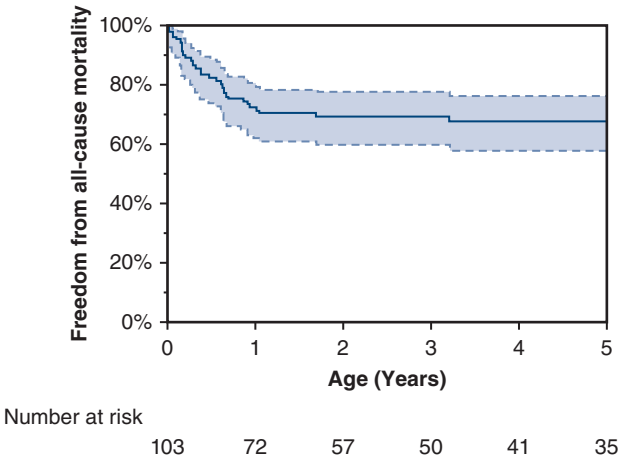

FIGURE 1. Kaplan-Meier curves for freedom from all-cause mortality.

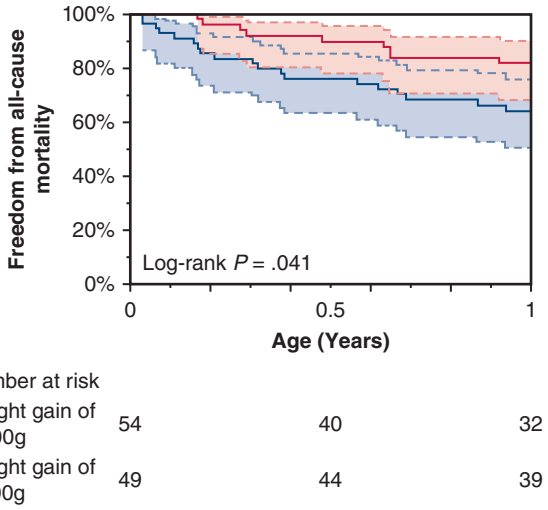

FIGURE 2. Kaplan-Meier curves for freedom from all-cause 1-year mortality; the weight gain ≥300 g group and the weight gain <300 g group.

TABLE 4. Risk analysis for multivariable Cox-regression analysis of all-cause mortality within 1 year

Variable	Bivariable		Multivariable	
	Hazard ratio (95% CI)	*P* value	Hazard ratio (95% CI)	*P* value
Genetic syndrome	3.29 (1.55-7.24)	.002	3.54 (1.67-7.82)	<.001
Weight change from birth to surgery, +1 kg	0.53 (0.26-0.98)	.04	0.49 (0.24-0.90)	.02
Gestational age at surgery, +1 wk	0.93 (0.84-1.01)	.08		
Preoperative shock	2.34 (0.78-5.70)	.12		
Preoperative mechanical ventilation	1.65 (0.75-3.53)	.21		
Male sex	1.11 (0.51-2.33)	.78		
Birth weight, +1 kg	1.05 (0.40-3.21)	.93		

This improvement was found both in patients with single-ventricle CHD, both simple and complex, and in those requiring CPB.

Based on these findings, we believe that delaying surgery in a very-low-birth-weight neonate is reasonable to consider if weight gain can be accomplished. This strategy might result in a more favorable prognosis.

We have tried various strategies in small newborn infants with single ventricle lesions during the past 2 decades. In the past 5 years, we have also added to our armamentarium of practice a hybrid strategy with bilateral pulmonary artery banding in small babies.[13] In the present study, out of 19 patients who underwent attempted staged single-ventricle repair, 6 patients (32%) progressed to become candidates for Fontan surgery. We believe that the bilateral pulmonary artery banding approach enabled us to extend the boundaries of care for newborn infants with very low birth weight who have single-ventricle CHD.

Limitations

With the retrospective nature of the study, it is difficult to ascertain the exact intent to treat and whether or not the decision to wait or to proceed with early surgery was deemed necessary by the clinical status of the patients. In addition, the comparison of the 2 groups may be confounded by other differences than weight gain at time of surgery. It cannot be

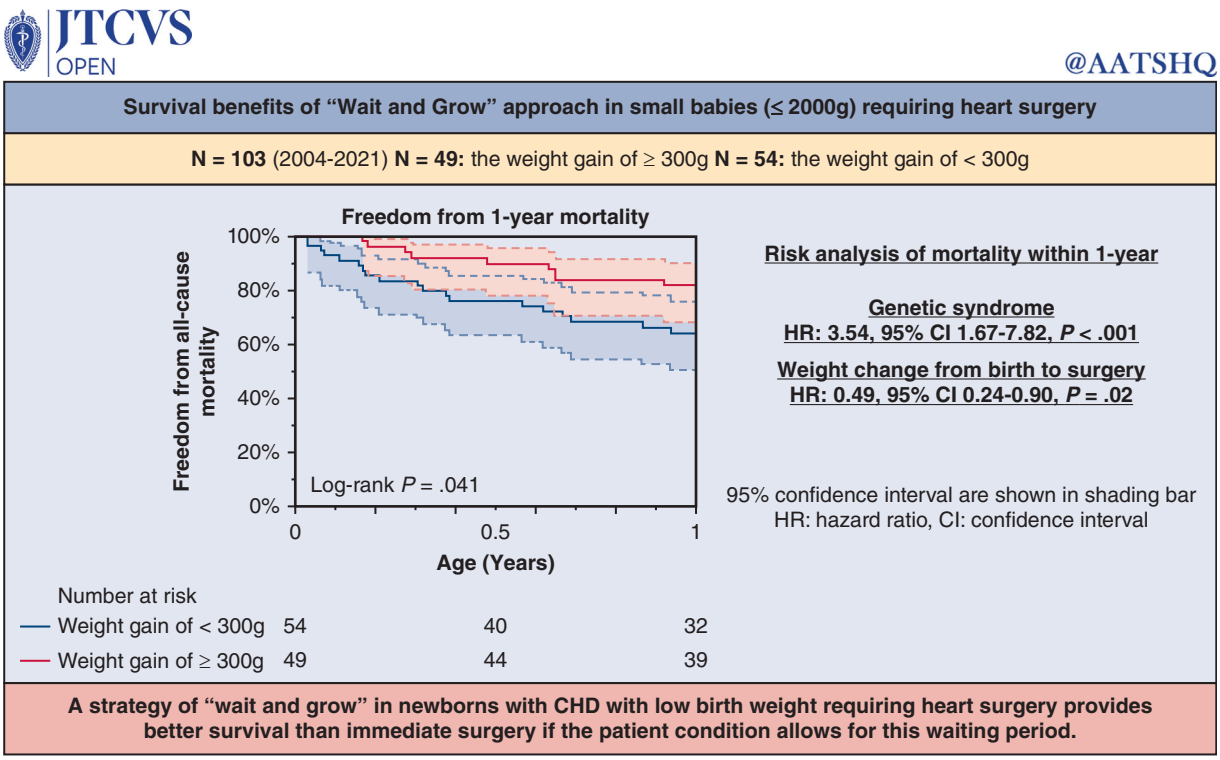

FIGURE 3. Graphical abstract. A strategy of "wait and grow" for very-low-birth-weight newborn infants requiring heart surgery results in better survival than immediate surgery provided that the patient condition allows for this waiting period. *HR*, Hazard ratio; *CHD*, congenital heart disease.

determined whether other important factors influenced weight gain, clinical course, and surgical outcomes.

CONCLUSIONS

A strategy of "wait and grow" in newborn infants with CHD with low birth weight who require heart surgery provides better survival than immediate surgery if the patient's condition allows for this waiting period with minimal risk (Figure 3). Further work is needed to determine optimal growth and best time frame minimize morbidity while maximizing survival.

Conflict of Interest Statement

The authors reported no conflicts of interest.

The *Journal* policy requires editors and reviewers to disclose conflicts of interest and to decline handling or reviewing manuscripts for which they may have a conflict of interest. The editors and reviewers of this article have no conflicts of interest.

References

1. Chu PY, Li JS, Kosinski AS, Hornik CP, Hill KD. Congenital heart disease in premature infants 25-32 weeks' gestational age. *J Pediatr*. 2017;181:37-41.e1.
2. Curzon CL, Milford-Beland S, Li JS, et al. Cardiac surgery in infants with low birth weight is associated with increased mortality: analysis of the Society of Thoracic Surgeons Congenital Heart Database. *J Thorac Cardiovasc Surg*. 2008;135:546-551.
3. Henmi S, Essa Y, Öztürk M, et al. Cardiovascular surgery in very low birth weight (≤1500 g) neonates. *Eur J Cardiothorac Surg*. 2022;63:ezac552 https://doi.org/10.1093/ejcts/ezac552
4. Chang AC, Hanley FL, Lock JE, Castaneda AR, Wessel DL. Management and outcome of low birth weight neonates with congenital heart disease. *J Pediatr*. 1994;124:461-466.
5. Marino BS, Bird GL, Wernovsky G. Diagnosis and management of the newborn with suspected congenital heart disease. *Clin Perinatol*. 2001;28:91-136.
6. Pawade A, Waterson K, Laussen P, Karl TR, Mee RB. Cardiopulmonary bypass in neonates weighing less than 2.5 kg: analysis of the risk factors for early and late mortality. *J Card Surg*. 1993;8:1-8.
7. Numa A, Butt W, Mee RB. Outcome of infants with birthweight 2000 g or less who undergo major cardiac surgery. *J Paediatr Child Health*. 1992;28:318-320.
8. Reddy VM, McElhinney DB, Sagrado T, Parry AJ, Teitel DF, Hanley FL. Results of 102 cases of complete repair of congenital heart defects in patients weighing 700 to 2500 grams. *J Thorac Cardiovasc Surg*. 1999;117:324-331.
9. Haas F, Goldberg CS, Ohye RG, Mosca RS, Bove EL. Primary repair of aortic arch obstruction with ventricular septal defect in preterm and low birth weight infants. *Eur J Cardiothorac Surg*. 2000;17:643-647.
10. Hickey EJ, Nosikova Y, Zhang H, et al. Very low-birth-weight infants with congenital cardiac lesions: is there merit in delaying intervention to permit growth and maturation? *J Thorac Cardiovasc Surg*. 2012;143:126-136.
11. Sudarshan CD, Cochrane AD, Jun ZH, Soto R, Brizard CP. Repair of coarctation of the aorta in infants weighing less than 2 kilograms. *Ann Thorac Surg*. 2006;82:158-163.
12. Reddy VM, Hanley FL. Cardiac surgery in infants with very low birth weight. *Semin Pediatr Surg*. 2000;9:91-95.
13. Ozturk M, d'Udekem Y, Yerebakan C. Hypoplastic left heart syndrome pushing the limits. *J Thorac Cardiovasc Surg Tech*. 2022;13:165-166.

Key Words: low birth weight, cardiovascular surgery, single ventricle, delayed surgery

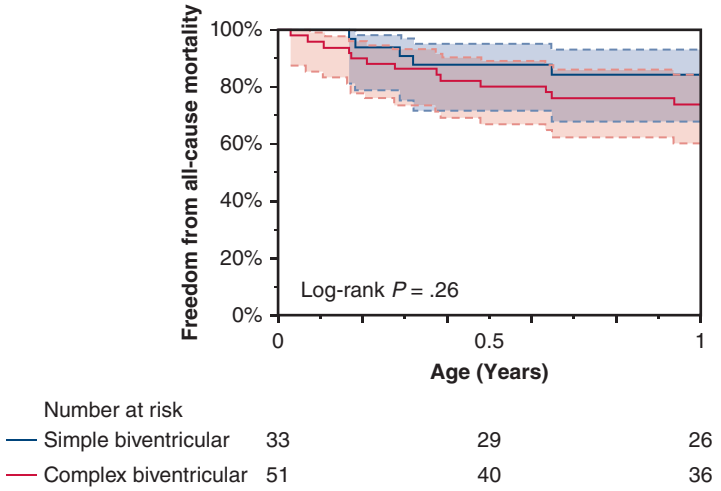

FIGURE E1. Kaplan-Meier curves for freedom from all-cause 1-year mortality; simple biventricular lesion and complex biventricular lesion.

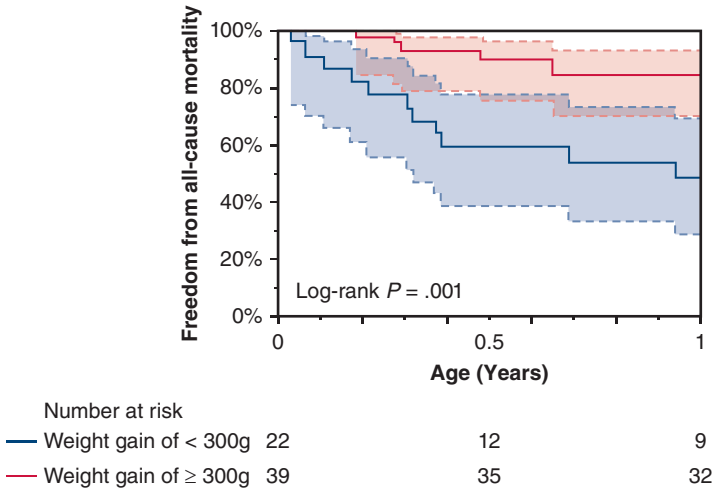

FIGURE E2. Kaplan-Meier curves for freedom from all-cause 1-year mortality in patients who underwent surgery with cardiopulmonary bypass; the weight gain ≥300 g group and the weight gain <300 g group.

TABLE E1. Diagnosis of congenital heart diseases

Type of lesion	Diagnosis	Result
Single ventricle CHD		19 (18)
	Hypoplastic left heart syndrome	6 (6)
	DORV with remote VSD	3 (3)
	Pulmonary atresia with IVS	3 (3)
	Tricuspid atresia	2 (2)
	Mitral atresia	2 (2)
	DILV	1 (1)
	Completed AVSD with unbalanced atrioventricular valve and hypoplastic ventricle	1 (1)
	CCTGA with VSD	1 (1)
Complex biventricular CHD		51 (50)
	Coarctation of the aorta with VSD	16 (16)
	Tetralogy of Fallot with PS	14 (14)
	Truncus arteriosus	4 (4)
	Completed AVSD	4 (4)
	TGA	2 (2)
	DORV	2 (2)
	Tetralogy of Fallot with pulmonary atresia	2 (2)
	Pulmonary atresia with VSD	2 (2)
	Coarctation of aorta with MS	1 (1)
	Coarctation of aorta with partial AVSD	1 (1)
	Mitral regurgitation	1 (1)
	Infective endocarditis	1 (1)
Simple biventricular CHD		33 (32)
	VSD	18 (17)
	Coarctation of the aorta	13 (13)
	ASD	2 (2)

Values are presented as n (%). *CHD*, Congenital heart disease; *DORV*, double outlet right ventricle; *VSD*, ventricular septal defect; *IVS*, intact ventricular septum; *DILV*, double inlet left ventricle; *AVSD*, atrioventricular septal defect; CCTGA, congenitally corrected transposition of the great arteries; *PS*, pulmonary stenosis; *TGA*, transposition of the great arteries; *MS*, mitral stenosis; *ASD*, atrial septal defect.

TABLE E2. The details of patients on whom single ventricular repair was attempted

Group	Diagnosis	Birth weight (kg)/ weight at surgery (kg)	Primary intervention	Reintervention*	Current status
Weight gain ≥300 g (n = 3)					
	DORV with remote VSD	1.7/2.6	Simple PA banding	-	Dead (age 11 mo)
	Mitral atresia	1.2/1.8	Bilateral PA banding	2nd: PDA stenting (age 3 mo) 3rd: Norwood (age 6 mo) 4th: Size up Sano shunt (age 10 mo)	Alive, Fontan candidate (age 2 y, 5 mo)
	Pulmonary atresia with IVS	1.2/3.1	PA construction and systemic-to-pulmonary shunt	2nd: Modified Glenn (age 4 mo)	Alive, Fontan candidate (age 2 y, 6 mo)
Weight gain <300 g (n = 16)					
	Tricuspid atresia	1.9/2.2	ALCAPA repair	-	Dead (age 1 mo)
	DORV with remote VSD	1.6/1.6	Simple PA banding	-	Dead (age 1 mo)
	Pulmonary atresia with IVS	1.8/1.7	Systemic-to-pulmonary shunt	-	Dead (age 2 mo)
	HLHS	1.9/2.0	Aortic arch repair and Simple PA banding	-	Dead (age 4 mo)
	CCTGA with VSD	1.4/1.4	Simple PA banding	2nd: Glenn (age 3 mo)	Dead (age 7 mo)
	HLHS	1.5/1.7	Bilateral PA banding	-	Dead (age 7 mo)
	DILV	1.9/1.9	Bilateral PA banding	2nd: Pulmonary artery embolectomy	Dead (age 8 mo)
	HLHS	1.8/1.8	Norwood	2nd: Modified Glenn (age 3 mo)	Dead (age 8 mo)
	Mitral atresia	1.8/1.9	Bilateral PA banding	2nd: Norwood (age 3 mo)	Dead (age 11 mo)
	Pulmonary atresia with IVS	1.4/1.4	PDA stenting	2nd: Glenn (age 4 mo)	Dead (3 y, 3 mo)
	DORV with remote VSD	1.1/1.2	Bilateral PA banding	2nd: Aortic arch repair and de-banding (age 6 mo) 3rd: Re-PA banding 4th: Pulmonary valve closure and A-P shunt	Alive (age 1 y, 2 mo)
	HLHS	2.0/1.7	Bilateral PA banding	2nd: Rastelli (2 mo)	Alive, Fontan candidate (1 y 3 mo old)
	Completed AVSD with unbalanced atrioventricular valve and hypoplastic ventricle	1.8/1.8	PDA stenting and Bilateral PA banding	2nd: Arch repair, AVSD repair and PA de-banding	Alive (age 1 y, 3 mo)

(Continued)

TABLE E2. Continued

Group	Diagnosis	Birth weight (kg)/ weight at surgery (kg)	Primary intervention	Reintervention*	Current status
	Tricuspid atresia	1.5/1.5	Simple PA banding	2nd: Glenn (7 mo)	Alive, Fontan candidate (age 1 y, 10 mo)
	HLHS	1.9/2.0	Simple PA banding	2nd: Norwood 3rd: Modified Glenn	Alive, Fontan candidate (age 2 y, 6 mo)
	HLHS	1.9/1.9	PDA stenting	2nd: Norwood 3rd: Pulmonary artery embolectomy	Alive, Fontan candidate (age 4 y, 2 mo)

DORV, Double outlet right ventricle; *VSD*, ventricular septal defect; *PA*, pulmonary artery; *PDA*, patent arteriosus ductus; *IVS*, intact ventricular septum; *ALCAPA*, anomalous left coronary artery from the pulmonary artery; *HLHS*, hypoplastic left heart syndrome; *CCTGA*, congenitally corrected transposition of the great arteries; *DILV*, double inlet left ventricle; *A-P*, hepatic arterioportal; *AVSD*, atrioventricular septal defect. *Time from primary surgery.