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The impact of a dedicated single-ventricle home-monitoring program on interstage somatic growth, interstage attrition, and 1-year survival

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Objective: There has been considerable improvement in survival after the first stage of palliation for single-ventricle heart disease. Yet, interstage mortality continues to plague this population. Home monitoring has been proposed to reduce interstage mortality. We review our experience after creation of a Single Ventricle Program.

Methods: All infants with a single ventricle heart defect who were admitted to Texas Children's Hospital from the inception of the Single Ventricle Program on September 1, 2007, to January 1, 2010, were included in the Single Ventricle Program cohort. Infants with a single ventricle presenting between January 1, 2002, and August 31, 2007, comprised the pre-Single Ventricle Program group. Anatomic, operative, and postoperative details were noted for all patients. End points included in-hospital death after the first stage of palliation, interstage death (defined as after discharge from the first stage of palliation and before the second stage of palliation), and death or heart transplantation by 1 year of age. Interstage weight gain was also compared.

Results: A total of 137 infants with a single ventricle were included in the pre-Single Ventricle Program cohort, and 93 infants were included in the Single Ventricle Program cohort. Anatomic subtypes were similar between groups. There was significant improvement in rate of interstage weight gain, whereas age at the second stage of palliation was significantly reduced in the Single Ventricle Program group. In-house mortality decreased during the Single Ventricle Program era ($P = .021$). Interstage mortality did not significantly decrease in the Single Ventricle Program group. However, 1-year transplant-free survival improved during the Single Ventricle Program era ($P = .002$).

Conclusions: The Single Ventricle Program improved interstage weight gain, thereby allowing for early second-stage palliation at an equivalent patient weight. Interstage mortality was not significantly reduced by our program. However, 1-year transplant-free survival was significantly improved in patients in the Single Ventricle Program. (J Thorac Cardiovasc Surg 2011;142:1358-66)

Operative survival after stage 1 surgical palliation (S1P) for single-ventricle heart disease has improved significantly over the past 2 decades.[1-3] This improvement is thought to be due to earlier detection and diagnosis of single-ventricle heart disease, improved pre- and postoperative management strategies, and refinements in surgical technique. Nonetheless, interstage mortality—death after discharge from S1P and before stage 2 surgical palliation (S2P) —persists at rates varying from 5% to 19%.[4-6] Most commonly, the cause of interstage mortality is unknown, although thrombosis of the systemic-to-pulmonary artery shunt and arrhythmia are believed to be significant contributors to interstage mortality.

The results of an intensive home-monitoring program, which included home pulse-oximetry, daily weight checks, and close clinic follow-up, were reported recently.[7] This report demonstrated a significant improvement in interstage mortality. There were no early postoperative deaths or interstage deaths (IDs) noted during the study period. One aspect proposed in this report was earlier timing of S2P, thus reducing the length of the interstage period. It remained unclear whether these results would be generalizable to other institutions with more diverse populations. It was also unclear whether reduction in ID was simply a reflection of a shorter interstage period, while the overall mortality at 1 year would remain unchanged. Nevertheless, this report has prompted many centers to consider the creation of dedicated outpatient programs to monitor infants with single-ventricle heart disease. We report on our early experience after creation of a dedicated Single Ventricle Program (SVP), which includes both home monitoring—pulse

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Abbreviations and Acronyms

BT = Blalock–Taussig
CAVC = complete atrioventricular canal
DORV = double-outlet right ventricle
G-tube = gastrostomy tube
HLHS = hypoplastic left heart syndrome
ID = interstage death
RVPA = right ventricle-to-pulmonary artery
S1P = stage 1 surgical palliation
S2P = stage 2 surgical palliation
SVP = Single Ventricle Program

oximetry and daily weight checks—and access to a dedicated physician and nurse practitioner team who maintain close outpatient contact with our infants with a single ventricle awaiting S2P. We describe our experience since the inception of our program and compare interstage mortality, patient weight gain, and 1-year mortality before and after the program was initiated.

MATERIALS AND METHODS

Patient Characteristics

All patients with single-ventricle anatomy from January 1, 2002, to February 1, 2010, were included in this study. Patient data were attained after a careful review of both the cardiac surgical and the cardiology patient databases. Patients enrolled in the SVP had multiple anatomic subtypes of single ventricle, including hypoplastic left heart syndrome (HLHS), unbalanced complete atrioventricular canal (CAVC), tricuspid atresia, double-inlet left ventricle, and double-outlet right ventricle (DORV) with mitral atresia/stenosis. Not all patients underwent Norwood-type palliation at the initial neonatal surgery. Accordingly, the comparison groups, drawn from the period between January 1, 2002, and August 31, 2007, included all patients with the same range of diagnoses.

Patient characteristics, including birth weight, gestational age, age and weight at S1P, and associated genetic lesions, were noted. Details of S1P were also noted, including need for pulmonary vein or atrioventricular valve repair, type of pulmonary blood flow source at S1P (modified Blalock–Taussig [BT] shunt or right ventricle-to-pulmonary artery [RVPA] conduit), and time to discharge from S1P. Nutritional details were reviewed from both the time of discharge from S1P and the interstage period; such details included route of enteral feeding (oral vs nasogastric or gastrostomy tube [G-tube]), formula calorie content, and patient weight at time of birth, S1P, discharge from S1P, and S2P.

Mortality details were carefully reviewed for all patients. Mortality at any point within the first year of life was noted. In-hospital mortality was defined as death after S1P and before discharge. Interstage mortality was defined as death after discharge from S1P and before S2P. One-year mortality was also reviewed, and all deaths (in-hospital, interstage, and post-S2P death) were included in this review. One-year mortality also included those patients with a single ventricle who underwent heart transplantation within the first year of life.

Single Ventricle Program

The SVP began on September 1, 2007, at Texas Children's Hospital. As noted above, patients with many various anatomic subtypes of single ventricle are included. The goal of the program has been to optimize nutrition and medical management, and to reduce ID among all patients with a single ventricle. The SVP is composed of 6 pediatric cardiologists, 6 nurse practitioners, a social worker, a nutritionist, and a developmental pediatrician, all of whom participate in the SVP in addition to their primary heart center responsibilities. Parents of all patients with a single ventricle are prospectively approached and consented for enrollment into the SVP at the time of initial presentation in the neonatal period. All pertinent patient variables—demographics, single ventricle type, patient size/age at S1P, type of S1P, and associated noncardiac problems—are included in our SVP database. Operative variables evaluated include type of S1P performed, placement of a systemic-to-pulmonary artery (modified BT shunt) or a ventriculo-pulmonary (RVPA) conduit, need for atrioventricular valve repair or pulmonary vein repair, and other associated surgical interventions. Patients are officially enrolled into the SVP on discharge from S1P and are discharged from SVP after their first outpatient visit after S2P.

Members of the SVP meet with the parents on a number of occasions before discharge from S1P. In particular, when there are protracted difficulties with oral feeds, the SVP may recommend G-tube placement. This recommendation is only made after a thorough evaluation by our feeding team and speech therapists. The recommendation for G-tube is made with input from the inpatient and surgical teams, and the parents.

Patients are seen in the designated SVP outpatient clinic located within the hospital. The frequency of outpatient visits is determined by a number of factors, including patient age, medical status, and nutritional status. The nurse practitioners maintain at least weekly telephone contact with all SVP families during the interstage period. Decreased oxygenation (pulse-oximetry $< 75\%$) or failure to gain weight on at least 3 successive days may prompt an outpatient visit or inpatient admission. Weekly meetings of the SVP team are held to discuss each interstage patient and to formulate his/her medical plan, including the pre-S2P evaluation and timing of S2P. The SVP team attempted not only to attain a close partnership with each family during the interstage period but also to achieve a consistency in the medical and nutritional management of patients with a single ventricle. Consistency in the timing of S2P was thought to be critically important, and patients were routinely scheduled to undergo S2P between 4 and 5 months of age provided they were growing well and were thought to be good candidates for promotion to cavopulmonary physiology.

Statistical Analysis

Data are expressed as mean $\pm$ standard deviation or median (range) where appropriate. Characteristics of the pre-SVP and SVP cohorts were compared using nonpaired t test and Fisher exact test where appropriate. We sought to determine the incidence of the following clinical end points: (1) in-hospital death after S1P, (2) ID, and (3) death or transplant at 1 year. For in-hospital death and 1-year survival end points, we compared patients by era (pre-SVP era vs SVP era) rather than by SVP enrollment, because patients who died before discharge from S1P were not enrolled in the SVP. For ID comparisons, SVP enrollment was evaluated. We compared the rates of the above end points between the pre-SVP and SVP cohorts using Kaplan–Meier analysis. For time-dependent end points, Cox multivariate analysis was performed to identify factors associated with development of those outcomes. For 1-year mortality comparison, binary logistic regression was performed to identify risk factors. We also compared patient weight at time of S1P, discharge from S1P, and discharge from S2P between the pre-SVP and SVP cohorts. Weight-for-age z scores were calculated using the Anthro (Version 3.1) calculator provided by the World Health Organization. Rate of weight gain during the interstage period and weight-for-age z scores were compared using a standard nonpaired t test.

Finally, the same analyses listed above were performed for the subgroup of patients with a single ventricle associated with systemic outflow obstruction (HLHS, DORV/mitral atresia, and unbalanced CAVC) who underwent Norwood-type palliation at S1P. For the Norwood subgroup, comparisons between SVP and pre-SVP cohorts were made. Further, comparison between Norwood types (aortopulmonary shunt versus ventriculo-pulmonary conduit)

TABLE 1. Patient characteristics

	Pre-SVP era (n = 137)	SVP era (n = 93)	*P* value
Preoperative characteristics			
Birth weight (kg)	3.05 ± 0.50	3.08 ± 0.50	.67
Gestational age (wk)	38.2 ± 1.5	38.4 ± 1.4	.44
Age at S1P (d)	13.8 ± 12.4	8.5 ± 6.6	.01
Weight at S1P (kg)	3.17 ± 0.66	3.09 ± 0.51	.36
Diagnoses			
HLHS	82 (59.8%)	49 (55.7%)	.28
Unbalanced CAVC	43 (31.4%)	23 (26.1%)	.45
DILV	5 (3.6%)	2 (2.3%)	.71
Heterotaxy syndrome	36 (26.3%)	17 (19.3%)	.36
S1P operative characteristics			
BT shunt	110 (80.3%)	56 (63.6%)	.02
RVPA conduit	1 (0.7%)	21 (23.9%)	.01
PA banding	29 (21.2%)	11 (12.5%)	.16
Pulmonary vein repair	19 (13.9%)	8 (9.1)	.38
Atrioventricular valve repair	3 (2.1%)	8 (9.1%)	.03
Interstage characteristics			
Age at D/C from S1P (d)	43.8 ± 30.6	37.5 ± 19.3	.07
Weight at D/C from S1P (kg)	3.4 ± 0.7	3.5 ± 0.7	.17
Weight at S2P (kg)	6.5 ± 1.8	6.3 ± 1.2	.29
Weight-for-age *z* score at S1P	–1.08 ± 1.30	–0.95 ± 1.14	.43
Weight-for-age *z* score at S2P	–1.84 ± 1.53	–1.38 ± 1.27	.03
Age at S2P (d)	221.4 ± 112.2	157.6 ± 49.4	<.01
Daily weight gain from S1P to S2P (g/d)	19.8 ± 8.4	23.6 ± 7.9	<.01
Outpatient clinic frequency (visits/30 d)	1.1 ± 1.0	1.5 ± 0.7	<.01
ED encounter frequency (visits/30 d)	0.1 ± 0.3	0.1 ± 0.2	.78
Unplanned admissions (admits/30 d)	0.4 ± 0.6	0.3 ± 0.3	.21
Nutrition details			
Formula concentration (cal/oz)	21.8 ± 2.8	23.8 ± 2.0	<.01
PO feeding at D/C from S1P (%)	87 (75%)	73 (83%)	.03
NG-tube dependency from S1P-S2P (%)	18 (16%)	5 (6%)	.06
G-tube dependency from S1P-S2P (%)	8 (7%)	13 (15%)	.03
S2P operative details			
Aortic arch repair (%)	5	3	.75
Atrioventricular valve repair (%)	11	6	.50
Pulmonary vein repair (%)	8	8	.55
Mortality			
In-hospital death after S1P (predischarge)	21 (15%)	4 (4%)	<.01
ID	14 (12%)	7 (8%)	.49
Cause of ID			
Sudden/unknown cause	10	4	NS
Shunt occlusion	2	2	NS
Respiratory (eg, infection, aspiration)	2	1	NS
Any pre-S2P death (in-hospital or ID)	35 (26%)	11 (12%)	.01
1-y transplant-free survival	97 (71%)	78 (84%)	.02

Pre-SVP, Infants who underwent S1P before SVP inception; *SVP,* infants who underwent S1P during SVP and who enrolled in the program; *D/C,* discharge; *LOS,* length of stay; *DILV,* double-inlet left ventricle; *PA,* pulmonary artery; *ED,* emergency department; *PO,* oral; *NG,* nasogastric.

was also performed. The institutional review board approved this study. For statistical analysis, SPSS version 18 was used (SPSS Inc, Chicago, Ill).

RESULTS

A total of 230 infants with various forms of single ventricle underwent S1P at Texas Children's Hospital between January 1, 2002, and December 30, 2009. Of this total, 137 patients underwent S1P pre-SVP (January 2002 to August 2007), and 93 infants underwent S1P during the SVP era (September 2007 to February 2010). One patient who underwent S1P during the SVP period did not enroll in the SVP because of out-of-state residency, and 4 patients during the SVP era died in-hospital before discharge from S1P and were therefore not enrolled in the SVP. Thus, although there were 93 patients who underwent S1P during the SVP era, the SVP enrollment cohort included 88 patients. The most common diagnosis for both groups was HLHS, followed by right-dominant CAVC defect (Table 1). There were no significant differences in prevalence of diagnoses between the pre-SVP and SVP groups.

Timing of S1P was earlier in the SVP group, who underwent initial palliation at 8.3 ± 6.5 days of life, compared with 13.8 ± 12.4 days of life in the pre-SVP group ($P = .03$). Components of the S1P between both groups are detailed in Table 1. There were no differences in rates of heterotaxy syndrome, pulmonary vein repair, or atrioventricular valve repair at S1P between the pre-SVP and SVP groups. However, use of the RVPA conduit increased from 1 of 137 infants in the pre-SVP era to 21 of 93 infants in the SVP era. This change was due to individual surgeon preference and did not reflect a program-wide change. Because some patients, particularly those with tricuspid atresia or double-inlet left ventricle, presented with congestive heart failure rather than systemic arterial obstruction, pulmonary artery banding was occasionally used during S1P, and the Damus–Kaye–Stansel reconstruction or palliative arterial switch was deferred in these patients until S2P. Patients in both the SVP and pre-SVP cohorts were similar in age and weight at time of discharge from S1P (Table 1).

Interstage Period

The SVP cohort was observed more frequently during the interstage period. There were 1.60 ± 0.76 outpatient clinic

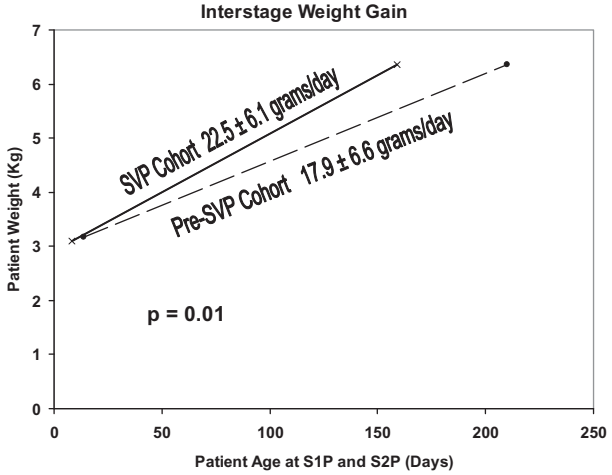


FIGURE 1. Interstage weight gain in the SVP group outpaced the growth rate in the pre-SVP group. The SVP group was promoted to S2P at an earlier age and yet had achieved a similar weight at an earlier time compared with the pre-SVP group. *SVP,* Single Ventricle Program; *S1P,* stage 1 palliation; *S2P,* stage 2 palliation.

visits per patient per 30 days for the SVP cohort, compared with 0.99 ± 1.12 visits per patient per 30 days for pre-SVP patients ($P < .01$). Rates of unplanned admissions to the hospital and emergency department visits did not differ between the groups (Table 1). Patients enrolled in the SVP were more likely to receive fortified formula, with an average caloric content of 23.9 ± 2.0 calories/ounce, compared with 21.8 ± 2.8 calories/ounce in the pre-SVP group ($P = .021$). SVP patients were more likely to be completely orally fed at the time of discharge from S1P, where only 12.2% required tube feed supplementation, compared with 27.3% of patients in the pre-SVP group ($P = .004$). However, when tube supplementation was required, there was a higher rate of G-tube use in the SVP group ($P = .016$) and a higher rate of nasogastric tube use in the pre-SVP group ($P = .003$).

Timing of S2P differed significantly between the pre-SVP cohort (210 ± 114 days) and the SVP cohort (159 ± 52 days) ($P < .001$). The variation in timing was reduced as well, from a standard deviation of ± 114 days for the pre-SVP group to ±52.4 days for the SVP group. Although weight-for-age z score did not differ between the eras at S1P, the SVP group had a higher weight-for-age z score of –1.38 ± 1.27 compared with –1.84 ± 1.53 for the pre-SVP group at S2P ($P = .029$). The average patient weight at S2P was 6.35 ± 1.23 kg for the SVP group compared with 6.36 ± 1.49 for the pre-SVP group ($P =$ NS). Thus, average daily weight gain was greater in the SVP group at 22.5 ± 6.1 g/d compared with 17.9 ± 6.6 g/d for the pre-SVP group ($P = .01$) (Figure 1).

Before discharge from S1P, 21 of 137 infants (15.3%) in the pre-SVP cohort died, whereas 4 of 93 infants (4.5%) in the SVP era died ($P = .021$). Binary logistic regression

TABLE 2. Multivariate analyses

Risk factor	Hazard ratio (95% CI)	*P* value
In-hospital death (post-S1P)		
Age at S1P > 14 d	3.41 (1.2–11.4)	.046
Weight at S1P (kg)	0.69 (0.3–1.4)	.315
HLHS	1.11 (0.41–3.0)	.833
BT shunt at S1P	3.12 (1.5–5.9)	.012
AV valve repair at S1P	1.0 (0.9–11.1)	.889
SVP era	0.258 (0.1–0.8)	.024
ID		
HLHS	10.9 (2.2–53)	.016
Higher weight at S1P (kg)	0.33 (0.1–0.8)	.015
BT shunt at S1P	0.53 (0.1–1.9)	.341
AV valve repair at S1P	7.4 (1.0–54)	.069
SVP member	1.06 (0.3–3.4)	.924
Death or transplant at 1 y		
Single RV	1.24 (0.1–16)	.871
Pre-SVP era	6.96 (1.2–52)	.049
Age at S2P (d)	0.01 (0.00–0.02)	.001
BT shunt at S1P	8.76 (1.6–67)	.037
Death or transplant at 1 y, Norwood cohort		
Pre-SVP era	2.13 (1.1–5.6)	.031
Age at S1P (d)	1.10 (1.1–1.2)	.043
Weight at S1P (kg)	0.41 (0.1–0.8)	.029
BT shunt at S1P	1.20 (0.3–4.3)	.783

AV, Atrioventricular; *SVP era,* pre-SVP era for infants who underwent S1P before September 1, 2007, post-SVP era for infants who underwent S1P after September 1, 2007; *single RV,* single-ventricle type with morphologic right ventricle.

revealed that age more than 14 days at S1P ($P = .046$), S1P with a BT shunt ($P = .012$), and S1P during the pre-SVP era ($P = .024$) were associated with predischarge mortality (Table 2).

There were 14 cases of ID in the pre-SVP group (12.1%) and 7 cases of ID in the SVP group (8.3%) ($P = .924$). Cox regression analysis demonstrated that low weight at S1P ($P = .043$) and diagnosis of HLHS ($P = .010$) were associated with increased risk of ID (Table 2). No association was found between ID and pulmonary vein repair, atrioventricular valve repair, or the additional diagnosis of heterotaxy syndrome. An autopsy was performed in 10 of 21 patients who experienced ID and demonstrated BT shunt thrombosis in 4 patients, whereas no cause was found in 6 patients. The majority of ID cases (14/21) were sudden and unexpected deaths of unknown cause (Table 2). HLHS was the diagnosis in 19 of 21 patients (90%) with ID. When evaluated collectively, pre-S2P mortality, defined as either in-hospital or post-discharge death after S1P, was higher in the pre-SVP era ($P = .003$) and in patients with the diagnosis of HLHS ($P = .001$) (Figure 2).

One-Year Survival

At 1 year of age, 55 of 230 patients had died (n = 52) or undergone heart transplantation (n = 3), giving a 1-year survival of 76.3% for the entire cohort (Figure 3). Attrition occurred primarily before S2P (46/55, 84%) (Figure 4). There

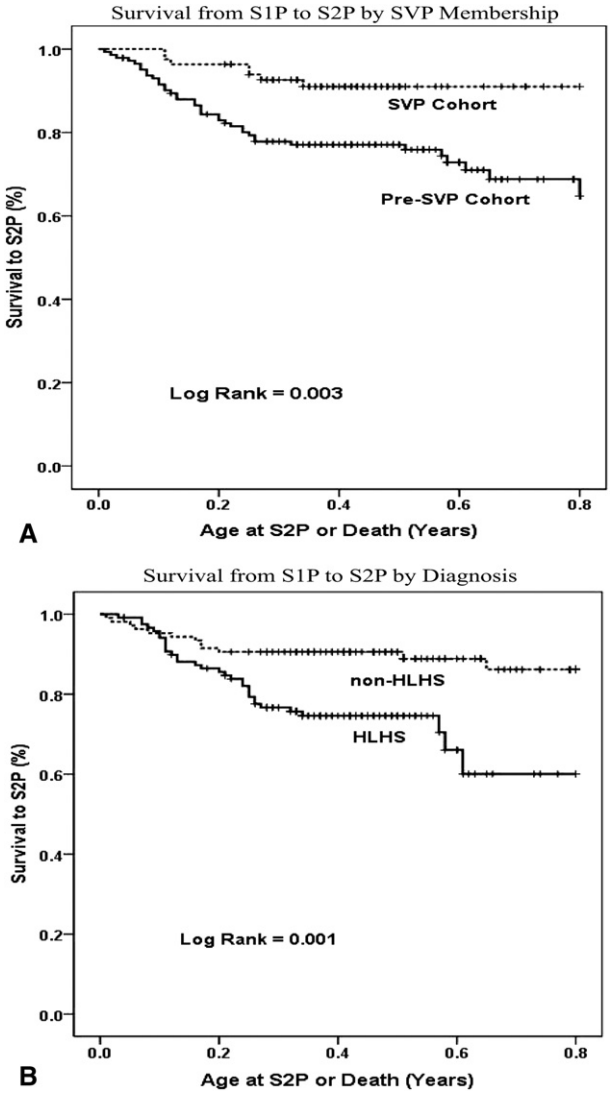


FIGURE 2. Kaplan–Meier analysis of survival between S1P and S2P. Both in-hospital death after S1P and ID are included in the mortality for these analyses. *A,* Survival between the SVP and the pre-SVP cohorts is compared. The SVP cohort has a lower rate of in-hospital and ID. B, Among the entire cohort, patients with HLHS are at higher risk for pre-S2P mortality when they are compared with the remainder of the cohort. *SVP,* Single Ventricle Program; *S1P,* stage 1 palliation; *S2P,* stage 2 palliation; *HLHS,* hypoplastic left heart syndrome.

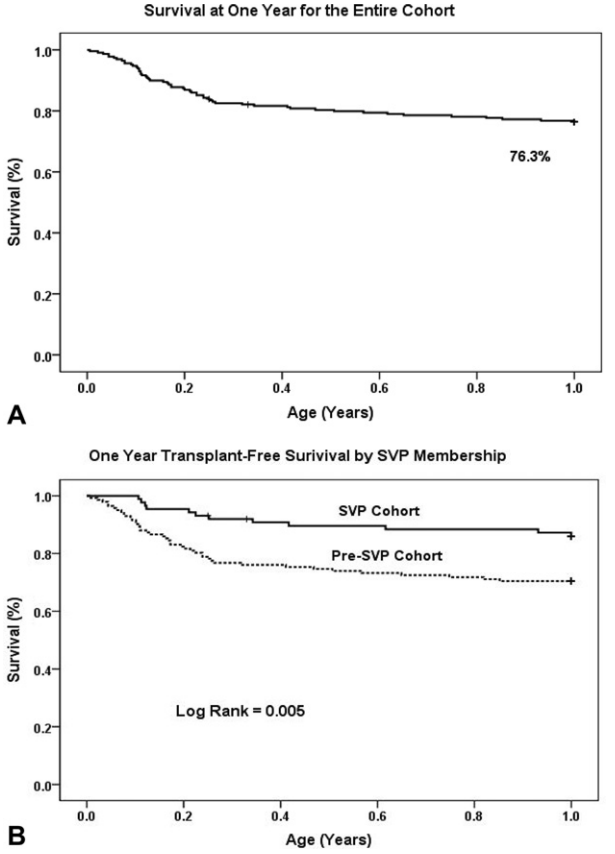


FIGURE 3. Kaplan–Meier analysis of 1-year transplant-free survival. A, Among the entire single-ventricle cohort (both SVP and pre-SVP), the 1-year transplant-free survival is 76.3%. The majority of events occur before 0.3 years. B, There is improvement in 1-year transplant-free survival in the SVP cohort. *SVP,* Single Ventricle Program.

was a significant improvement in 1-year survival in the SVP era in 78 of 93 patients (83.8%) compared with the pre-SVP era in 97 of 137 patients (70.8%) ($P = .002$). Binary logistic regression analysis demonstrated that pre-SVP era ($P = .019$) and low weight at S1P ($P = .026$) were associated with 1-year mortality/transplantation (Table 2).

Norwood Cohort

Of the 230 patients, 151 (66%) underwent Norwood-type palliation at S1P, of whom 87 (58%) were pre-SVP and 64 (42%) were SVP members. The most common diagnoses among this subgroup were HLHS (80%), unbalanced CAVC (15%), and DORV/mitral atresia (4%). A total of 22 patients (15%) underwent RVPA conduit with a Norwood procedure, with the remaining patients having a BT shunt; as noted above, 21 of 22 (96%) RVPA Norwood procedures were performed during the SVP era ($P < .01$). Predischarge mortality after S1P was 14 of 87 (16.1%) during the pre-SVP era and 4 of 64 (6.2%) during the SVP era ($P = .065$). ID occurred in 10 patients in the pre-SVP cohort (13.7%) and in 4 patients (7.1%) in the SVP cohort ($P = .28$). Multivariate regression analysis revealed that among the Norwood cohort, placement of a BT shunt ($P = .04$) and low patient weight at S1P ($P = .03$) were associated with ID, whereas membership in the SVP was not protective against ID ($P = .94$).

By 1 year, 30 of 87 (34.4%) of the pre-SVP Norwood cohort had undergone heart transplantation (n = 2) or died (n = 28). In the SVP Norwood cohort, 15 of 64 patients (23.4%) underwent heart transplantation (n = 1) or died (n = 14) by 1 year of age (Figure 5). Binary logistic

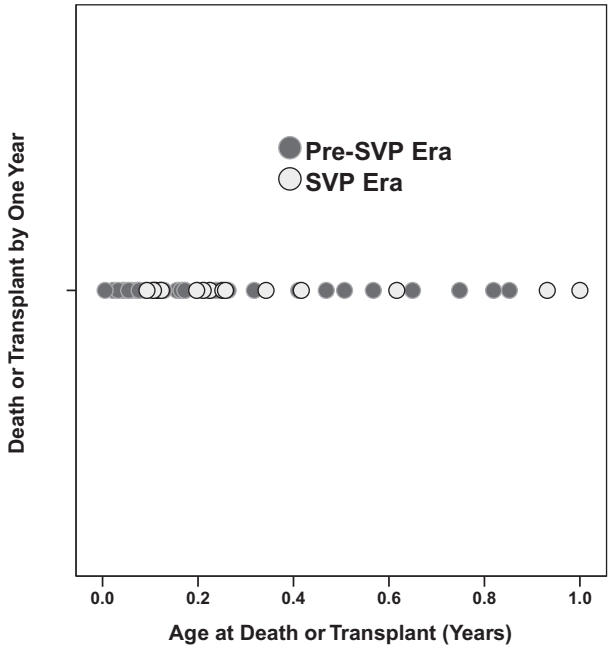


FIGURE 4. Timeline of mortality events (death or heart transplantation) in pre-SVP (dark grey) and SVP (light grey) groups. The timeline demonstrates that the majority of events occurred early (<0.4 years). *SVP,* Single Ventricle Program.

regression demonstrated that, among the Norwood subgroup, higher weight at S1P ($P = .045$), younger age at S1P ($P = .033$), and SVP era ($P = .031$) were associated with improved 1-year transplant-free survival (Table 2). Pulmonary blood flow source type was not associated with 1-year transplant free survival (Figure 5, *B*).

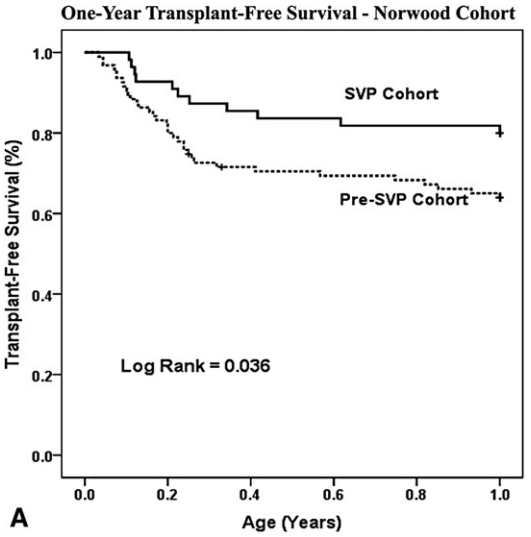
DISCUSSION

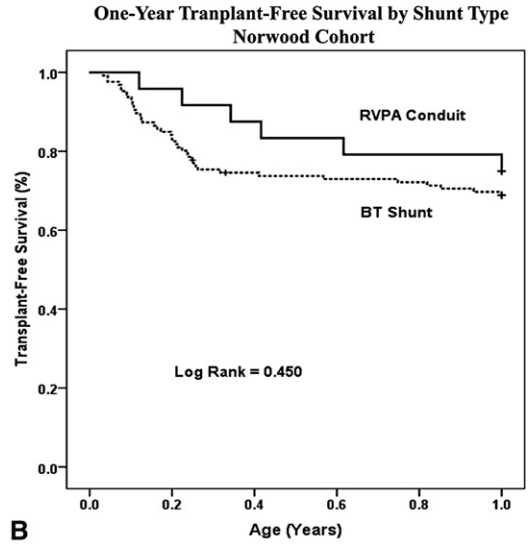
Over the past 2 decades, there has been adoption of a more or less uniform staged palliative approach to the patient with single-ventricle anatomy. Survival after S1P continues to improve since the inception of the Norwood operation.[1-3] A significant effort has been taken by a number of academic centers to identify risk factors that relate to mortality, both before initial stage palliation and between stages. These efforts have resulted in a collective improvement, among a number of centers, in outcomes for infants with single-ventricle anatomy.[8-10] The commonly accepted reasons for improved outcomes include technical advancements and modifications associated with S1P, earlier detection of heart disease, and improvements in preoperative and postoperative care of neonates after S1P reconstruction.[3,11] The impact of close outpatient surveillance remains unclear.

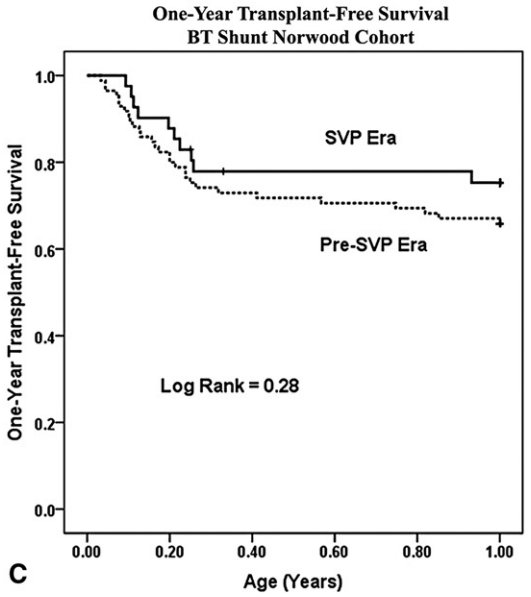
In our retrospective analysis, we found that mortality before S2P continues to be an important problem in patients with single-ventricle anatomy. Although early postoperative mortality was reduced during the SVP era, interstage mortality did not significantly decrease. Although postoperative management continues to evolve at Texas Children's Hospital, there was no identifiable shift in the pre- and postoperative medical management that could account for the decrease in predischarge mortality. Surgical management of these patients did evolve over this time period: RVPA conduit use increased during the SVP era, and this had a demonstrable effect on predischarge survival. We believe that earlier timing of S1P also played a large role in the reduction in predischarge mortality. During the SVP era at Texas Children's Hospital, patients underwent S1P at an earlier age secondary to multiple factors: expansion of the cardiac intensive care unit and operating rooms, and a greater impetus toward earlier surgery. A number of studies have demonstrated that delay beyond 7 to 14 days of age for S1P is associated with mortality.[2,4]

It was disappointing that the interstage mortality did not decrease after initiation of a comprehensive outpatient program at Texas Children's Hospital, given the published data from other centers.[7,12] In the report by Ghanayem and colleagues,[7] interstage mortality was eliminated with the use of outpatient home pulse-oximetry and daily weight monitoring after S1P. These infants were put forward for S2P at less than 5 months of age. The patients reported by Ghanayem and colleagues were often followed by cardiologists outside of the primary institution. The experience at the Children's Hospital of Wisconsin had a large impact on the formation of our program. However, in contrast with the program described in their report, all patients in our SVP were followed primarily by the designated SVP clinicians. In addition, before discharge from S1P all patients in our SVP had rhythm monitoring and airway and feeding evaluations to carefully identify those patients known to be at highest risk for ID. Nonetheless, interstage mortality continued at a rate of 8.3%, despite close outpatient follow-up and home monitoring.

The causes of interstage mortality have been extensively studied. Simsic and colleagues[5] described a higher rate of postoperative arrhythmia in infants who experienced ID. Mahle and colleagues[13] reviewed an extensive variety of preoperative and perioperative factors and found that only earlier era of S1P and history of arrhythmia were associated with ID. Likewise, Hehir and colleagues[4] noted that the majority of IDs were sudden, unexpected events in infants with a history of arrhythmia. Thus, even with vigilant outpatient monitoring of at-risk infants with a single ventricle, there may be a limited ability to reduce interstage mortality. Indeed, although outpatient pulse-oximetry may act as a reliable screening tool for shunt thrombosis or stenosis, it seems that many instances of ID are not associated with shunt occlusion. In a multi-institutional study by Li and colleagues,[14] the mortality rate after Norwood palliation in infants exceeded the rate of thrombosis within systemic-to-pulmonary shunts. The authors postulated that coronary







hypoperfusion in these patients may have contributed to ID. It does seem that the Norwood circulation, in particular, often results in a tenuous balance among the systemic, pulmonary, and coronary circulation. Thus, it is likely that no tool currently available can reliably screen for and prevent all instances of sudden ID.

Earlier timing of S2P has been proffered as a means to reduce interstage mortality. Although some reports have indicated poorer outcomes associated with S2P at less than 4 months of age, others have indicated that earlier S2P is safe.[15-17] In our experience with the SVP, patients were brought forward for S2P as early as 3 months of age and were rarely held for more than 5 months before S2P. To study the efficacy of such a strategy, we thought it important to review the 1-year mortality of the SVP group. We note that there is a significant improvement in 1-year transplant-free survival during the SVP era. Yet, most attrition occurred pre-S2P, and although in-hospital mortality was lower during the SVP era, interstage mortality was not significantly reduced. Thus, improved 1-year survival may be secondary to other factors, including earlier promotion to S1P in neonates with single-ventricle anatomy.

The most significant reduction in mortality was seen before discharge from S1P. Both earlier age at S1P and the limited use of the RVPA conduit were found to be protective against early in-hospital mortality. However, there was little attrition after S2P in either the pre-SVP or SVP era, indicating that the benefits, if any, of early promotion to cavopulmonary circulation cannot be appreciated by 1 year of age.

Patient growth during the interstage period is a crucial factor in allowing for early S2P surgery, and studies have shown that weight gain in infants with a single ventricle is particularly challenging.[18,19] The study by Kelleher and colleagues[20] demonstrated that somatic growth is restricted in patients with a single ventricle, particularly in the interstage period. Their report demonstrated that low weight-for-age *z* score was associated with poorer outcomes, including more frequent interstage admissions. Low patient weight at S2P has also been associated with longer inpatient stay, longer duration of pleural drainage, and longer duration of mechanical ventilation.[17] The study by Hsu and colleagues[21] demonstrated that the mean weight-for-age *z* score at the time of S2P was –1.6, and the *z* score average remained below zero well beyond S2P. Cognizant of the risks of S2P in growth-restricted infants, we used a nutritionist and feeding

FIGURE 5. Kaplan–Meier analysis of 1-year transplant-free survival in the subgroup of patients with a single ventricle who underwent Norwood-type palliation at S1P. A, The SVP cohort experienced improved 1-year transplant-free survival. B, There is no statistically significant improvement in 1-year transplant-free survival with the modified Norwood with RVPA conduit. C, BT shunt group appears to have improved survival at 1 year, but this difference in survival fails to reach statistical significance. *SVP,* Single Ventricle Program; *BT,* Blalock–Taussig.

team to optimize caloric delivery in the interstage period. Patient growth was improved with this approach, and by the time of S2P, patients had achieved a higher weight-for-age z score than their predecessors in the pre-SVP era. Thus, the SVP patients were able to attain an equivalent weight to the pre-SVP group in a shorter period of time, which allowed them to undergo S2P at equivalent size but at a younger age. Indeed, the rate of recovery and time to discharge from S2P were the same between the 2 groups, indicating that the SVP group underwent earlier S2P at no additional risk. Aside from the nutritional and growth benefits attained by this approach, it remains uncertain what other benefits will be derived from the earlier S2P itself.

Texas Children's Hospital is somewhat unique in its limited adoption of the RVPA conduit at S1P. There is a significant body of literature supporting the early benefits of RVPA conduit use in neonates with single-ventricle anatomy.[9,10,22] Since Sano and colleagues[23] reported their experience with the RVPA conduit, many centers have reproduced the improved interstage survival at a cost of earlier S2P because of decreased systemic oxygen saturations.[24-26] Indeed, a recent multicenter randomized study indicated a significantly improved 12-month survival with use of the RVPA conduit.[22] In our center's experience, we did find that in comparison with the RVPA conduit group, the BT shunt group had a higher rate of early, in-hospital death, and a higher rate of ID among the HLHS cohort. Indeed, the difference in 1-year transplant-free survival between the RVPA conduit group and the BT shunt group did not reach statistical significance in our study. Nevertheless, our data support the use of the RVPA conduit at S1P, and it may be particularly useful in low-birthweight neonates.

This report differs from other published reports in that our SVP enrolled infants with a wide range of single-ventricle heart disease, including patients without systemic outflow obstruction and patients with single, morphologic left ventricles. However, this heterogeneity reflects the population served at Texas Children's Hospital. Of course, at Texas Children's Hospital, infants who underwent Norwood palliation also had improved survival at 1 year of age. That outcomes improved in a heterogeneous population with single-ventricle anatomy after initiation of the dedicated program suggests that these results are generalizable and reproducible at other centers.

This study had a number of limitations, including its retrospective nature. The heterogenous nature of our cohort made it difficult to control for a number of factors, particularly in the more complex heterotaxy population. The higher incidence of early mortality in the pre-SVP group may have affected the 1-year survival significantly; thus, reduction in early mortality before the intensive home monitoring certainly played a large role in improvement in 1-year survival.

CONCLUSIONS

Since the initiation of the SVP at Texas Children's Hospital, there has been a significant reduction in early in-hospital mortality and improved interstage growth. Although the SVP did not succeed in reducing interstage mortality, the 1-year transplant-free survival was significantly improved during the SVP era. This may reflect the success of a strategy that included earlier promotion to S1P and optimizing interstage weight gain, with subsequent earlier second-stage surgical palliation.

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