Survival and right ventricular performance for matched children after stage-1 Norwood: Modified Blalock-Taussig shunt versus right-ventricle-to-pulmonary-artery conduit

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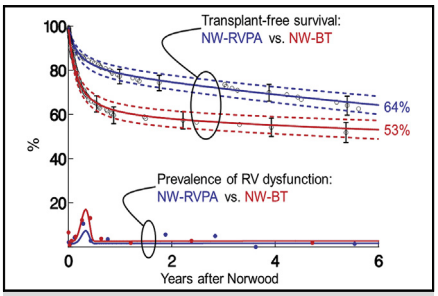
ABSTRACT

Objective: Early survival advantages after Norwood with right-ventricle-(RV)-to-pulmonary-artery conduit (NW-RVPA) over Norwood-operation with a Blalock-Taussig shunt (NW-BT) are offset by concerns regarding delayed RV dysfunction. We compared trends in survival, RV dysfunction, and tricuspid valve regurgitation (TR) between NW-RVPA and NW-BT for propensity-matched neonates with critical left ventricular outflow tract obstruction (LVOTO).

Methods: In an inception cohort (2005-2014; 21 institutions), 454 neonates with critical LVOTO underwent Norwood stage 1. Propensity-score matching paired 169 NW-RVPA patients with 169 NW-BT patients. End-states were compared between NW-RVPA and NW-BT using competing-risks, multiphase, parametric, hazard analysis. Post-Norwood echocardiogram reports (n = 2993) were used to grade RV dysfunction and TR. Time-related prevalence of ≥moderate RV dysfunction and TR were characterized using nonlinear mixed-model regression, and compared between groups via multiphase, parametric models.

Results: Overall 6-year survival was better after NW-RVPA (70%) versus NW-BT (55%; $P < .001$). Additionally, transplant-free survival during this time was better after NW-RVPA (64%) versus NW-BT (53%; $P = .004$).

Overall prevalence of ≥moderate RV dysfunction reached 11% within 3 months post-Norwood. During this time, RV dysfunction after NW-BT was 16% versus 6% after NW-RVPA ($P = .02$), and coincided temporally with an increased early hazard for death. For survivors, late RV dysfunction was <5%



Transplant-free survival and trends in right ventricle dysfunction after NW-RVPA and NW-BT. *NW-RVPA*, Norwood operation with a right-ventricle-to-pulmonary-artery conduit; *NW-BT*, Norwood operation with a modified Blalock-Taussig shunt; *RV*, right ventricle.

Central Message

In neonates with critical left ventricular outflow tract obstruction, NW-RVPA has better 6-year survival, and comparable late RV dysfunction and TR, compared with NW-BT.

Perspective

Norwood-RVPA has been shown to have better early survival than NW-BT. However, concerns about late RV dysfunction have diminished enthusiasm for NW-RVPA. The Congenital Heart Surgeons' Society experience demonstrated better survival at 6 years for NW-RVPA, and comparable late RV dysfunction between groups. For neonates with critical LVOTO, NW-RVPA may be preferable to NW-BT.

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Abbreviations and Acronyms

LVOTO = left ventricular outflow tract obstruction
NW-BT = Norwood operation with a modified Blalock-Taussig shunt
NW-RVPA = Norwood operation with a right-ventricle-to-pulmonary-artery conduit
RV = right ventricular
SVR = Pediatric Heart Network Single Ventricle Reconstruction Trial
TR = tricuspid valve regurgitation

and was not different between groups ($P = .36$).Overall prevalence of ≥moderate TR reached 13% at 2 years post-Norwood and was increased after NW-BT (16%) versus NW-RVPA (11%; $P = .003$). Late TR was similar between groups.ConclusionsAmong propensity-score–matched neonates with critical LVOTO, NW-RVPA offers superior 6-year survival with no greater prevalence of RV dysfunction or TR than conventional NW-BT operations. (J Thorac Cardiovasc Surg 2015;■:1-13)

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For patients with hypoplastic left heart syndrome and related variants, Norwood operations with a right-ventricle-to-pulmonary-artery conduit (NW-RVPA) have been associated with a more stable early postoperative recovery and improved early survival, compared with Norwood operations with a modified Blalock-Taussig shunt (NW-BT).[1] However, early survival advantages associated with NW-RVPA are offset by concerns regarding delayed right ventricle (RV) dysfunction.[2,3] The increased prevalence of late RV dysfunction after NW-RVPA has been suggested to account for, at least partially, the late equalization of transplant-free survival between groups.

Recent reports have demonstrated statistically significant, although relatively slight, decrements in RV function after NW-RVPA.[2,3] Despite the reported association between NW-RVPA and decreased RV function,[2] the clinical impact and associated cause of these small decreases in RV function remain unknown. Furthermore, the relationship between Norwood operations and tricuspid valve regurgitation (TR), and the overall impact on survival, has not been extensively explored.

In 2005, the Congenital Heart Surgeons' Society initiated the critical left ventricular outflow tract obstruction (LVOTO) inception cohort. Most of the neonates enrolled (66%) have undergone a stage-1 Norwood operation. Additionally, for all patients who underwent a Norwood operation, the society data center has collected 4783 echocardiogram reports throughout follow up. Thus, the data center is uniquely positioned to explore differences in survival, postoperative RV dysfunction, and TR among Norwood strategies.

In a propensity-matched, multi-institutional cohort of neonates with critical LVOTO who had undergone either NW-RVPA or NW-BT, we sought to determine: (1) late survival differences; (2) differences in the prevalence of RV dysfunction; and (3) differences in the prevalence of TR.

METHODS

Between 2005 and 2014, an inception cohort of 692 consecutive neonates diagnosed with critical LVOTO were prospectively enrolled by 21 institutions (Table E1). All neonates were admitted within 30 days of birth. Critical LVOTO was defined as stenosis occurring at any level, from the subvalvar region to the innominate artery, with or without left ventricular hypoplasia, such that systemic circulation was ductal dependent.[4] A staged, single-ventricle strategy with an initial Norwood operation was undertaken in 454 (66%) neonates who had hypoplastic left heart syndrome and its variants, such as "borderline left ventricle," for whom single-ventricle palliation was favored. The NW-RVPA was undertaken in 222 (49%), and the NW-BT in 232 (51%). Selection of treatment strategy (including source of pulmonary blood flow) was made at the discretion of the treating physicians.

Similar neonates from each group (NW-RVPA and NW-BT) were statistically matched using propensity scores generated from baseline morphologic, demographic, and clinical characteristics (n = 338). For this study, analyses focused on 169 neonates who underwent NW-RVPA and were propensity-score matched with 169 neonates who underwent NW-BT. Details of all interventions and clinical investigations were acquired by the data center, including reports of all available echocardiograms throughout follow-up. The analysis strategy involved: (1) parametric risk-adjusted comparisons of survival, transplantation, and other competing end-states; and (2) risk-adjusted comparisons of the time-related prevalence of important (≥moderate) RV dysfunction and TR, using nonlinear, multiphase mixed-model techniques (Appendix 1).[5-7]

Data Acquisition and Follow-up

Participation in the study and submission of patient information was voluntary and confidential. Parental consent for enrollment and ethics board approval were obtained by individual institutions and the data center. Admission, diagnostic, and surgical patient data were abstracted from institutional medical records, echocardiogram reports, and surgical reports, as previously described.[8] Patients' families were contacted annually by data center staff to obtain details of subsequent clinical history, investigations, and interventions. Reports of all such investigations and interventions were then obtained from each institution to complete longitudinal follow-up. Median follow-up among survivors for the 338 propensity-matched children was 4.8 years (7 days to 8.6 years), and in 2014, the process had been completed for 79% of patients.

Statistical Analysis

Demographic, morphologic, and clinical information preceding stage-1 Norwood operations were included as baseline variables. Variables were

processed as described in detail previously.[8] Measurements of cardiac dimensions were standardized as z-scores, based on published normative data, if available, or otherwise indexed to height or body surface area.[9] Missing values for baseline covariables were estimated using multiple imputation.[10] Missing values for outcome variables, however, were not imputed. For regression analyses and propensity matching, final variable selection was guided by bootstrap resampling for reliability (n = 500 resamples threshold for inclusion $P < .1$).[11]

Continuous variables were compared with the Wilcoxon rank-sum test, using Wilcoxon rank scores, and these are summarized as median with range, mean ± SD, or as equivalent 15th, 50th (median), and 85th percentiles. Categoric variables were compared using a χ^2; test of independence or Fisher's exact test, when appropriate, and are presented as frequencies and percentages. Parametric estimates of postoperative echocardiographic measurements are accompanied by asymmetric, 68% confidence limits (comparable to ±1 SE), obtained using bootstrap percentile methods.[5,12] Data analyses were performed with SAS statistical software (version 9.2; SAS Institute, Inc, Cary, NC). Additional information regarding statistical analyses is provided in Appendix 1.

Propensity-score matching. To adjust for potential differences between neonates who underwent an NW-RVPA versus an NW-BT, propensity-score matching was used.[13-15] This process included: (1) incorporating baseline demographic, morphologic, and clinical parameters that met bootstrap criteria, into a logistic regression equation, modeling the probability of any given neonate belonging to the NW-RVPA versus NW-BT group. (2) This parsimonious model was augmented with important clinical variables, including baseline RV dysfunction and TR from echocardiogram reports (13 variables, c-statistic = 0.71; Table E2). (3) Neonates were matched with a 1:1 greedy-matching algorithm between NW-RVPA and NW-BT, based on propensity scores.[16] (4) The difference between the 2 groups before and after propensity-score matching was compared, using the standardized differences for mean value of important baseline characteristics (Figure E1).[17]

Table E3 summarizes the values for all variables before propensity-score matching (including those not selected into the final propensity score) used for determining the propensity score. Of the 454 neonates who underwent Norwood stage1, a total of 116 (26%) remained unmatched, indicating that their demographic, morphologic, and clinical features were less comparable to those in the remainder of the cohort. Propensity-score matching yielded 338 (74%) paired neonates: 169 NW-RVPA and 169 NW-BT (Figure E2). These 2 groups comprised the study population of focus for the remaining analyses.

Analysis of competing end-states. Kaplan-Meier estimates of time-to-event were constructed, and used to create parametric multiphase models defining transition to various end-states. These models utilize shaping parameters that capture various phases of risk, each of which can independently be subjected to risk-hazard regression analysis.[18] (For additional details, see http://www.lerner.ccf.org/qhs/software/hazard.) Mutually exclusive end-states for analysis included death, transplantation, and transition to other mutually exclusive competing end-states, such as Fontan operation or biventricular repair.

Analysis of repeated measurements of RV dysfunction and TR. All available echocardiogram reports were acquired throughout the follow-up period, for all patients. Reported subjective grades of RV dysfunction and TR were abstracted and categorized into a 6-category, ordinal scale of severity, ranging from no dysfunction or TR to severe dysfunction and/or TR. For nonlinear, mixed-model analysis, RV dysfunction and TR were dichotomized by the presence of moderate-or-worse disease (≥moderate). Follow-up was censored for echocardiograms after transplantation, or conversion to biventricular repair. For analysis of TR, follow-up was censored for echocardiograms after tricuspid valve interventions (repair and/or replacement).

Time-related trends for the prevalence of ≥moderate RV dysfunction and TR were evaluated using nonlinear mixed-model regression (SAS PROC NLMIXED; SAS Institute, Inc, Cary, NC). This technique is similar to logistic regression in that it allows for the detection and characterization of nonlinear trends for each outcome parameter. Additionally, all available data points for each patient are utilized. Therefore, rather than aggregating data to be used in analysis, data are adjusted for repeated measures.[5,6] Nonlinear models were then used for multivariable regression analysis, in a manner similar to nonproportional hazard analysis. In total, 2993 post-Norwood echocardiogram reports were available for 309 propensity-matched neonates (91% of the population). Reliable evaluation for the time-related trends in RV dysfunction and TR was permitted for up to 6 years after Norwood stage 1.

RESULTS

Group Characteristics

Baseline characteristics for propensity-matched neonates who underwent NW-RVPA and NW-BT were similar (Table 1). No differences were found in median birth weights for neonates who underwent NW-RVPA (3.1 kg, from 1.8 to 4.4 kg) versus NW-BT (3.2 kg, from 1.9 to 4.5 kg; $P = .92$). No significant difference was found between groups for neonates with ≥moderate RV dysfunction ($P = .97$) or TR ($P = .42$) on baseline echocardiogram.

Outcomes

After Norwood stage 1, all neonates transitioned to various mutually exclusive competing end-states. Overall, 52% of neonates transitioned to a Fontan operation by 6 years after stage 1 (54% after NW-RVPA vs 49% after NW-BR; Figure 1). Additionally, 4% of neonates underwent transplantation (6% after NW-RVPA vs 2% after NW-BT), and 2% of neonates converted to biventricular repair (exclusively after NW-RVPA). A total of 11 patients underwent a tricuspid valve intervention. Of these, 7 occurred after NW-RVPA; 4 occurred after NW-BT ($P = .36$).

Overall survival. Overall survival for all 338 propensity-matched neonates at 6 years after Norwood stage 1 was 62% ± 3%. Independent of time, 115 patients died (NW-RVPA = 44; NW-BT = 71; $P = .002$). Overall survival was significantly better after NW-RVPA (70% ± 4%) versus NW-BT (55% ± 3%, at 6 years; log-rank, $P < .001$). Survival differences were predominantly attributable to a significantly greater hazard for death within the initial 1.5 years after NW-BT ($P < .0001$; Figure 2, *A*). Beyond this initial 1.5 years, the hazard for death reflected a slow, constant attrition (approximately 5 deaths per year; $P = .76$) and was comparable between groups.

Transplant-free survival. For the composite end-state of transplantation or death, 126 total events occurred (113 deaths and 13 transplants). Transplant-free survival was 58% ± 3% 6 years after stage 1, for all neonates. Transplantation was performed in 13 children (NW-RVPA = 9; NW-BT = 4; $P = .16$), with late transplant-free survival significantly better after NW-RVPA (64% ± 4%) versus

TABLE 1. Selected baseline characteristics for 338 neonates after propensity-score matching

Variable	NW-RVPA (n = 169)			NW-BT (n = 169)			*P* value
	n	Mean ± SD	Percentiles or frequency (%)	n	Mean ± SD	Percentiles or frequency (%)	
General							
Gender, male	169		105 (62)	169		113 (67)	.43
Age at Norwood (d)*	169	6.3 ± 4.5	3/5/9	169	6.5 ± 4.6	4/6/8.5	.14
Age at stage-2 SCPC (mo)	125	5.7 ± 2.8	4.1/4.9/7.2	108	5.9 ± 2.3	3.6/5.7/7.8	.44
Birth weight (kg)	164	3.2 ± 0.5	2.7/3.1/3.7	168	3.2 ± 0.4	2.8/3.2/3.6	.92
Birth weight <2.5 kg	168		11 (7)	164		9 (5)	.61
Birth BSA (m^2)	152	0.21 ± 0.02	0.19/0.21/0.23	162	0.21 ± 0.02	0.19/0.21/0.22	.57
Weight at Norwood (kg)	166	3.2 ± 0.48	2.7/3.1/3.7	169	3.2 ± 0.46	2.7/3.2/3.6	.67
BSA at Norwood (m^2)*	160	0.21 ± 0.02	0.18/0.2/0.23	166	0.21 ± 0.02	0.19/0.21/0.22	.71
Associated lesions							
Anomalous coronary artery	169		4 (2)	169		3 (2)	.70
Transverse arch coarctation*	164		50 (30)	164		52 (32)	.81
Septum/endocardium							
Small/restrictive ASD*	120		49 (41)	124		54 (44)	.67
Unrestrictive VSD	110		19 (17)	102		20 (20)	.66
EFE (any level)	30		27 (90)	39		35 (90)	.97
LVOT							
Minimum LVOTO size (cm)	157	0.16 ± 0.2	0/0/0.4	164	0.17 ± 0.2	0/0/0.5	.55
Minimum LVOTO z-score	153	−23 ± 10	−31/−31/−9	163	−22 ± 11	−31/−31/−7	.37
Aortic valve annulus (cm)*	145	0.14 ± 0.2	0/0/0.4	149	0.15 ± 0.2	0/0/0.4	.82
Aortic valve annulus z-score	142	−23 ± 10	−31/−31/−9	148	−23 ± 11	−31/−31/−8	.65
Ascending aorta (cm)	129	0.34 ± 0.2	0.18/0.26/0.5	137	0.35 ± 0.2	0.2/0.26/0.6	.41
Ascending aorta index (cm/m^2)	118	1.6 ± 0.9	0.9/1.2/2.6	133	1.7 ± 0.9	0.9/1.3/2.8	.40
Transverse arch (cm)	81	0.37 ± 0.1	0.25/0.4/0.5	77	0.37 ± 0.1	0.27/0.4/0.5	.96
Transverse arch index (cm/m^2)	78	1.8 ± 0.5	1.2/1.8/2.3	76	1.8 ± 0.5	1.3/1.8/2.2	.85
Aortic valve atresia	157		89 (57)	164		90 (55)	.74
Functional aortic valve atresia†	169		116 (69)	169		116 (69)	1.0
AI (any degree)*	141		19 (13)	148		22 (15)	.74
Left ventricle							
EDD (cm)	23	1.5 ± 0.5	1.1/1.5/2	35	1.3 ± 0.5	0.7/1.3/1.9	.10
ESD (cm)	22	1.1 ± 0.4	0.7/1.1/1.6	30	1 ± 0.5	0.4/1/1.6	.56
Shortening fraction	22	29 ± 13	14/28/44	30	30 ± 17	8.7/28/47	.99
Functional atresia†	75		35 (47)	74		37 (50)	.68
Dysfunction (any degree)*	81		53 (65)	77		57 (74)	.24
Atrioventricular valve							
MV annulus (cm), 4-chamber view	109	0.22 ± 0.4	0/0/0.7	116	0.24 ± 0.3	0/0/0.7	.44
MV z-score	108	−17 ± 7.4	−22/−22/−6	115	−17 ± 7	−22/−22/−6	.44
TV annulus (cm)	19	1.3 ± 0.2	1.07/1.3/1.5	47	1.3 ± 0.2	1.1/1.3/1.5	.77
TV annulus z-score*	18	−1 ± 1.5	−2.5/−0.5/1.4	47	−1 ± 1.8	−3/−11/1	.64
MV atresia	156		75 (48)	155		70 (45)	.61
Functional mitral valve atresia*,†	153		133 (85)	153		140 (89)	.31
Grade TR*	164			161			.19
No TR (0)			37 (23)			23 (14)	
Trivial (1)			5 (3)			8 (5)	
Mild (2)			66 (40)			80 (50)	
Mild+ (3)			42 (26)			40 (25)	
Moderate (4)			12 (7)			10 (6)	
Moderate+ (5)			2 (1)			0	
TR (≥moderate)	164		14 (9)	161		10 (6)	.42
Right ventricle							
EDD (cm)	7	1.5 ± 0.6	.9/1.5/2.4	22	1.2 ± 0.4	0.9/1.3/1.6	.36
Grade dysfunction*	161			156			.34
No dysfunction			140 (85)			134 (86)	

(Continued)

TABLE 1. Continued

Variable	NW-RVPA (n = 169) n	Mean ± SD	Percentiles or frequency (%)	NW-BT (n = 169) n	Mean ± SD	Percentiles or frequency (%)	*P* value
Trivial (1)			8 (5)			13 (8)	
Mild (2)			8 (5)			7 (5)	
Mild+ (3)			3 (2)			0	
Moderate (4)			1 (1)			2 (1)	
Moderate+ (5)			1 (1)			0	
Dysfunction ≥moderate	161		2 (1)	156		2 (1)	.97
RVOT							
PV annulus (cm)	26	1 ± 0.2	0.8/1.1/1.2	45	1 ± 0.1	0.85/1/1.1	.22
PV z-score	24	1.37 ± 1.27	−0.03/1.3/2.9	44	1 ± 1	−0.03/1.1/2.9	.71
Minimum BPA (cm)	46	0.47 ± 0.1	0.38/0.46/0.6	48	0.45 ± 0.1	0.37/0.45/0.6	.36
Minimum BPA z-score	45	−1 ± 1.4	−2/−0.5/1	47	−1 ± 1.4	−2.3/−0.5/1	.60
Stenosis	155		4 (3)	156		6 (4)	.53
Preoperative							
Mechanical ventilation	169		74 (44)	169		69 (41)	.58
Identifiable genetic syndrome	169		3 (2)	169		7 (4)	.20
Renal insufficiency*	169		2 (1)	169		1 (1)	.56
Metabolic acidosis*	169		20 (12)	169		20 (12)	1.0
CNS: seizure, bleeding, stroke	169		4 (2)	169		3 (2)	.70
Outcomes							
Total dead	169		44 (26)	169		71 (42)	.002
Total transplant	169		9 (5)	169		4 (2)	.16
Fontan operation	169		65 (38)	169		52 (31)	.14
Stage-2 SCPC	169		125 (74)	169		108 (64)	.05
Tricuspid valve intervention	169		7 (4)	169		4 (2)	.36
Biventricular repair	169		6 (4)	169		0	.014

Percentiles are 15th/50th/85th. Values for baseline morphologic and demographic characteristics (including variables not used for determining the propensity score), along with outcome measures for 338 propensity-score matched neonates. Stratified by NW-RVPA (n = 169) versus NW-BT (n = 169). *NW-RVPA*, Norwood operation with right-ventricle-to-pulmonary-artery conduit; *NW-BT*, Norwood operation with modified Blalock-Taussig shunt; *SD*, standard deviation; *SCPC*, superior cavopulmonary connection; *BSA*, body surface area; *ASD*, atrial septal defect; *VSD*, ventricular septal defect; *EFE*, endocardial fibroelastosis; *LVOT*, left ventricular outflow tract; *LVOTO*, left ventricular outflow tract obstruction; *AI*, aortic insufficiency; *EDD*, end diastolic dimension; *ESD*, end systolic dimension; *MV*, mitral valve; *TV*, tricuspid valve; *TR*, tricuspid regurgitation; *PV*, pulmonary valve; *RVOT*, right ventricular outflow tract; *BPA*, branch pulmonary artery; *CNS*, preoperative stroke, seizure or central nervous system/intracranial hemorrhage. *Designates variables used to create the propensity score. †Functional aortic valve atresia and functional mitral valve atresia designate an aortic or mitral valve that is either atretic or associated with severe stenosis or hypoplasia.

NW-BT (53% ± 4% at age 6 years; log-rank $P = .004$; Figure 2, *B*). At all time points, transplant-free survival was significantly greater after NW-RVPA. However, the magnitude of the difference in transplant-free survival diminished over time (late convergence) between the groups.

Right Ventricular Dysfunction After Norwood Stage 1

For all 338 propensity-matched patients, the time-related prevalence of ≥moderate postoperative RV dysfunction peaked to 11% ± 3% during the initial 3 to 6 months after Norwood palliation (Figure E3). Thereafter, the prevalence of ≥moderate postoperative RV dysfunction remained at a constant level of <5%.

The NW-BT procedure was associated with a significantly greater prevalence of RV dysfunction in the initial 6 months (16%), compared with NW-RVPA (6%; $P = .019$; Figure 3). However, beyond 1 year after Norwood stage 1, both groups exhibited a low and comparable prevalence of ≥moderate RV dysfunction. Both NW-RVPA and NW-BT demonstrated a similar prevalence of late (6-year follow-up) RV dysfunction for survivors not undergoing transplantation or biventricular repair (<5%; $P = .36$).

The increased early prevalence of RV dysfunction coincides temporally with the early hazard for death or transplantation (Figure 4), and corresponds to the pre–stage-2 period (often termed ''interstage''). Stage-2 superior cavopulmonary connection was undertaken at a median interval of 4.7 months (2.1-24 months) and 5.4 months (1.5-16 months) after stage 1, for NW-RVPA and NW-BT, respectively ($P = .61$).

Right ventricular dysfunction and survival before stage 2 or biventricular repair. Trends for RV dysfunction during the interstage period before stage-2 or biventricular repair showed that the peak prevalence for RV dysfunction (10% ± 2%) occurred between 3 and 4 months after the

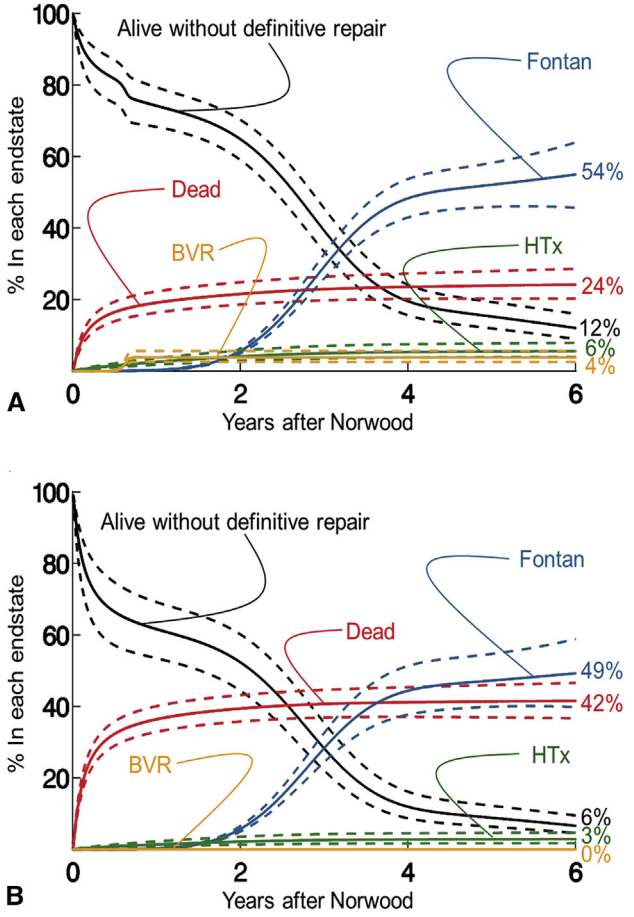

FIGURE 1. A, Competing end-states after (A) NW-RVPA versus (B) NW-BT. The transition to competing end-states for 169 propensity-score matched neonates after (A) NW-RVPA and (B) NW-BT. All neonates begin alive immediately after the Norwood operation (time = 0); thereafter, they remained in this state (*black curve*), or entered 1 of 4 additional mutually exclusive end-states, including: (1) transition to Fontan operation (*blue curve*); (2) HTx (*green curve*); (3) conversion to BVR (*yellow curve*); and (4) death without definitive repair (*red curve*). At any point in time, the sum of proportions of patients in each end-state must be 100%. (A) By 6 years after NW-RVPA, 12% of children were alive without definitive repair, 54% underwent Fontan operation, 6% reached HTx, 4% converted to BVR, and 24% died without definitive repair. (B) By 6 years after NW-BT, 6% of children were alive without definitive repair, 49% underwent Fontan operation, 3% reached HTx, none had converted to a BVR, and 42% died without definitive repair. *Solid lines* show parametric estimates defined by the hazard function and are enclosed within *dashed* 68% confidence bands equivalent to ±1 SE. *BVR*, Biventricular repair; *HTx*, heart transplantation.

Norwood operation. During this time, transplant-free survival ($P = .0019$) and the prevalence of ≥moderate postoperative RV dysfunction ($P = .0026$) were significantly better for NW-RVPA versus NW-BT (Figure E4). For both groups, the prevalence of ≥moderate RV dysfunction began to decline after 4 to 5 months, corresponding temporally with the approximate timing of stage 2 and with the end of the early hazard for death.

Right ventricular dysfunction and survival after stage 2. For 233 neonates (NW-RVPA = 125; NW-BT = 108; $P = .05$) who underwent stage 2, the prevalence of ≥moderate postoperative RV dysfunction showed progressive and similar declines for both groups, reaching <5% for survivors 5 years after stage 2 (Figure 5, *A*; $P = .66$). Furthermore, transplant-free survival after transition to stage 2 was similar for NW-RVPA (81% ± 3%) and NW-BT (80% ± 4%; log-rank, $P = .69$; Figure 5, *B*) at 5 years. Immediately after stage 2 was a low, early hazard for death, followed by a low, constant rate thereafter.

Tricuspid Valve Regurgitation After Norwood Stage 1

The peak prevalence of ≥moderate TR was 13% ± 3% at 2 years after the Norwood operation, for all patients (Figure E5). For survivors not undergoing transplantation, biventricular repair, or tricuspid valve intervention, the prevalence of ≥moderate postoperative TR was 11% at 6 years after Norwood stage 1. The NW-BT procedure was associated with a greater prevalence of ≥moderate TR during the initial 2 years (15%), compared with NW-RVPA (11%; $P = .003$). Thereafter, NW-BT was associated with a decreasing prevalence of tricuspid valve regurgitation (12% at 6 years); whereas NW-RVPA plateaued to a 10% prevalence for ≥moderate TR (Figure 6).

Tricuspid valve regurgitation before and after stage 2. During the interstage period before stage 2, TR demonstrated an increasing prevalence, reaching 12% ± 3% at 5 months. Shortly after transition to stage 2, the prevalence of TR peaked to 13% (2 years after stage-1 Norwood), which was followed by a gradual decline.

Tracking the prevalence of ≥moderate postoperative TR during the interstage period before and after stage 2 showed that the most significant difference in the prevalence of TR between NW-RVPA and NW-BT occurred before stage 2 ($P = .001$). Thereafter, NW-BT tended to be associated with an increased prevalence of ≥moderate TR relative to NW-RVPA (12% vs 10% at 6 years, respectively); however, this difference was not statistically significant ($P = .25$).

DISCUSSION

For neonates with critical LVOTO and similar baseline characteristics undergoing a Norwood stage-1 operation, the 6-year overall survival and transplant-free survival were significantly better after NW-RVPA versus NW-BT. Although a relative convergence occurred for transplant-free survival between groups, NW-RVPA was associated with significantly better transplant-free survival at all time points during follow-up. For all survivors not undergoing transplantation or biventricular repair, the prevalences of

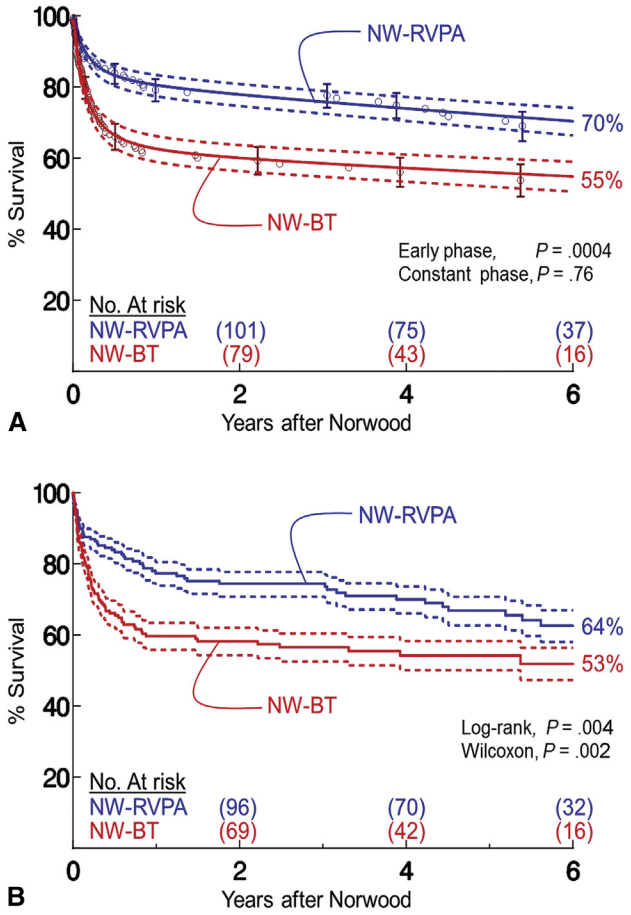

FIGURE 2. A, Overall survival and (B) transplant-free survival for 338 propensity-score matched neonates after Norwood stage 1. A, Overall 6-year survival after Norwood stage 1 for 169 propensity-score matched neonates after Norwood operation with NW-RVPA (*blue curve*), and 169 propensity-matched neonates after NW-BT (*red curve*). Independent of time, 44 deaths occurred after NW-RVPA, and 71 after NW-BT. The 6-year survival after NW-RVPA (70% ± 4%) was significantly better than that after NW-BT (55% ± 3%). The difference in survival was predominantly related to an increased early (<1.5 years) hazard (PE = 0.85; $P = .0004$). Thereafter, a constant hazard demonstrated similar low rates of attrition between groups (PE = −0.18; $P = .76$). Each *circle* represents a death positioned on the vertical axis by the Kaplan-Meier estimator. *Vertical bars* are confidence limits equivalent to ±1 SE. *Solid lines* are PEs enclosed within *dashed* 68% confidence bands equivalent to ±1 SE. *In parentheses* are the numbers of patients at risk at each associated time. PEs were determined from multiphase risk-hazard analysis and represent the magnitude of NW-BT as a risk factor for death. B, Kaplan-Meier curve for 6-year, transplant-free survival for 169 propensity-score matched neonates after NW-RVPA (*blue curve*) and 169 propensity-score matched neonates after NW-BT (*red curve*). Independent of time were 52 events after NW-RVPA (43 deaths, 9 transplants) and 74 events after NW-BT (70 deaths, 4 transplants). At all time points, NW-RVPA was associated with significantly better transplant-free survival versus NW-BT (64% ± 4% vs 53% ± 4% at 6 years, respectively; log-rank, $P = .004$). In a multiphase, parametric hazard analysis, NW-BT was associated with an increased risk of death or transplant in the early (<1.5 years) hazard phase (PE = 0.83; $P = .0004$). This phase was followed by a constant hazard phase, which did not demonstrate a significant difference in transplant-free survival between groups (PE = −0.80; $P = .26$). *Solid lines* are Kaplan-Meier estimates enclosed within 68% confidence bands equivalent to ±1 SE (*dashed lines*). *In parentheses* are the numbers of patients at risk at each associated time. PEs were determined from multiphase risk-hazard analysis and represent the magnitude of NW-BT as a risk factor for death. *NW-RVPA*, Norwood operation with right-ventricle-to-pulmonary-artery conduit; *NW-BT*, Norwood operation with modified Blalock-Taussig shunt.

late, ≥moderate RV dysfunction and tricuspid valve regurgitation were similar in the NW-BT and NW-RVPA groups, at 6 years, without evidence of increased RV dysfunction for patients who underwent NW-RVPA.

Trends for Survival, Right Ventricular Dysfunction, and Tricuspid Valve Regurgitation

The Norwood operation places the systemic and pulmonary circulations in parallel. As such, the RV must generate higher than normal cardiac output, and is placed in a state of relative volume overload.[19,20] The increased cardiac demand placed on the systemic RV after a Norwood operation is considered to play an important role in the early risk of death.[19] Consistent with previous reports, our results demonstrate an early hazard for death after Norwood stage 1.[1,19,21] Specifically, most deaths occurred before transition to stage-2 superior cavopulmonary connection; with a low, constant rate of attrition thereafter. This finding is congruous with reports that show excellent survival for all patients after stage 2 (95% survival, 1-year post–superior cavopulmonary connection).[20,22,23]

The risk of death early after Norwood stage 1 may be due partly to the increased prevalence of important (≥moderate) RV dysfunction that occurs during the interstage period between a Norwood operation and conversion to stage 2. For all neonates, the peak prevalence of RV dysfunction coincided temporally with the maximum rate of death after Norwood stage 1. Although a causal link between these 2 time-related events cannot be made directly, they suggest that poor RV function contributes to the early hazard for death. The peak prevalence, and long-term trends of important postoperative RV dysfunction and TR, did not coincide. The RV dysfunction begins to decline before the median age of stage 2, whereas TR does not peak until after transition to stage 2. Thereafter, TR remained elevated at 6 years, relative to the prevalence of important RV dysfunction.

Potential implications of these findings include: (1) the transition to stage 2 is not entirely responsible for the decreased prevalence of RV dysfunction. The declining prevalence of RV dysfunction may, in part, be related to early mortality, resulting in selective ‘‘dropout’’ of patients

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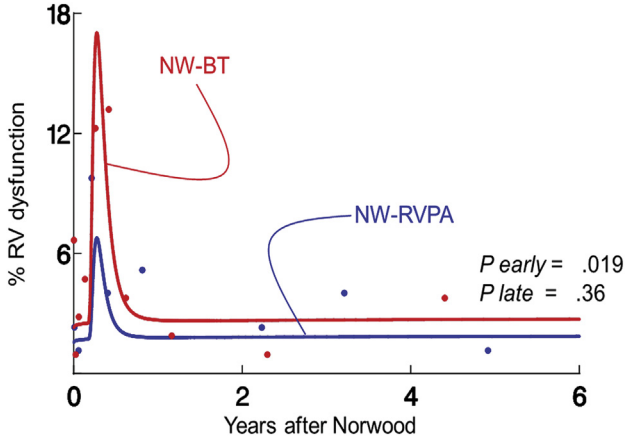

FIGURE 3. Overall, postoperative RV dysfunction for NW-RVPA and NW-BT. Relationship between the prevalence of ≥moderate postoperative RV dysfunction for patients who NW-RVPA (*blue curve*) versus patients who underwent NW-BT (*red curve*). NW-BT was associated with a significantly greater prevalence of RV dysfunction during the initial 6 months, (16%) relative to NW-RVPA (6%; PE = 1.7, $P = .019$). Beyond 1 year after Norwood stage 1, both groups exhibited a comparable, low (<5%) prevalence of ≥moderate postoperative RV dysfunction (PE = 0.48; $P = .36$). The increased early prevalence of RV dysfunction coincides temporally with the early hazard for death. Therefore, the decreased late prevalence of RV dysfunction does not necessarily reflect the potential for individual recovery. RV dysfunction was evaluated for 292 children (2474 echocardiogram reports). *Solid lines* indicate the estimated prevalence for ≥moderate RV dysfunction. *Circles* represent data grouped by associated operation (without regard to repeated measurements) within timeframes, to provide crude verification of model fit. PEs were determined from multiphase, nonlinear, mixed-model regression and represent the magnitude of association with RV dysfunction for NW-BT. *NW-BT*, Norwood operation with modified Blalock-Taussig shunt; *NW-RVPA*, Norwood operation with right-ventricle-to-pulmonary-artery conduit; *RV*, right ventricular.

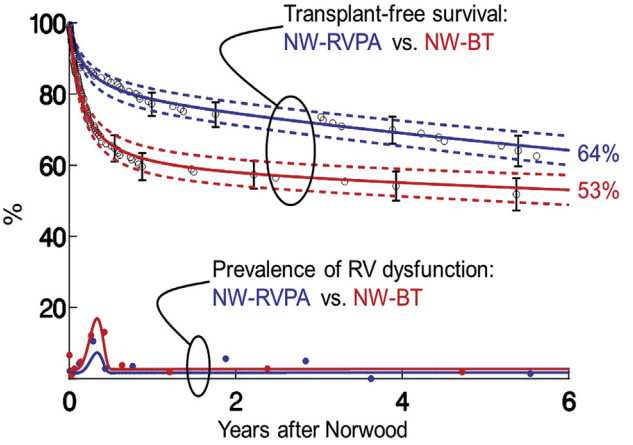

FIGURE 4. Transplant-free survival and prevalence of RV dysfunction for NW-RVPA and NW-BT. Transplant-free survival versus the prevalence of ≥moderate postoperative RV dysfunction for patients who underwent NW-RVPA (*blue curve*) versus NW-BT (*red curve*). The early prevalence of RV dysfunction coincides temporally with the early hazard for death, both of which were significantly better after NW-RVPA versus NW-BT. *Open blue circles* represent an event (death or transplant) after NW-RVPA, and *open red circles* are events after NW-BT positioned on the vertical axis by the Kaplan-Meier estimator. *Vertical bars* are confidence limits equivalent to ±1 SE. *Solid black lines* are parametric estimates enclosed within *dashed* 68% confidence bands equivalent to ±1 SE. The *solid blue line* shows the estimated probability for ≥moderate RV dysfunction after NW-RVPA. The *solid red line* is the estimated probability for ≥moderate RV dysfunction after NW-BT. *Closed circles* represent data grouped by associated operation (without regard to repeated measurements) within timeframes to provide crude verification of model fit. *NW-RVPA*, Norwood operation with right-ventricle-to-pulmonary-artery conduit; *NW-BT*, Norwood operation with modified Blalock-Taussig shunt; *RV*, right ventricular.

with poor RV function, resulting in better RV function for the remaining population. (2) Patients with important TR may not be subject to the same early "dropout" associated with poor RV function. Given this possibility, an increased prevalence of important TR early may not affect survival to the same degree as early RV dysfunction.

Comparison Between NW-RVPA and NW-BT

The increased hazard for death and the prevalence of RV dysfunction, which occurred early after NW-BT relative to NW-RVPA, suggest that the "cost" of NW-BT, in survival and RV dysfunction, occurs during the volume-loaded, pre–stage-2 interval. After stage 2, the hazard for death and the prevalence of RV dysfunction were comparable between groups, implying that NW-RVPA is not associated with a "cost" of late RV dysfunction.

The SVR trial compared outcomes after Norwood operations for 549 infants randomized to NW-RVPA and NW-BT.[1] The initial trial, along with extensions of follow-up, has generated important contributions in describing outcomes between NW-RVPA and NW-BT.[1-3,19,24-26] A key finding of the SVR trial was the increased early (<1-year) survival after NW-RVPA, compared with NW-BT (74% vs 64%, respectively).[1] Thereafter, transplant-free survival between groups was similar. Follow-up of the SVR trial demonstrated that 3- and 5-year survival was not significantly different with NW-BT (61% and 60%, 3 and 5 years) versus NW-RVPA (67% and 64%, 3 and 5 years).[3] Our series, using data from an inception cohort, identified similar trends for transplant-free survival between groups.

Transplant-free survival versus overall survival. The slightly increased late attrition in transplant-free survival after NW-RVPA seems to be related to—at least in part—the influence of late transplantation. Although speculative, 1 possibility is that survival after NW-RVPA is improved during the early, "high-risk" postoperative period, thereby increasing the probability of late transplantation; by contrast, struggling NW-BT patients may not survive

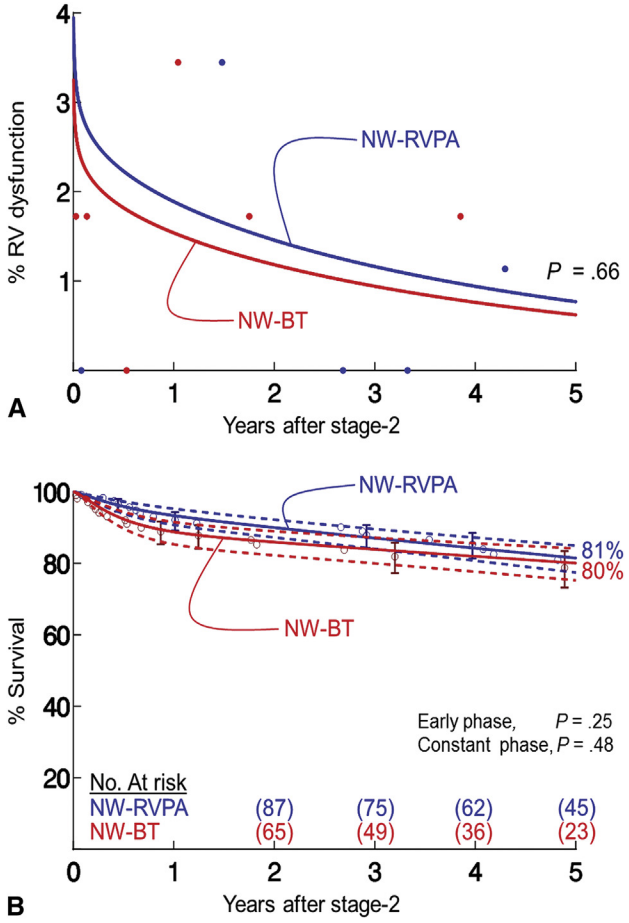

FIGURE 5. A, Post–stage-2 RV dysfunction, and (B) transplant-free survival. A, Relationship between the prevalence of ≥moderate postoperative RV dysfunction after transition to stage-2 SCPC for patients who underwent NW-RVPA (*blue curve*) versus patients who underwent NW-BT (*red curve*). The NW-RVPA and NW-BT had a similar low prevalence of postoperative RV dysfunction (<5%) after stage 2 (PE = −0.23; $P = .66$). RV dysfunction was evaluated for 187 patients (1265 echocardiogram reports). *Solid lines* are the estimated prevalence for ≥moderate RV dysfunction after stage 2. *Circles* represent data grouped by associated operations (without regard to repeated measurements) within timeframes, to provide crude verification of model fit. PEs were determined from multiphase, nonlinear, mixed-model regression and represent the magnitude of association with RV dysfunction for NW-BT. B, The 5-year, transplant-free survival after transition to stage-2 SCPC among 233 propensity-score matched neonates, stratified by NW-RVPA (n = 125; *blue curve*) versus NW-BT (n = 108; *red curve*). Independent of time were 20 events after NW-RVPA (13 deaths, 7 transplants), and 17 events after NW-BT (16 deaths, 1 transplant). At 5 years after stage 2, no significant difference was found in transplant-free survival between NW-RVPA (81% ± 3%) and NW-BT (80% ± 4%; log-rank, $P = .69$). Multiphase, parametric hazard analysis demonstrated a short early hazard before 1 year (PE = 0.95; $P = .25$) followed by a constant phase thereafter (PE = −0.38; $P = .48$). Each *circle* represents a death, positioned on the vertical axis by the Kaplan-Meier estimator. *Vertical bars* are confidence limits equivalent to ±1 SE. *Solid lines* are PEs enclosed within *dashed* 68% confidence bands equivalent to ±1 SE. *In parenthesis* are the numbers of patients at risk at each associated time. PEs were determined from multiphase risk-hazard analysis and represent the magnitude of NW-BT as a risk factor for death. *NW-RVPA*, Norwood operation with right-ventricle-to-pulmonary-artery conduit; *NW-BT*, Norwood operation with modified Blalock-Taussig shunt; *RV*, right ventricular.

to transplant eligibility. Transplant-free survival after Norwood operations is a useful clinical endpoint that focuses on the durability of the single-ventricle heart for supporting the circulation. However, from the perspective of a child and family, the differences in overall survival seen here are particularly important. Specifically, at all time points, a child is significantly more likely to be alive, irrespective of underlying physiology, after having undergone NW-RVPA.

Norwood strategy impact on RV dysfunction and TR. Enthusiasm for the early survival benefits associated with NW-RVPA has been mitigated somewhat by concerns regarding poor long-term RV function.[1,2] Specifically, the ventriculotomy required for NW-RVPA is a site of myocardial injury, thought to lead, potentially, to late aneurysm formation, arrhythmias, and ventricular failure.[2] In our series, NW-RVPA was associated with a decreased prevalence of early RV dysfunction, compared with NW-BT, and the 6-year prevalence of RV dysfunction was comparable between groups. However, the adverse manifestations of a ventriculotomy may not become apparent for years, meaning that the "true" long-term differences between strategies may not be well defined for years, and perhaps even decades, after stage-1 palliation. Finally, despite the qualitative nature of the data used for this analysis, our results may be similar to the early results of the SVR trial. An early finding was that the median RV end-diastolic dimension indexed to body surface area was significantly decreased, and the median RV ejection fraction was significantly increased before stage 2 for patients who underwent NW-RVPA.[1,3,26]

To date, the most recent follow-up publication from the SVR trial reported that NW-BT and NW-RVPA had similar indices for RV function and tricuspid valve performance 14 months after randomization.[2] These indices included measurements of global RV systolic and diastolic function, cardiac dimensions, and tricuspid valve annulus dimensions and function.[2] In comparing similar indices for NW-RVPA and NW-BT from pre-Fontan echocardiograms, NW-RVPA was associated with a significant decrease in RV ejection fraction, compared with NW-BT (42% ± 7% vs 45% ± 6%, respectively).[2] However, the clinical significance of this small difference is not clear. Furthermore, global measurements of RV dysfunction, such as myocardial performance index, were found to be "remarkably stable and similar for both groups."[2] Markers

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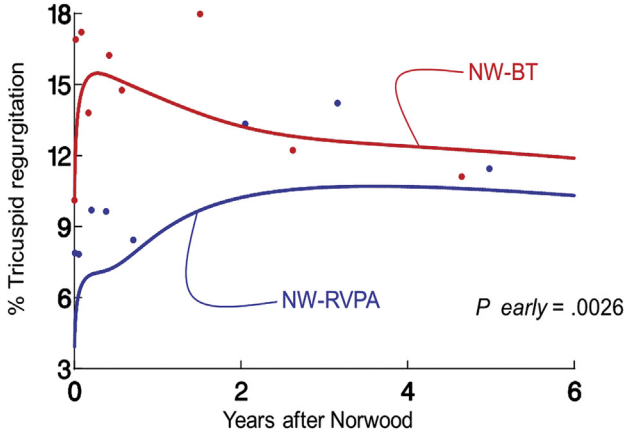

FIGURE 6. Overall, postoperative prevalence of TR for NW-RVPA and NW-BT. Relationship between the prevalence of ≥moderate postoperative TR for patients who underwent NW-RVPA (*blue curve*) versus patients who underwent NW-BT (*red curve*). NW-BT was associated with significantly greater prevalence of TR in the initial year (15%) relative to NW-RVPA (11%; PE = −1.4, P = .0026). Beyond 1 year after Norwood stage 1, NW-BT demonstrated a persistent and steady decline in the prevalence of TR (12% at 6 years), whereas NW-RVPA plateaued at 10% (PE = −.26; P = .68). TR was evaluated for 288 children (2423 echocardiogram reports). *Solid lines* are the estimated prevalence for ≥moderate TR. *Circles* represent data grouped by associated operation (without regard to repeated measurements) within timeframes, to provide crude verification of model fit. PEs were determined form multiphase, nonlinear mixed-model regression and represent the magnitude of association with TR for NW-BT. *NW-RVPA*, Norwood operation with right-ventricle-to-pulmonary-artery conduit; *NW-BT*, Norwood operation with modified Blalock-Taussig shunt.

for diastolic dysfunction (tricuspid valve E/E′ ratio) improved for patients in the NW-RVPA group, between the echocardiogram 14 months after randomization and the pre-Fontan echocardiogram.[2]

Qualitative echocardiographic measures for RV dysfunction and TR, as used in our series, are difficult to relate directly to detailed quantitative measures, such as those analyzed in the SVR trial. However, in many respects, the clinical messages are similar; for both NW-BT and NW-RVPA, survivors demonstrate reasonable, systemic ventricular and tricuspid valve function. Additionally, it is reassuring that the trends for survival and transplantation between NW-BT and NW-RVPA here are similar to those reported in the SVR trial and subsequent follow-up investigations.[1,3,25] Given the relative difficulties associated with creating a randomized trial for patients with congenital heart disease, our results speak to the potential merits of applying propensity-matching techniques to a multicenter inception cohort. Furthermore, utilization of these methodologies may allow incorporation of a broader and less-exclusive population from multiple institutions.

Study Limitations

We recognize that use of echocardiogram reports from multiple institutions is inherently predisposed to interobserver error and subjective values. However, using repeated measures statistical methodology to analyze thousands of data points over time greatly reduces the variance associated with such measurements. This technique is more robust, for example, than selecting and reporting values from the "predischarge," 1-year, and latest echocardiograms, as it makes use of all available echocardiogram reports.

Although propensity-score matching is an effective method for "balancing" patient-specific characteristics, an important limitation is the inability to account for unmeasured factors.[13,27] Despite our rigorous statistical methodology, important factors, such as center and era-effect, remain inherently unaccounted for with propensity matching. The role of center and surgeon volume, distribution of operation per institution, and era of operation are important factors, having been linked to patient outcomes after congenital heart surgery.[28-33]

However, methods to evaluate these effects are themselves associated with limitations.[29-32] Specifically, as it pertains to our study, submission of data is voluntary; therefore, center volume, procedural distribution, and era of operation can be estimated based on enrollment only. Given this limitation, adjustment factors for these effects are subject to nonrandom selection bias, precluding them from incorporation into the propensity score. Additionally, previous analysis of lesion-specific outcomes from the Congenital Heart Surgeons' Society found that center volume was influential for some complex lesions, whereas patient-specific and management factors were more important for others, including the Norwood operations.[31] This analysis does not disregard the importance of institutional factors on outcomes, but it does acknowledge the difficulties associated with accurately quantifying these factors via voluntary-based, clinical datasets.

Despite these difficulties, however, the importance of center-effect and era-effect on outcomes is an important consideration. Therefore, institutional enrollment, and era of operation were evaluated informally for this analysis, via risk-hazard analysis; none of these factors significantly influenced the results. Furthermore, this cohort is comprised of a significant number of patients, enrolled from multiple institutions, and is representative of the Congenital Heart Surgeons' Society member surgeon experience.

CONCLUSIONS

Neonates with critical LVOTO who undergo stage-1 palliation with NW-RVPA are more likely to be alive, having achieved a definitive end-state by 6 years after

surgery, versus neonates who undergo stage-1 palliation with NW-BT. Furthermore, our results suggest that among survivors, the late prevalence of RV dysfunction and TR is comparable in the 2 strategies. These data imply that NW-RVPA may be preferable to NW-BT for stage-1 palliation.

Conflict of Interest Statement

Authors have nothing to disclose with regard to commercial support.

The authors thank the Congenital Heart Surgeons' Society Data Center staff, including Sally Cai, Annette Flynn, Susan McIntyre, Ilina Ristevska, and Veena Sivarajan, for coordinating patient enrollment, and the collection, abstraction, and management of data. Additionally, we thank the Cleveland Clinic Foundation, Department of Quantitative Health Sciences, for their assistance with statistical analysis. Finally, we are grateful to all members of the Congenital Heart Surgeons' Society and their colleagues for their ongoing contributions to this study.

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Key Words: single ventricle, critical left ventricular outflow tract obstruction, hypoplastic left heart syndrome, Norwood operation, congenital heart disease

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Discussion

Dr R. Ohye *(Ann Arbor, Mich)*. Thank you, President del Nido and Dr Moon. Travis, congratulations on your presentation and also on nearing the conclusion of your Kirklin-Ashburn Fellowship. For those of you who are unfamiliar with the Kirklin-Ashburn Fellowship, it is a 2-year research fellowship supported by the Congenital Heart Surgeons' Society Data Center. Travis performed this research project during his fellowship, as well as working toward a Master's degree at the University of Toronto.

I would also like to just briefly acknowledge the 2 gentlemen for whom the fellowship is named. I do not need to introduce John W. Kirklin to this audience, but he was, of course, a pioneer in congenital heart surgery, as well as in research and education. David Ashburn did this fellowship several years ago, prior to coming to us as a thoracic resident at the University of Michigan. Tragically, David perished in a transplant procurement plane crash just a few weeks prior to beginning his congenital fellowship with us at Michigan.

Travis, well done, well conceived, well executed, and well presented. I have 3 straightforward questions for you. One, since this is not a randomized prospective trial, one of the components of the study that is very important is your propensity matching. In your paper, which you kindly supplied to me, you noted that, for missing baseline covariates, you imputed the data. Do you have any estimate that you can give us to aid in understanding the completeness of these baseline data? Do you know what percentage of patients had complete baseline covariates; or was there a certain number of missing data points at which time they were no longer eligible for enrollment?

Dr T. Wilder *(Toronto, Ontario, Canada)*: Excellent question, and thank you for the kind words, Dr Ohye.

First, to briefly expand on the process of creating a propensity score—which in our case was a fairly rigorous undertaking—we initially create a score from nonimputed data, to identify the most statistically significant variables. This so-called parsimonious model is then augmented with additional variables considered to be clinically important, to create the final propensity score. You are correct that the final score does incorporate data for which the missing values were imputed. Understandably, this raises potential concern and is a potential limitation. To account for this, we first eliminate—or do not consider in the propensity score—variables with excessive missing values. Second, our method of imputation for these missing variables has 2 properties that make it a very reliable and robust technique for addressing missing data. The properties are: (1) It is informative, meaning it uses all other data for an individual patient to impute the missing value; (2) We impute each missing value 5 times, and then take the mean of the 5 imputed data sets. So you can see, although it is not perfect, it is a very robust method to account for missing data.

To address the question regarding how much data, and which variables are missing—on the whole, there are always some missing variables; for some, or maybe most, variables, the missing data range is roughly 10% to 15%, and for some, there is more than 25% missing. For some collected variables, there may even be up to 75% missing, and we typically exclude these unless we feel it is a very important variable. For variables included in the final propensity score, the majority of variables had more than75% available data. This included important variables such as: (1) aortic atresia, which was consistently reliable, for about 90% of the patients; (2) left ventricular outflow tract composite diameter; (3) the diameter of the ascending aorta; and (4) mitral valve diameter. They were all very consistent, with more than 75% available.

Dr Ohye. I think another important factor, since the study is nonrandomized, is whether you were able to bring center effects into the analysis—whether it is by center, by center volume, or surgeon volume? We saw in the SVR (Single Ventricle Reconstruction) trial that center volume and surgeon volume had a strong effect in a number of our associations and outcomes. In addition, the choice of shunt is likely co-linear with center, in that as surgeons or centers, we have our favorite shunts. This surgeon and center bias then brings into play everything we do preoperatively, intraoperatively, and postoperatively in our patient management, as well as in some of the important study outcomes, such as the echocardiograms, which are obviously center specific.

Dr Wilder. Again, a very important, very clinically relevant question, and one that we have tried to address to the best of our ability. Unfortunately, when we analyze center volume, we can only do so based on the reported volume. Because this has been an ongoing project, with various subset analyses, we have controlled for institution volume as best we can, both before and after propensity matching. This included introducing variables to control for the total reported volume of an institution, the absolute number of a reported case or procedure at each institution, and the percentage of a procedure performed as a representation of which procedure an institution may prefer. When we control for institution to the best of our ability, it does not seem to ever influence the final outcome. Now, admittedly, the limitation is that we are at the mercy of what each institution presents to us in terms of enrollment.

Dr Ohye. I think probably one of the difficulties for this study was that you had to rely on the echocardiogram reports and you did not have an echocardiogram core laboratory. Were there any thoughts of taking a limited cross-section of the echocardiograms to see if there were differences in how TR and RV function were graded, among either readers or centers?

Dr Wilder. We have not done that yet, mostly because collecting thousands of echocardiogram data reports and introducing them into the data set and preparing them is a large task that requires a tremendous amount of effort and person power. So for the purposes of this first analysis, we focused strictly on qualitative measurements interpreted by each review, and this is an admitted limitation that cannot be overcome right now. We are in the process of developing an echocardiogram core laboratory at the data center, which will look at each echocardiogram provided by the institution, with a single blinded reviewer, in an attempt to answer this question, but for this analysis and moving forward in the short term, we are relying on this interpretation.

Dr Ohye. We will look forward to that. Thank you very much, and again, congratulations on this project and the completion of your fellowship. Best of luck as you return to your general surgery residency at the University of California, San Diego.

Dr Wilder. Thank you, sir. I appreciate it.

Dr P. del Nido *(Boston, Mass)*. First of all, congratulations again. This is a tremendous amount of work and a very important study. This obviously has huge implications, because all of us have preferences as to which procedure we do, but that gets back to the issue that because of the system that you have for collecting data, you are at risk for having institutions that have larger volume influencing the final decision or the final outcome.

You said there were patient factors as well as institutional factors that you tried to match in the propensity-score matching. Is that true? Did you do both, or is it primarily patient factors that you match?

Dr Wilder. Thanks, Dr del Nido. We only matched on patient factors. In an attempt to control for potential institutional influence, after matching, we did risk-stratify based on institutional factors.

Dr del Nido. Because if an institution is large and only does one procedure, they will tend to really outweigh or at least influence the results inordinately, I would think.

Dr Wilder. It is true that the potential bias of a large institution that enrolls only one subset of a procedure potentially introduces bias. Our feeling is that that is going to be counterbalanced, because there are large institutions that enroll a subset of both groups of patients, and there are a number of ''small'' institutions that are enrolling only a low number of patients. The feeling is that the broad array of institutions—both small and large—may actually be a strength of this study in that it provides a true representation of the cases performed by Congenital Heart Surgeons' Society surgeons.

Dr Osman Al-Radi *(Jeddah, Saudi Arabia)*. Travis, thank you very much for an excellent study. Were you able to identify any subset of patients where the BT was equal to or better than the RVPA (Sano operation); for instance, with patients who started with RV dysfunction? That is my first question. The other question is, was there any difference in the mode of failure? In the patients who died in the BT group and the RVPA group, was the mode of death or failure the same?

Dr Wilder. To address your first question, we did not look at specific characteristics predictive of survival of each group. I will say that the amount of RV dysfunction prior to Norwood was very low for both groups. And this is something that, from behind the scenes, we have looked at and studied in a standard risk-adjusted analysis, and for our data set, there is nothing that will select improved survival for a BT versus a RVPA.

In regard to mode of failure, we did not look at that, other than plotting tricuspid regurgitation and RV dysfunction for each group. However, this is relatively powerful circumstantial evidence to suggest that RV dysfunction is playing a large role in the mortality of both groups, especially the BT group.

APPENDIX 1. ANALYSIS OF COMPETING END-STATES

Competing end-states analyses were used to examine rates of transition from an initial state (hazard function) to mutually exclusive time-related end-states. Each competing end-state was estimated via hazard-function multiphase parametric modeling (for additional details, see http://www.lerner.ccf.org/qhs/software/hazard).[18] All neonates began alive, immediately after a Norwood operation (time = 0). Thereafter, they remained in this state, or entered 1 of 4 mutually exclusive end-states: (1) alive, without definitive operation; (2) transition to Fontan operation; (3) transplantation; (4) conversion to biventricular repair; and (5) death without definitive repair. At any point in time, the sum of proportions of children in each end-state must be 100%. Competing end-states methodology integrates each individual hazard function to give the actual proportion of neonates in each end-state at any point in time.[34] For each hazard function, factors associated with each end-state can be determined independently (eg, via multivariable risk adjustment). However, the focus of this analysis was to compare the risk of death without definitive repair for NW-RVPA versus NW-BT.

LONGITUDINAL (REPEATED MEASURES) DATA ANALYSIS

Nonlinear mixed-model regression analysis was used to characterize the time-related prevalence for ≥moderate (moderate or worse) postoperative RV dysfunction and TR from the repeated measures data (PROC NLMIXED; SAS Institute, Cary, NC), using a multiphase parametric model.[6] In total, 2993 post-Norwood echocardiogram reports were available for 309 propensity-score–matched neonates (91% of the population). A total of 2474 echocardiogram reports had available data for RV dysfunction, and 2423 had available data for TR. Therefore, reliable evaluation for the time-related trends in RV dysfunction and TR was possible for the time period of up to 6 years after Norwood stage 1.

We, in collaboration with the Quantitative Health Sciences Department Heart and Vascular Institute at the Cleveland Clinic Foundation (which developed and validated these methodologies for cardiovascular research[5,6]), have incorporated the use of multiphase, nonlinear mixed-effects models for longitudinal data analysis recently. These methods provide the ability to account for varying influence of factors on the temporal rate of each postoperative parameter measured. It does so by identifying additive time phases. Each phase is created from a set of shaping parameters designed to fit the underlying data (similar to nonproportional hazards in a survival analysis). However, the use of mixed models (PROC NLMIXED) accounts for the correlation within subjects. Model selection is guided by the corrected Akaike's information criterion, and the concordance correlation coefficient (r_c) between observed and predicted values.

Given that the primary objectives were to determine: (1) the difference in survival; and (2) the time-related prevalence of ≥moderate RV dysfunction and TR between propensity-score–matched neonates after NW-RVPA versus NW-BT, hazard and regression models were not subject to multivariable analysis.[6] Instead, the variables for NW-RVPA and NW-BT were manually entered into hazard models and regression models. Baseline continuous variables with excessive missing values (>75%), and categoric or ordinal variables with ≤5 associated events, were excluded to minimize the risk of model overdetermination (unless deemed important to the specific analysis). Various mathematical transformations of continuous variables were tested for optimal calibration with the relationship to procedure type, for entry into the propensity score. Missing values for baseline covariables were estimated by 5-fold multiple imputation using the Markov Chain Monte Carlo method.[10]

PROPENSITY MATCHING AND INSTITUTIONAL INFLUENCE

An important objective for all studies comparing multiple treatment strategies—including randomized and nonrandomized studies—is to control for the potential bias that results from differences in baseline characteristics among groups. Unlike randomized studies, in which observed and unobserved bias is controlled fundamentally through study design, nonrandomized studies rely on various statistical methodologies to mitigate potential bias.

Proven strategies employed by the Congenital Heart Surgeons' Society Data Center to adjust for potential bias include: multivariable parametric risk-hazard analysis and propensity-score matching. However, all statistical techniques—and randomized trials—are associated with limitations. For example, although multivariable risk-hazard analysis incorporates all study subjects and is an effective approach to identifying important risk factors, multivariable analyses are limited by the number of covariables that can be reliably included.

Propensity-scores models, however, are not obligated to be parsimonious. The use of a propensity score permits inclusion of a wide range of variables, regardless of statistical significance.[27] Furthermore, propensity-score matching has been demonstrated to be an effective method of adjusting for potential bias related to the differences in baseline, patient-specific characteristics.[13,27] However, an important limitation of propensity scores is the inability to account for unobserved or unmeasured variables.[13] Therefore, despite our rigorous statistical methodology and scrutiny in generating the propensity score, we cannot eliminate all potential bias. Of primary importance, as it pertains to

our study, is the influence of center-specific factors and era-effect, including: total institution and surgeon volume, distribution of procedure at each institution and era of operation.

In studies for which participation and data submission are voluntary, the ''true'' volume and distribution of operations at each institution can be estimated based on enrollment only. Similarly, the era for enrolled operations may not represent the total operations performed in a given era. As a result, adjustment factors for these effects potentially can introduce nonrandom, selection bias. For example, an institution may have started enrollment after a change in operative management strategy, or limited enrollment to a specific subset of eligible patients. The potential limitations associated with estimating the influence of center and era, based on enrollment, precluded us from incorporating these factors in the propensity score. However, reported enrollment and era-effect were informally evaluated for this analysis (and formally evaluated for previous analysis with this cohort) via risk-hazard analysis. Variables tested as independent risk factors for death, both before and after propensity matching, included: (1) the total number of reported Norwood operations per institution; (2) the absolute number of each type of Norwood operation reported per institution; (3) the percentage of each type of Norwood operation reported per institution; and (4) individual institutions. The potential era-effect was evaluated as the date of operation and by classifying era into 3 categories: (1) 2005 to 2007; (2) 2008 to 2011; and (3) 2012 to 2014 (NW-RVPA tended to have an increased distribution in the early era). Parametric risk hazards for these factors did not significantly alter survival outcomes among groups.

References cited in Appendix 1 are available in the main article text.

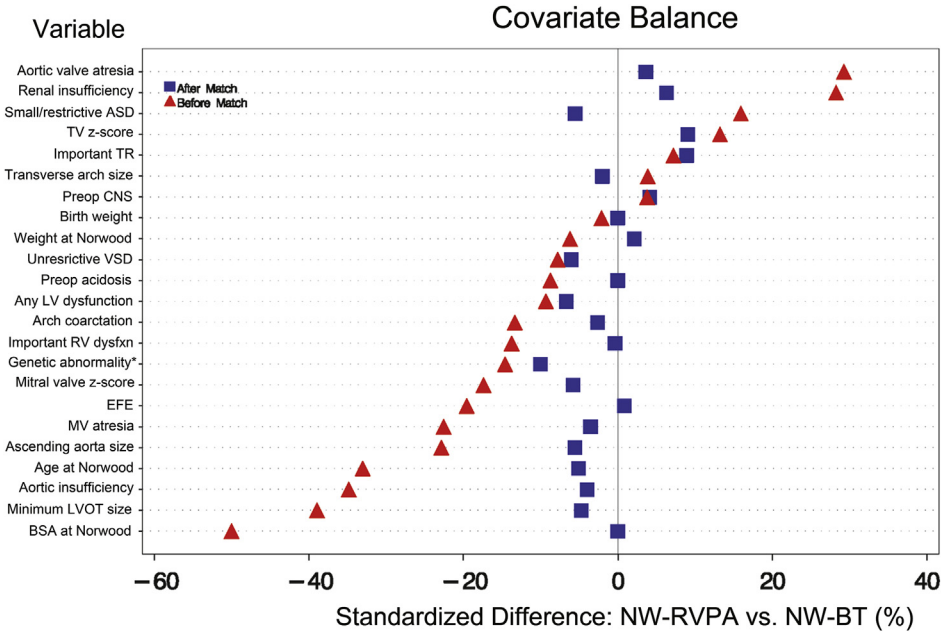

FIGURE E1. Standardized difference for key variables before and after propensity-score matching. Covariate balance for selected preoperative variables before (*triangles*) and after (*squares*) propensity-score matching, showing contrast in characteristics of patients undergoing NW-RVPA versus NW-BT. Magnitude of standardized difference relates directly to magnitude of relative difference between the 2 groups. Variable definition key: Arch coarctation is the transverse aortic arch coarctation. Ascending aorta size is the ascending aorta indexed to BSA. The TV z-score is the TV annulus z-score. Important TR is ≥moderate TR. Important RV dysfunction is ≥moderate RV dysfunction. Minimum LVOT size is the minimum diameter of the LVOT in cm. Preop acidosis is the preop lactic/metabolic acidosis. CNS is preop stroke, seizure or CNS/intracranial hemorrhage. The transverse arch size is the transverse aortic arch diameter indexed to BSA. *ASD*, atrial septal defect; *BSA*, body surface area; *VSD*, ventricular septal defect; *LV*, left ventricle; *RV*, right ventricle; *EFE*, endocardial fibroelastosis; *MV*, mitral valve; *preop*, preoperative; *CNS*, central nervous system; *NW-RVPA*, Norwood operation with right-ventricle-to-pulmonary-artery conduit; *NW-BT*, Norwood operation with modified Blalock-Taussig shunt; *LVOT*, left ventricular outflow tract; *TV*, tricuspid valve; *TR*, tricuspid regurgitation. *Any identifiable genetic syndrome.

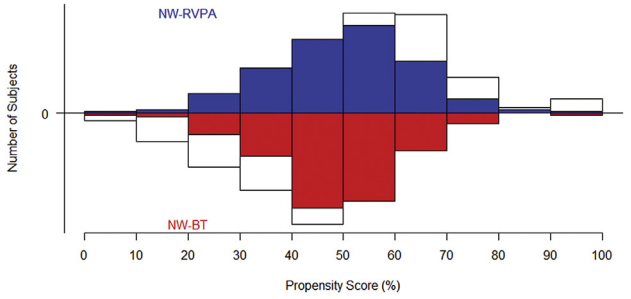

FIGURE E2. Distribution of propensity scores. Mirrored histogram of distribution of propensity scores for neonates who underwent a stage-1 NW-RVPA (*blue*) versus NW-BT (*red*). The propensity score is the probability of belonging to NW-RVPA versus NW-BT based on pre-procedure variables. *Blue and red areas* represent 169 matched patient pairs; *uncolored portions of bars* represent unmatched patients (NW-RVPA, n = 53; NW-BT, n = 63). *NW-RVPA*, Norwood operation with right-ventricle-to-pulmonary-artery conduit; *NW-BT*, Norwood operation with modified Blalock-Taussig shunt.

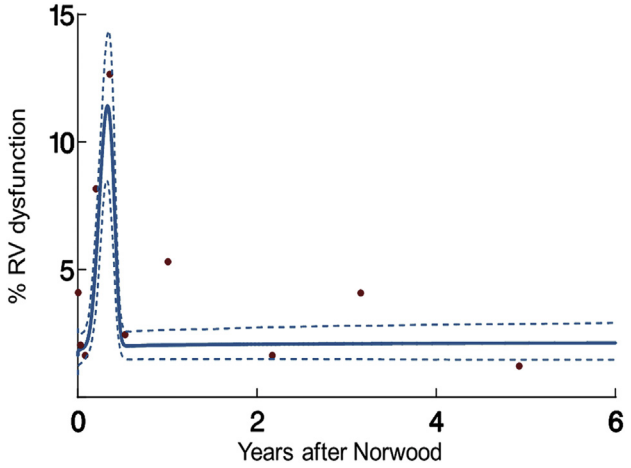

FIGURE E3. Overall prevalence of ≥moderate RV dysfunction after Norwood stage 1. Overall prevalence of ≥moderate RV dysfunction after Norwood stage 1, as evaluated from 2474 echocardiogram reports for 292 children. The prevalence of RV dysfunction demonstrated a significant early peak to 11% ± 3% during the first 3 to 6 months after Norwood palliation. Thereafter, the prevalence of ≥moderate postoperative RV dysfunction remained at a constant level (<5%) for survivors not undergoing transplantation or biventricular repair. *Solid line* represents the unadjusted estimates of the temporal trend for the prevalence of ≥moderate RV dysfunction enclosed in the 68% bootstrap confidence intervals (*dashed lines*). *Circles* are data grouped by associated degree of RV dysfunction (without regard to repeated measurements) within time-frames, to provide crude verification of model fit. *RV,* Right ventricular.

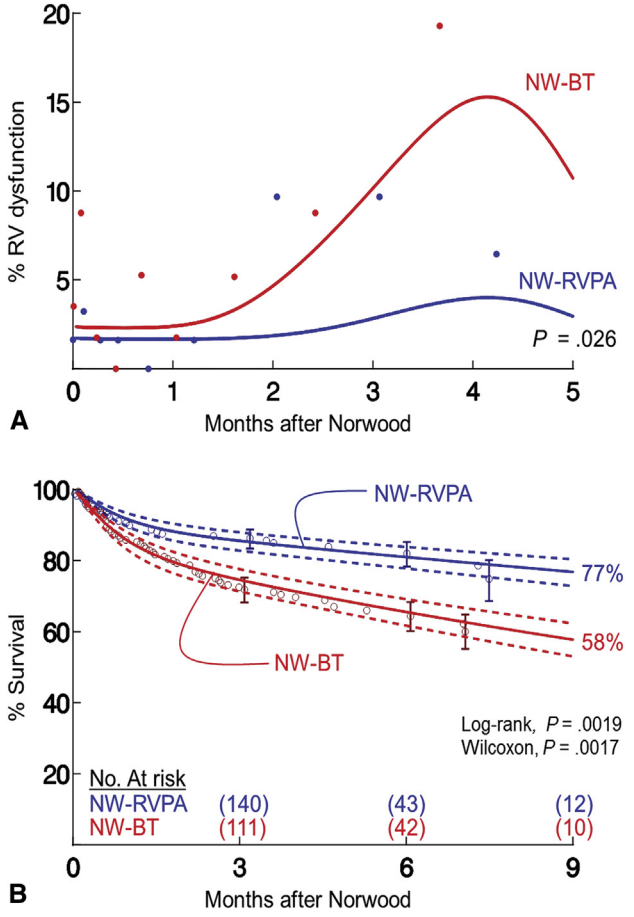

FIGURE E4. A, Postoperative RV dysfunction and (B) transplant-free survival before stage 2 or biventricular repair. A, Relationship between the prevalence of ≥moderate postoperative RV dysfunction before transition to stage-2 superior cavopulmonary connection or conversion to biventricular repair; stratified by patients who underwent NW-RVPA (*blue curve*) versus NW-BT (*red curve*). NW-BT was associated with significantly greater prevalence of RV dysfunction during the initial 4 months (peaking at 15%) relative to NW-RVPA (5%; PE = 3.0, $P = .026$). At 4 to 5 months after Norwood stage 1, both groups exhibited a decline in the prevalence of ≥moderate RV dysfunction (PE = 0.48; $P = .55$) corresponding temporally with transition to stage 2 and the early hazard for death. RV dysfunction was evaluated for 269 children (1209 echocardiogram reports). *Solid lines* are the estimated prevalence for ≥moderate RV dysfunction. *Circles* represent data grouped by associated operation (without regard to repeated measurements) within timeframes, to provide crude verification of model fit. PEs were determined form multiphase, nonlinear mixed-model regression and represent the magnitude of association with RV dysfunction for NW-BT. B, The 9-month, transplant-free survival among 338 propensity-score–matched neonates before transition to stage-2 superior cavopulmonary connection or conversion to biventricular repair after Norwood stage 1; stratified by NW-RVPA (*blue curve*) versus NW-BT (*red curve*). Independent of time, 32 events occurred after NW-RVPA (31 deaths; 1 transplant), and 57 events after NW-BT (54 deaths; 3 transplants). NW-RVPA (77% ± 4%) was associated with better transplant-free survival before stage 2, compared with NW-BT (58% ± 5% at 9 months; log-rank, $P = .0019$). Parametric hazard analysis demonstrated NW-BT was a risk factor for death or transplant before stage 2 (PE = 0.87; $P = .003$). *Circles* represent an event (death or transplant) positioned along the vertical axis by the Kaplan-Meier estimator. *Vertical bars* are the confidence limits equivalent to ±1 SE. *Solid lines* are PEs enclosed within *dashed* 68% confidence bands equivalent to ±1 SE. *In parentheses* are the numbers of patients at risk at the associated time. PEs were determined from multiphase risk-hazard analysis and represent the magnitude of NW-BT as a risk factor for death. *NW-BT*, Norwood operation with modified Blalock-Taussig shunt; *RV*, right ventricular; *NW-RVPA*, Norwood operation with right-ventricle-to-pulmonary-artery conduit.

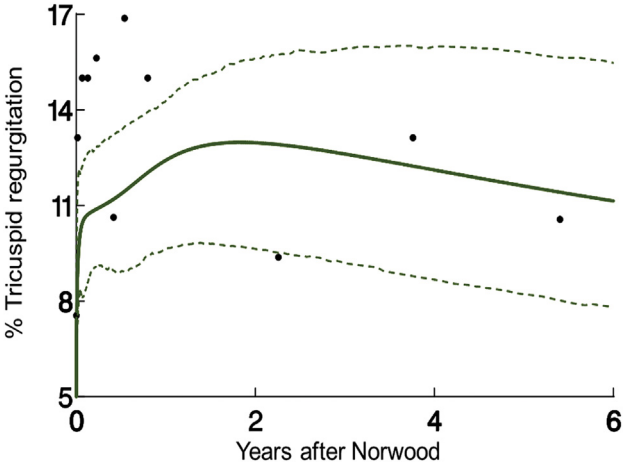

FIGURE E5. Overall prevalence of ≥moderate TR after Norwood stage 1. Overall prevalence of ≥moderate TR after Norwood stage 1, as evaluated from 2423 echocardiogram reports for 288 children. TR demonstrated a significant early peak to 13% ± 3% during the first 2 years after Norwood palliation. Thereafter, the prevalence of ≥moderate TR remained constant, but persistently elevated (11%) for all survivors not undergoing transplantation, biventricular repair, or tricuspid valve intervention. *Solid line* represents the unadjusted estimates of the temporal trend for the prevalence of ≥moderate TR enclosed in the 68% bootstrap confidence intervals (*dashed lines*). *Circles* are data grouped by associated degree of TR (without regard to repeated measurements) within timeframes, to provide crude verification of model fit.

TABLE E1. Participating Congenital Heart Surgeons' Society member institutions

Alfred I. duPont Hospital for Children, Wilmington, Del
All Children's Hospital, St. Petersburg, Fla
Ann & Robert H. Lurie Children's Hospital of Chicago, Chicago, Ill
Children's Hospital of Alabama, Birmingham, Ala
Children's Hospital of Michigan, Detroit, Mich
Children's Hospital of Pittsburg, Pittsburg, Pa
Children's Mercy Hospitals and Clinics, Kansas City, Mo
Children's National Heart Institute, Children's National Medical Center, Washington, DC
Children's Hospital of Wisconsin, Milwaukee, Wis
Cincinnati Children's Hospital, Cincinnati, Ohio
C. S. Mott Children's Hospital, Ann Arbor, Mich
Inova Fairfax Hospital for Children, Falls Church, Va
Kosair Children's Hospital, Louisville, Ky
Lucile Packard Children's Hospital Stanford, Palo Alto, Calif
Milton Hershey Medical Center, Hershey, Pa
Primary Children's Medical Center, Salt Lake City, Utah
Rady Children's Hospital, San Diego, Calif
Riley Hospital for Children, Indianapolis, Ind
St. Louis Children's Hospital, St. Louis, Mo
The Children's Heart Clinic of Minnesota, Minneapolis, Minn
The Hospital for Sick Children, Toronto, Ontario

TABLE E2. The 13 variables used to generate the propensity score

	NW-RVPA (n = 169)		NW-BT (n = 169)		
Variable	**n available**	**Value**	**n available**	**Value**	***P* value**
Age at Norwood (d)	169	6.3 ± 4.5	169	6.5 ± 4.6	.14
BSA at Norwood (m^2)	160	0.21 ± 0.02	166	0.21 ± 0.02	.71
Aortic valve annulus (cm)	145	0.14 ± 0.2	149	0.15 ± 0.2	.82
Tricuspid valve annulus z-score	18	−0.7 ± 1.5	47	−1 ± 1.8	.64
Functional mitral valve atresia*	153	127 (83)	153	129 (84)	.76
AI (any degree)	141	19 (13)	148	22 (15)	.74
Transverse arch coarctation	164	50 (30)	164	52 (32)	.81
Small/restrictive ASD	120	49 (41)	124	54 (44)	.67
LV dysfunction (any degree)	81	53 (65)	77	57 (74)	.24
Grade TR at baseline†	164	14 (9)	161	10 (6)	.42
Grade RV dysfunction at baseline*,†	161	2 (1)	156	2 (1)	.97
Renal insufficiency	169	2 (1)	169	1 (1)	.56
Metabolic acidosis	169	20 (12)	169	20 (12)	1

Values are M ± SD, or n (%), unless otherwise indicated. Baseline characteristics, number available and values for each variable that were selected to create the propensity score for matched neonates. The generated propensity score was used to match neonates with similar baseline characteristics who underwent NW-RVPA (n = 169) versus NW-BT (n = 169). A total of 338 neonates who underwent a stage-1 Norwood operation were matched using a propensity score generated from 13 variables (c-statistic = .71). The c-statistic is a measure of how well the propensity score controls for confounders. A score between 0.65 and 0.85 is associated with an adequate match. *NW-RVPA*, Norwood operation with right-ventricle-to-pulmonary-artery conduit; *NW-BT*, Norwood operation with modified Blalock-Taussig shunt; *BSA*, body surface area; *AI*, aortic insufficiency; *ASD*, atrial septal defect; *LV*, left ventricular; *TR*, tricuspid valve regurgitation; *RV*, right ventricular. *Functional mitral valve atresia designates a valve that is either atretic or associated with severe stenosis or hypoplasia. †Values reported are for ≥moderate RV dysfunction and TR.

TABLE E3. Baseline morphologic and demographic characteristics used in determining the propensity score for all 454 neonates before propensity-score matching

	NW-RVPA (n = 222)			NW-BT (n = 232)			
Variable	n available	Mean ± SD	Percentiles or frequency (%)	n available	Mean ± SD	Percentiles or frequency (%)	*P* value
General							
Gender, male	222		145 (65)	232		147 (63)	.70
Age at Norwood (d)	222	6.0 ± 4.2	3/5/9	232	7.7 ± 5.5	4/6/11	<.001
Birth weight (kg)	217	3.15 ± 0.47	2.71/3.1/3.64	231	3.16 ± 0.48	2.7/3.14/3.64	.77
Birth weight <2.5 kg	217		15 (7)	231		15 (6)	.86
Birth BSA (m^2)	201	0.21 ± 0.02	0.19/0.21/0.23	222	0.21 ± 0.02	0.19/0.21/0.23	.90
Weight at Norwood (kg)	219	3.14 ± 0.48	2.7/3.1/3.6	232	3.17 ± 0.49	2.7/3.15/3.6	.70
BSA at Norwood (m^2)	210	0.2 ± 0.02	0.18/0.2/0.23	227	0.21 ± 0.02	0.19/0.21/0.23	.23
Associated lesions							
Anomalous coronary artery	222	8 (4)		232		6 (3)	.53
Transverse arch coarctation	217		63 (29)	227		80 (35)	.16
Septum/endocardium							
Small/restrictive ASD	159	75 (47)		173		68 (39)	.15
Unrestrictive VSD	142	20 (14)		142		24 (17)	.51
EFE (any level)	37		31 (84)	62		56 (90)	.33
LVOT							
Minimum LVOTO size (cm)	208	0.14 ± 0.2	0/0/0.4	224	0.22 ± 0.2	0/0.21/0.5	<.001
Minimum LVOTO z-score	204	−23 ± 10	−31/−31/−9	220	−20 ± 11	−31/−19/−6	<.001
Aortic valve annulus (cm)	192	0.13 ± 0.2	0/0/0.4	202	0.2 ± 0.2	0/0.1/0.45	.001
Aortic valve annulus z-score	189	−24 ± 10	−31/−31/−9	198	−21 ± 11	−31/−31/−7	.001
Ascending aorta (cm)	166	0.33 ± 0.2	0.18/0.26/0.5	187	0.37 ± 0.2	0.2/0.3/0.6	.03
Ascending aorta index (cm/m^2)	152	1.6 ± 0.9	0.88/1.3/2	180	1.8 ± 0.9	0.92/1.5/3	.043
Transverse arch (cm)	109	0.37 ± 0.1	0.25/0.39/0.47	112	0.37 ± 0.1	0.28/0.38/0.47	.54
Transverse arch index (cm/m^2)	104	1.8 ± 0.5	1.2/1.9/2.3	108	1.8 ± 0.53	1.3/1.7/2.2	.54
Aortic valve atresia	207		124 (60)	220		100 (45)	.003
Functional aortic valve atresia*	213		156 (73)	226		138 (61)	.007
AI (any degree)	190		21 (11)	195		47 (24)	<.001
Left ventricle							
Functional LV atresia	97		44 (45)	102		51 (50)	.51
LV Dysfunction (any degree)	105		66 (63)	109		85 (78)	.015
Atrioventricular valve							
MV annulus (cm), 4-chamber view on echocardiogram	134	0.2 ± 0.4	0/0/0.7	164	0.3 ± 0.3	0/0/0.7	.066
TV annulus (cm)	21	1.3 ± 0.2	1.1/1.3/1.6	65	1.3 ± 0.2	1.1/1.3/1.5	1
MV z-score	133	−18 ± 7	−22/−22/−6	162	−16 ± 7	−22/−22/−6	.072
TV z-score	20	−0.7 ± 1.6	−2.5/−0.5/1.4	64	−0.8 ± 1.9	−3/−0.5/1.3	.95
MV atresia	205		94 (46)	214		93 (43)	.62
Functional mitral valve atresia*	204		170 (83)	215		196 (91)	.016
Grade TR	216			221			.50
No TR (0)			40 (18)			29 (13)	
Trivial (1)			6 (3)			11 (5)	
Mild (2)			94 (44)			104 (47)	
Mild+ (3)			55 (25)			60 (27)	
Moderate (4)			19 (9)			15 (7)	
Moderate+ (5)			2 (1)			2 (1)	
TR (≥moderate)	216		21 (10)	221		17 (8)	.45
Right ventricle							
Grade RV dysfunction	213			215			.18
No RV dysfunction			185 (86)			182 (84)	
Trivial (1)			9 (4)			17 (8)	
Mild (2)			13 (6)			9 (4)	
Mild+ (3)			4 (2)			1 (1)	

(Continued)

TABLE E3. Continued

Variable	NW-RVPA (n = 222)			NW-BT (n = 232)			*P* value
	n available	Mean ± SD	Percentiles or frequency (%)	n available	Mean ± SD	Percentiles or frequency (%)	
Moderate (4)			1 (1)			5 (2)	
Moderate + (5)			1 (1)			1 (1)	
RV dysfunction (≥moderate)	213		2 (1)	215		6 (3)	.29
RVOT							
Minimum branch PA size (cm)	61	0.47 ± 0.1	0.4/0.46/0.56	65	0.46 ± 0.1	0.4/0.45/0.55	.78
Minimum branch PA z-score	58	−0.4 ± 1.4	−1.9/−0.4/1	62	−0.5 ± 1.5	−2.2/−0.3/0.9	.86
RVOT stenosis	205		5 (2)	210		8 (4)	.42
Preoperative							
Mechanical ventilation	222		92 (41)	232		97 (42)	.94
Identifiable genetic syndrome	222		4 (2)	232		10 (4)	.17
Renal insufficiency	222		11 (5)	232		1 (1)	.003
Metabolic acidosis	222		26 (12)	232		34 (15)	.35
CNS: seizure, bleeding, stroke	222		5 (2)	232		4 (2)	.75

Values for baseline morphologic and demographic characteristics used to determine the propensity score (including those not selected in the final model) for all 454 neonates who underwent NW-RVPAor NW-BT. Percentiles given are 15th/50th/85th. *NW-RVPA*, Norwood operation with right-ventricle-to-pulmonary-artery conduit; *NW-BT*, Norwood operation with modified Blalock-Taussig shunt; *SD*, standard deviation; *BSA*, body surface area; *ASD*, atrial septal defect; VSD, ventricular septal defect; *EFE*, endocardial fibroelastosis; *LVOT*, left ventricular outflow tract; LVOTO, left ventricular outflow tract obstruction; *AI*, aortic insufficiency; *LV*, left ventricular; *MV*, mitral valve; *TV*, tricuspid valve; *TR*, tricuspid valve regurgitation; *RV*, right ventricular. *RVOT*, right ventricular outflow tract; *PA*, pulmonary artery; *CNS*, preoperative stroke, seizure or central nervous system/intracranial hemorrhage. *Functional aortic valve atresia and functional mitral valve atresia designate an aortic or mitral valve that is either atretic or associated with severe stenosis or hypoplasia.

000 Survival and right ventricular performance for matched children after stage-1 Norwood: Modified Blalock-Taussig shunt versus right-ventricle-to-pulmonary-artery conduit

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In neonates with critical left ventricular outflow tract obstruction, NW-RVPA has better 6-year survival, and comparable late RV dysfunction and TR, compared with NW-BT.