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Impact of pre-stage II hemodynamics and pulmonary artery anatomy on 12-month outcomes in the Pediatric Heart Network Single Ventricle Reconstruction trial

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Objective: To compare the interstage cardiac catheterization hemodynamic and angiographic findings between shunt types for the Pediatric Heart Network Single Ventricle Reconstruction trial. The trial, which randomized subjects to a modified Blalock-Taussig shunt (MBTS) or right ventricle-to-pulmonary artery shunt (RVPAS) for the Norwood procedure, demonstrated the RVPAS was associated with a smaller pulmonary artery diameter but superior 12-month transplant-free survival.

Methods: We analyzed the pre-stage II catheterization data for the trial subjects. The hemodynamic variables and shunt and pulmonary angiographic data were compared between shunt types; their association with 12-month transplant-free survival was also evaluated.

Results: Of 549 randomized subjects, 389 underwent pre-stage II catheterization. A smaller size, lower aortic and superior vena cava saturation, and higher ventricular end-diastolic pressure were associated with worse 12-month transplant-free survival. The MBTS group had a lower coronary perfusion pressure (27 vs 32 mm Hg; $P < .001$) and greater pulmonary blood flow/systemic blood flow ratio (1.1 vs 1.0, $P = .009$). A greater pulmonary blood flow/systemic blood flow ratio increased the risk of death or transplantation only in the RVPAS group ($P = .01$). The MBTS group had fewer shunt (14% vs 28%, $P = .004$) and severe left pulmonary artery (0.7% vs 9.2%, $P = .003$) stenoses, larger mid-main branch pulmonary artery diameters, and greater Nakata indexes (164 vs 134, $P < .001$).

Conclusions: Compared with the RVPAS subjects, the MBTS subjects had more hemodynamic abnormalities related to shunt physiology, and the RVPAS subjects had more shunt or pulmonary obstruction of a severe degree and inferior pulmonary artery growth at pre-stage II catheterization. A lower body surface area, greater ventricular end-diastolic pressure, and lower superior vena cava saturation were associated with worse 12-month transplant-free survival. (*J Thorac Cardiovasc Surg* 2014;148:1467-74)

Despite significant advances in staged surgical repair for infants with single ventricle anatomy, the early- and intermediate-term outcomes have remained suboptimal.^{1,2} The palliative approach for these infants has consisted of a Norwood procedure using either a modified Blalock-Taussig shunt (MBTS) or right ventricle-to-pulmonary

artery shunt (RVPAS) to supply blood flow to the lungs. Then, usually at 3 to 7 months of age, a stage II procedure will be performed, most often after elective pre-stage II cardiac catheterization with angiography of the shunt and pulmonary arteries. Few data exist regarding the importance of the pre-stage II assessment using cardiac

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Abbreviations and Acronyms

BSA	= body surface area
CI	= confidence interval
EDP	= end-diastolic pressure
HR	= hazard ratio
LPA	= left pulmonary artery
MBTS	= modified Blalock-Taussig shunt
Qp/Qs	= pulmonary blood flow/systemic blood flow
RPA	= right pulmonary artery
RVPAS	= right ventricle-to-pulmonary artery shunt
SVC	= superior vena cava
SVR	= single ventricle reconstruction

catheterization and the importance of these findings to the outcomes.^{3,4}

Recently, several nonrandomized studies have reported improved early outcomes after Norwood procedures using a RVPAS.⁵⁻⁷ The Pediatric Heart Network Single Ventricle Reconstruction (SVR) trial was a multi-institutional trial that evaluated the early- and intermediate-term outcomes for infants undergoing a Norwood procedure randomized to either an MBTS or RVPAS. The initial SVR trial results⁸ demonstrated that the RVPAS, compared with the MBTS, was associated with superior 12-month transplant-free survival. However, at >12 months, no significant transplant-free survival difference was found between the 2 groups. However, that primary SVR analysis also demonstrated that the RVPAS subjects had undergone significantly more unintended cardiovascular procedures. In addition, analysis of the pre-stage II angiograms for pulmonary artery growth, a secondary endpoint of the SVR trial, demonstrated worse branch pulmonary artery growth before the stage II procedure for the RVPAS group compared with the MBTS group.⁸ However, the level of detail of the angiographic analysis was limited. The hemodynamic measures were not analyzed in the initial SVR publication.

The purposes of the present analysis were to describe in detail the cardiovascular hemodynamics and shunt or branch pulmonary artery angiographic findings from the pre-stage II cardiac catheterization; to assess the differences in these measures stratified by the shunt type; and to evaluate the effect of these factors on 12-month transplant-free survival.

METHODS**Study Population and Design**

From May 2005 to July 2008, 15 North American centers randomized 549 infants with single ventricle anatomy in the SVR trial to MBTS or RVPAS. Randomization was stratified by aortic atresia (presence vs

absence) and obstructed pulmonary venous return (presence vs absence), with dynamic allocation by the surgeon. Details regarding the trial design have been previously published.⁹ The institutional review board at all participating institutions approved the trial (ClinicalTrials.gov no. NCT00115934), and the parents or guardians provided informed consent for each subject.

All subjects enrolled in the SVR trial who had undergone pre-stage II cardiac catheterization were included in these analyses. Infants who had died before undergoing the stage II procedure but who had undergone cardiac catheterization and had acceptable angiograms were also included in the analyses. The only subjects excluded were those who had not undergone cardiac catheterization with angiography of the shunt and pulmonary arteries before the stage II procedure or those who survived but had never undergone stage II palliation. The subjects for whom the angiograms were deemed inadequate by the Angiography Core Laboratory were included for the hemodynamic analyses.

Catheterization Hemodynamic Variables

The hemodynamic variables were collected prospectively for each enrolled subject. These data were collected during catheterization at a baseline state, defined as the period when the subject was stable and before any intervention. The type of sedation and presence or absence of supplemental oxygen were recorded. If >1 measurement was obtained, the average of all stable baseline measurements was recorded. The coronary perfusion pressure was calculated as the aortic or femoral artery diastolic pressure minus the ventricular end-diastolic pressure (EDP).

Shunt and Pulmonary Angiographic Measurements

The Angiography Core Laboratory received the angiograms, which were blinded for the subjects' demographic data and medical center location. All angiograms were assessed for the presence of a reliable calibration factor, and the image quality was scored to determine whether the angiograms were acceptable to perform complete measurements. Each measurement was performed to the nearest 0.1 mm either digitally (Philips Inturis, Digital Angiographic Analysis, Eindhoven, The Netherlands) or using digital calipers (Absolute, Digimatic, Mitutoyo, Japan). The measurements were conducted separately by 2 physicians trained in angiography. If a significant discrepancy was present, the study was reviewed again and adjudicated such that discrepancies were resolved before entering the final data from the Angiography Core Laboratory. For the right and left pulmonary arteries (RPA and LPA, respectively), specific measurement locations (Figure 1) were defined as the mid-main branch pulmonary artery (between the shunt anastomosis and upper lobe branch or proximal to the upper lobe branch for the side contralateral to the shunt) and the proximal lower lobe branch pulmonary artery (between the takeoff of the upper lobe branch and the lower lobe segments). These specific locations were selected to avoid measuring stenotic areas as representative of pulmonary artery growth in the often-complex anatomy. The Nakata index was measured using the following formula: $\pi \times [\text{right mid-main pulmonary artery diameter (mm)}^2 + \text{left mid-main pulmonary artery diameter (mm)}^2] / [4 \times \text{body surface area (m}^2)]$.¹⁰ In addition, the angiograms were assessed for the presence of shunt stenosis (proximal or distal) and unilateral and bilateral branch pulmonary artery stenosis. The percentage of stenosis was calculated using the following formula: $[1 - (\text{diameter of narrowest portion of the stenotic branch pulmonary artery} / \text{diameter of ipsilateral proximal lower lobe branch})] \times 100$. The severity of branch pulmonary artery stenosis was quantified as none (<15%), mild (15%-35%), moderate (>35%-50%), or severe (>50%).

Statistical Analysis

Shunt comparisons were performed using the Student *t* test or Wilcoxon rank sum test, as appropriate, for continuous measures. Categorical

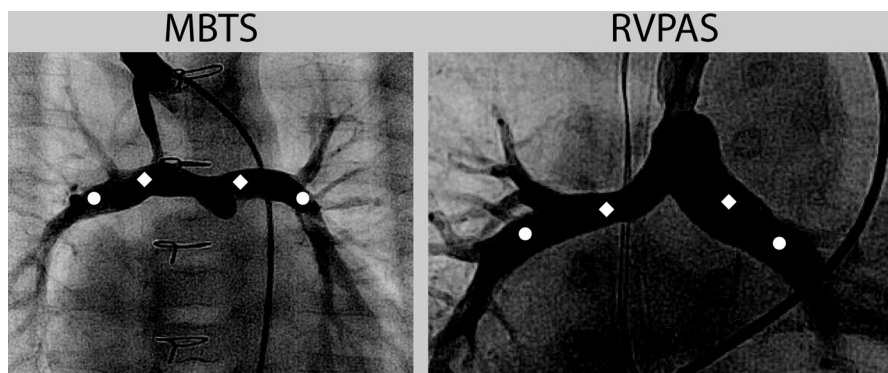


FIGURE 1. Location of branch pulmonary artery measurements. *Diamonds* mark the mid-main pulmonary artery measurement location, and *circles* mark the proximal lower lobe pulmonary artery measurement location. *MBTS*, Modified Blalock-Taussig shunt; *RVPAS*, right ventricle-to-pulmonary artery shunt.

measures were compared by shunt type using the Fisher exact test. Ordinal measures were also compared using the Mantel-Haenszel's test for trend. The shunt type used in statistical analyses was the actual shunt type in place at the end of the Norwood procedure and, thus, represented a non-intention-to-treat analysis. Hazard ratios (HRs) and the associations between the hemodynamic variables and angiographic measurements and 12-month transplant-free survival were examined using the Cox proportional hazards model. Interactions between the shunt type and the hemodynamic and angiographic measures were examined. Continuous measures were examined as quartiles when nonlinear associations were identified. Owing to the limited number of deaths and transplantations in the subjects with cardiac catheterization data, multivariate analysis was not practical; therefore, the associations with 12-month transplant-free survival were unadjusted. The proportional hazards assumption was examined for each measure. The incidence rates and 95% confidence intervals (CIs) for catheter interventions were calculated using Poisson's regression. The presented *P* values are raw and were not adjusted for multiple comparisons. Owing to the large number of comparisons performed, $P \leq .01$ was considered statistically significant. All analyses were performed using the Statistical Analysis Systems, version 9.2 (SAS Institute, Inc, Cary, NC) and R, version 2.12.0 (University of Auckland, Auckland, New Zealand).

RESULTS

Study Population

Of the 549 SVR trial subjects, the present analysis was restricted to the 389 subjects who had undergone prestage II cardiac catheterization, including 348 subjects with angiograms deemed adequate for analysis (MBTS, $n = 152$; RVPAS, $n = 196$; Figure 2). The reasons that catheterization was not performed are summarized in Figure 2 and included in-hospital death or transplant ($n = 97$), interstage death or transplantation ($n = 45$), and institutional preference ($n = 18$). Age, body surface area (BSA), and angiogram acceptability did not differ between shunt types (Table 1). The BSA at initial palliation also did not differ by shunt type ($P = .63$), and the frequency of a low BSA did not differ between the 2 groups at either the initial surgical palliation ($P = .30$) or catheterization ($P = .84$). Of those with adequate pre-stage II cardiac catheterization angiograms, 23 subjects (6.6%) had either died or underwent cardiac transplantation after the stage

II procedure and before the 12-month point after randomization (MBTS, 6%; RVPAS, 7%).

Sedation Type

For the entire cohort undergoing cardiac catheterization, the procedure was performed with the patient under general anesthesia for 63% of the patients and using intravenous sedation for the remaining 37%. The RVPAS patients were more likely to be placed under general anesthesia were the MBTS patients (69% vs 56%, $P = .01$).

Cardiovascular Hemodynamic Variables

For the entire cohort, 3 anthropometric or hemodynamic variables obtained at pre-stage II cardiac catheterization demonstrated associations on univariate analysis with transplantation or death at 12 months. These included the BSA (HR per standard deviation decrease, 1.87; 95% CI, 1.32-2.64; $P < .001$), superior vena caval saturation (HR per 1% decrease, 1.07; 95% CI, 1.03-1.12; $P = .002$), and ventricular EDP (HR per 1-mm Hg increase, 1.17; 95% CI, 1.07-1.30; $P = .006$). A larger pulmonary blood flow/systemic blood flow (Qp/Qs) ratio was associated with an increased risk only for the RVPAS group (HR per 0.1 increase, 1.11; 95% CI, 1.02-1.21; $P = .01$).

The hemodynamic data examined by shunt type (Table 2) demonstrated that the MBTS group, compared with the RVPAS group, had a greater Qp/Qs ratio, a significantly lower systemic diastolic pressure, and calculated coronary perfusion pressure but a similar systemic ventricle EDP.

Shunt and Pulmonary Artery Abnormalities

Overall, 55% of subjects had angiographic findings of shunt or branch pulmonary artery stenosis, including 33% with moderate or worse (>35%) branch pulmonary artery stenosis (Table 3). The RVPAS group demonstrated more frequent shunt stenosis (MBTS 14% vs RVPAS 28%; $P = .004$). When the location of shunt stenosis was

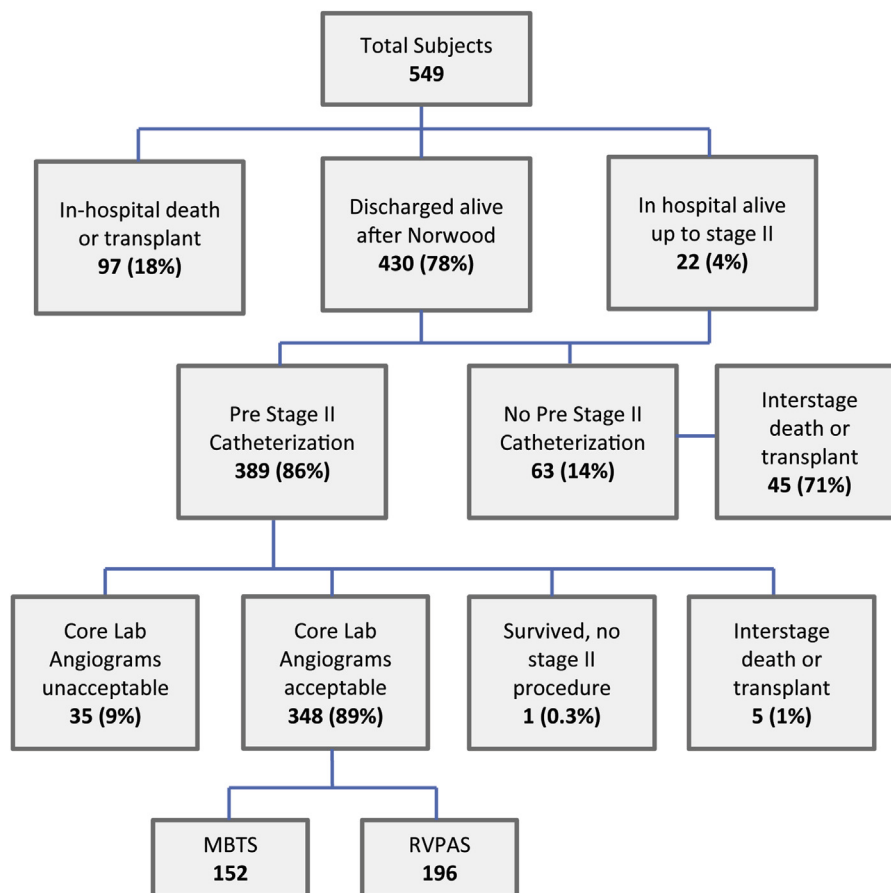


FIGURE 2. Single Ventricle Reconstruction trial subjects’ outcomes and subgroup with acceptable prestage II angiograms. *MBTS*, Modified Blalock-Taussig shunt; *RVPAS*, right ventricle-to-pulmonary artery shunt.

assessed, the RVPAS group had developed proximal shunt stenosis more often, and the distal shunt stenosis rates were similar between the 2 groups. The total pulmonary artery growth was also decreased in the RVPAS group, as reflected by the smaller right and left mid-main branch pulmonary artery diameters and the smaller proximal right lower lobe and lower Nakata index (Table 4). For the entire cohort, severe (>50%) branch pulmonary artery stenosis occurred in 9.5% in the RPA and 5.5% in the LPA. The rate of severe RPA stenosis did not differ between the 2 groups (MBTS 5.9% vs RVPAS 12%, $P = .18$). However, the MBTS subjects less often developed severe LPA

stenosis (MBTS 0.7% vs RVPAS 9.2%, $P = .003$). When comparing the narrowest diameter of the stenotic branch pulmonary artery segment, the RVPAS group had a smaller diameter for the stenotic portion of the RPA (2.9 ± 0.9 mm vs 4.0 ± 1.3 mm, $P < .001$) but not the LPA (2.9 ± 1.0 mm vs 3.3 ± 1.0 mm, $P = .06$).

For the entire cohort, no single angiographic measurement was associated with the 12-month transplant-free survival. The Nakata index also was not predictive of the 12-month transplant-free survival.

DISCUSSION

Our analysis represents the first prospective study to examine in detail the hemodynamic and angiographic variables and their relationship with the outcome in patients after Norwood procedure randomized to the MBTS or RVPAS.

Hemodynamic Parameters

The hemodynamic measures associated with an increased risk of death or transplantation at 12 months included a smaller size (as evidenced by a lower BSA), greater

TABLE 1. Demographic data by shunt type

Variable	Total	MBTS	RVPAS
Cardiac catheterization	389	170	217
Acceptable angiograms for analysis	348	152	196
Age at catheterization (mo)	4.4 ± 1.5	4.5 ± 1.5	4.4 ± 1.5
Body surface area (m ²)	0.31 ± 0.04	0.31 ± 0.04	0.31 ± 0.04

Data presented as n or mean ± standard deviation. *MBTS*, Modified Blalock-Taussig shunt; *RVPAS*, right ventricle-to-pulmonary artery shunt.

TABLE 2. Hemodynamic variables by actual shunt type

Hemodynamic variable	Total (n = 387)	MBTS (n = 170)	RVPAS (n = 217)	P value
Aortic diastolic pressure (mm Hg)	38 ± 8	35 ± 7	40 ± 7	<.001
Coronary perfusion pressure (mm Hg)	29 ± 8	27 ± 8	32 ± 8	<.001
Ventricular end diastolic pressure (mm Hg)	8.3 ± 3.3	8.7 ± 3.4	7.9 ± 3.2	.02
Aortic saturation (%)	75 ± 6	75 ± 5	74 ± 6	.09
Superior vena cava saturation (%)	50 ± 8	50 ± 8	50 ± 8	.54
Qp/Qs ratio	1.0 (0.8-1.4)	1.1 (0.8-1.5)	1.0 (0.8-1.3)	.009
Mean pulmonary artery pressure (mm Hg)	15 (13-17)	14 (13-17)	15 (12-18)	.98
Pulmonary vascular resistance (Wood unit × m ²)	2.0 (1.3-2.6)	2.0 (1.3-2.3)	2.0 (1.4-2.8)	.25
General anesthesia for procedural sedation	242 (63)	95 (56)	147 (69)	.01

Data presented as mean ± standard deviation, median (interquartile range), or n (%). P values comparing MBTS and RVPAS groups were determined using the Student *t* test for the mean values, Wilcoxon rank sum test for the median values, and Fisher exact test for frequencies. MBTS, Modified Blalock-Taussig shunt; RVPAS, right ventricle-to-pulmonary artery shunt; Qp, pulmonary blood flow; Qs, systemic blood flow.

ventricular EDP, and lower SVC saturation. A greater EDP, likely reflective of poor diastolic function or increased pulmonary blood flow, would also result in increased pulmonary artery pressure after the stage II procedure. A lower SVC saturation might have represented poor cardiac output or lower arterial oxygen saturation. It was not surprising that both parameters were associated with worse outcomes at 12 months. With respect to the comparison of hemodynamic parameters by shunt type, our analysis was consistent with previous reports regarding the retrograde aortic flow pattern,¹¹ lower aortic diastolic pressure, and lower coronary perfusion pressure in the MBTS subjects.¹² Although clear data are lacking, the latter finding might result in chronic injury to the ventricular myocardium in the MBTS subjects, which could explain the finding in the SVR trial of lower transplant-free survival at 12 months in the MBTS subjects. In contrast, RVPAS subjects will require a ventriculotomy, which could negatively affect late ventricular function and result in the development of ventricular arrhythmias. This could, in turn, offset the early advantages of greater coronary perfusion pressure.¹³ However, this potential disadvantage of a right ventriculotomy for RVPAS subjects has remained controversial. Tanoue and colleagues¹⁴ found that, after the stage II procedure, the RVPAS subjects had worse right ventricular systolic function than did the MBTS subjects. Owing to concerns regarding late ventricular dysfunction, Ballweg and colleagues³ analyzed 124 infants who had undergone a stage

II procedure for single ventricle physiology and reported no difference in 3-year survival, although the RVPAS subjects had a greater incidence of ventricular dysfunction by echocardiography at the stage II procedure. Graham and colleagues¹³ demonstrated no difference in hospital survival when comparing shunt types for 76 infants with single ventricle physiology but greater interstage mortality for MBTS subjects (22% vs 3%, *P* = .05). These results have been supported by Mahle and colleagues,¹⁵ who reported operative and 1-year survival of 81% for RVPAS subjects, with no difference in the Qp/Qs ratio or survival between shunt types, suggesting that equivalent pulmonary blood flow will result in equivalent survival.

Angiographic Findings

The analysis of our data have demonstrated that overall pulmonary artery growth was less in the RVPAS group and that no angiographic measurement was associated with the 12-month transplant-free survival. During the interstage period, pulmonary artery growth is dependent on the blood flow entering the branch pulmonary arteries across the surgical shunt. The potential explanations for the differences in branch pulmonary artery growth patterns include anatomic abnormalities with the shunt or branch pulmonary arteries¹⁶ and hemodynamic factors, such as shunt diameter¹² and pulsatile vs nonpulsatile shunt blood flow.¹¹ In contrast to our findings of inferior pulmonary artery growth in the RVPAS cohort, Januszewska and

TABLE 3. Angiographic pulmonary artery and shunt abnormalities by shunt type

Angiographic abnormality	Total (n = 348)	MBTS (n = 152)	RVPAS (n = 196)	P value
Mid main RPA stenosis	110 (32)	38 (25)	72 (37)	.02
Severe RPA stenosis, any location	33 (9)	9 (6)	24 (12)	.18
Mid main LPA stenosis	79 (23)	30 (20)	49 (25)	.30
Severe LPA stenosis, any location	19 (5)	1 (1)	18 (9)	.003
All shunt stenosis	75 (22)	21 (14)	54 (28)	.004
Proximal shunt stenosis	33 (10)	6 (4)	27 (14)	.008

Data presented as n (%). P values comparing MBTS and RVPAS group were determined using the Fisher exact test. MBTS, Modified Blalock-Taussig shunt; RVPAS, right ventricle-to-pulmonary artery shunt; RPA, right pulmonary artery; LPA, left pulmonary artery.

TABLE 4. Pulmonary artery measurements by shunt type

Measurement	Total (n = 348)	MBTS (n = 152)	RVPAS (n = 196)	P value
Mid-main LPA (mm)	4.5 (3.6-5.7)	4.8 (4.0-6.0)	4.3 (3.4-5.4)	.009
Mid-main LPA, indexed (mm/m ²)	15.1 (11.9-17.9)	15.8 (13.0-18.4)	14.2 (11.3-17.5)	.003
Mid-main RPA (mm)	4.6 (3.6-5.7)	5.0 (4.0-6.1)	4.2 (3.4-5.2)	<.001
Mid-main RPA, indexed (mm/m ²)	15.0 (11.6-18.4)	16.5 (13.0-19.9)	13.9 (10.7-17.1)	<.001
Proximal right lower lobe (mm)	5.7 ± 1.8	6.3 ± 2.1	5.1 ± 1.4	<.001
Proximal right lower lobe, indexed (mm/m ²)	18.4 ± 5.6	20.7 ± 6.2	16.7 ± 4.4	<.001
Proximal left lower lobe (mm)	5.3 ± 1.6	5.4 ± 1.6	5.2 ± 1.7	.54
Proximal left lower lobe, indexed (mm/m ²)	17.3 ± 5.2	17.6 ± 5.1	17.1 ± 5.4	.36
Nakata index (mm ² /m ²)	147 (110-196)	164 (125-226)	134 (100-180)	<.001

Data presented as mean ± standard deviation or median (interquartile range). Indexed data were indexed to the body surface area at catheterization. P values comparing MBTS and RVPAS groups were determined using the Student *t* test for the mean and Wilcoxon rank sum test for the median values. MBTS, Modified Blalock-Taussig shunt; RVPAS, right ventricle-to-pulmonary artery shunt; LPA, left pulmonary artery; RPA, right pulmonary artery.

colleagues¹⁷ reported that although the RVPAS subjects had a significantly lower Qp/Qs ratio (0.8 vs 1.2), lower aortic oxygen saturation (67.4% vs 75.3%), and lower SVC oxygen saturation (43.5% vs 49.7%), they had good, symmetric pulmonary artery growth before the stage II procedure. One purported advantage of the RVPAS is that it allows pulsatile flow into the branch pulmonary arteries, which might improve interstage pulmonary artery growth, compared with the MBTS, which provides continuous flow.

Shunt and Pulmonary Artery Stenosis

Stenoses of the shunt or branch pulmonary arteries can have significant adverse effects in this patient population. Obstruction to shunt-dependent blood flow will result in poor branch pulmonary artery growth,¹⁸ and branch pulmonary artery hypoplasia is a risk factor at the stage II procedure.^{19,20} In addition, the presence of central pulmonary artery stenoses frequently requires catheter-based interventions or surgical revision at the stage II procedure.^{4,16} For the entire cohort and irrespective of shunt type, branch pulmonary artery stenosis occurred nearly 50% of the time in both the LPA and the RPA. This finding was consistent with a report from Griselli and colleagues¹⁶ that 50% of infants undergoing a Norwood procedure developed central pulmonary artery stenosis that required surgical revision during the stage II procedure. In our angiographic analyses, the RVPAS subjects had more often had stenosis in the shunt, more often developed moderate-to-severe branch pulmonary artery stenosis, and had a significantly smaller absolute diameter of the stenotic portion of the RPA. Our data have demonstrated that the Nakata index before the stage II procedure was lower than that previously reported for both shunt types and was significantly lower for RVPAS subjects. This is in contrast to previous single-center, nonrandomized studies that have reported that subjects with an RVPAS, compared with an MBTS, have larger branch pulmonary arteries at the stage II procedure.²¹

By defining the specific branch pulmonary artery measurement locations (Figure 1), our analysis was potentially

able to avoid using the stenotic lesion for part of the measurement. In the presence of complex stenoses, the diameter of the proximal lower lobe pulmonary arteries might provide a more accurate assessment of the branch pulmonary artery growth. Determination of the clinical significance of the differences in branch pulmonary artery size among the survivors will require longer term follow-up. The RVPAS group had a significantly smaller mid-main LPA, mid-main RPA, and proximal right lower lobe pulmonary artery, and the proximal left lower lobe pulmonary artery diameters were similar. Moreover, the RVPAS subjects had a 1-year transplant-free survival advantage in the SVR trial.⁸ It is possible that the hemodynamic effects are more important and will ultimately outweigh the effects of smaller pulmonary arteries.

Study Limitations

Data on other factors that could affect survival, such as aortic arch obstruction, ventricular function, and atrioventricular valve regurgitation, were limited. We consciously did not analyze detailed surgical shunt features, such as size, length, insertion site, beveled anastomosis, and innominate artery size. Assumptions regarding the calculation of coronary perfusion pressure might have been erroneous in subjects with concomitant aortic arch obstruction. The mode of sedation was different between the 2 groups and might have affected the hemodynamic measures. Because of the study design, we had no hemodynamic or angiographic information for the subjects with interstage mortality. Also, because a greater number of MBTS subjects died during Norwood hospitalization or during the interstage period, the potential for a survivor bias was present and might have affected the shunt type comparisons. The shunt comparisons and associations with 12-month transplant-free survival were performed without adjustment for potential confounders owing to the limited number of deaths and cardiac transplants. Finally, because of the limited number of events in the transplant-free survival analyses, the statistical power to detect significant findings was limited.

CONCLUSIONS

Our analysis of pre-stage II catheterization data for SVR trial subjects has shown that, compared with the RVPAS subjects, the MBTS subjects had more hemodynamic abnormalities related to shunt physiology, including lower systemic diastolic and coronary perfusion pressures, greater ventricular EDPs, and greater Qp/Qs ratios. In contrast, the RVPAS subjects had more shunt or pulmonary obstruction of a severe degree and inferior pulmonary artery growth at pre-stage II catheterization. A lower BSA, greater ventricular EDP, and lower SVC saturation were associated with worse 12-month transplant-free survival for the entire cohort, and no single angiographic measurement had such an association.

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APPENDIX

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