Right Ventricle to Pulmonary Artery Conduit Improves Outcome After Stage I Norwood for Hypoplastic Left Heart Syndrome

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Background—Diastolic run off into the pulmonary circulation and labile coronary perfusion are thought to contribute to morbidity and mortality after the Norwood procedure (NP). We compared outcomes from the use of a RV to PA conduit (RV/PA) or a modified Blalock-Taussig shunt (BTS), physiologically distinct sources of pulmonary blood flow.

Methods and Results—Review of 56 consecutive patients who underwent a Norwood procedure with a RV/PA (n = 36) or a BTS (n = 20) between 2000 and 2002. Median age was 4.5 days (range 1 to 40) and median weight was 3.1 kg (range 1.8 to 4.1). The RV/PA was constructed with a 5-mm conduit. Patients in the BTS group received a 4-mm shunt.

Comparisons between RV/PA and BTS groups showed no difference for weight, gestational age, prenatal diagnosis, HLHS variant, associated diagnoses, ascending aortic size, ventricular function, AV valve function, and pulmonary venous obstruction. Operative survival was higher with RV/PA [33/36 (92%) versus 14/20 (70%); P = 0.05]. Patients with RV/PA had less need for ventilatory manipulations to balance the Qp/Qs (1/36 vs 8/20; P = 0.001), delayed sternal closure (6/36 vs 7/20; P = 0.001), and extracorporeal support (5/36 vs 7/20; P = 0.036). RV/PA patients had more favorable postoperative hemodynamics; higher diastolic blood pressure without changes in systolic blood pressure at 1, 8, 24, 48 hours after the NP (46.3 v/s 39.5; 47.2 v/s 42.1; 46.1 v/s 37.1; and 47.1 v/s 40.2; all P = 0.001).

Conclusion—RV/PA simplifies postoperative management and improves hospital survival after NP for HLHS.

Key Words: heart defects congenital heart surgery risk factors

The physiological palliation of hypoplastic left heart syndrome (HLHS) has evolved over more than 2 decades into a 3-staged operative strategy in which the initial intervention poses the greatest challenge. Although significant progress has been made in the perioperative management of the initial procedure, the early survival has plateaued.

Moreover, the interim mortality between the first two stages remains unsolved. The physiology of the initial stage is characterized by the presence of significant diastolic run off into the pulmonary vasculature away from coronary perfusion and persistent but necessary excessive volume load on the single ventricle. To modulate these detrimental physiological features, the use of a right ventricle to pulmonary artery conduit (RV/PA), initially reported in the early attempts of surgical palliation for HLHS by Norwood and colleagues, has been revisited.

This report compares the experience in two centers with the use of a RV to PA conduit to provide pulmonary blood flow as opposed to the conventional approach using a modified Blalock-Taussig shunt in neonates undergoing Stage I Norwood reconstruction for HLHS. No other aspect of the surgical technique or perioperative management has been altered.

Materials and Methods

The study had a cohort design without randomization. It included data collection from all patients with HLHS who underwent the Stage I Norwood procedure using a RV to PA conduit as the source of pulmonary blood flow between June 2001 and March 2002 at the Nemours Cardiac Center Wilmington, USA, and the Polish-American Hospital in Krakow, Poland. A control group was obtained by a retrospective review of 20 consecutive neonates with HLHS who underwent a Stage I Norwood procedure using a right modified Blalock-Taussig shunt at the Nemours Cardiac Center between 2000 and 2001. Data collection included demographic, preoperative, operative and postoperative variables, as well as follow up information obtained during office visits. The study was approved by the Institutional Review Boards of the Alfred I. duPont Hospital for Children and Polish–American Hospital.

The end points of this study included: (1) postoperative blood pressure measurements at 1 hour, 8 hour, 24 hour, 48 hour, and at hospital discharge; (2) Changes in postoperative diastolic flow reversal ratio (DFR) by echocardiography; (3) Use of ventilatory manipulations to balance Qp/Qs; (4) Use of extracorporeal circulatory support during the perioperative period; (5) Use of delayed...
The surgery was performed using a period of deep hypothermic circulatory arrest, and included atrial septectomy, association of the aortic root with the proximal main pulmonary artery, augmentation of the ascending aorta and aortic arch with cryopreserved pulmonary homograft. The source of pulmonary blood flow was a right ventricle to pulmonary artery conduit as the source of pulmonary artery blood flow.

Figure 1. Completed Stage I Norwood procedure with a right ventricle to pulmonary artery conduit as the source of pulmonary artery blood flow.

TABLE 1. Preoperative Variables (continuous)

<table>
<thead>
<tr>
<th>Preoperative Variables</th>
<th>BTS</th>
<th>RV/PA</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (days)</td>
<td>4.5±3.6</td>
<td>9.0±8.6</td>
<td>0.032</td>
</tr>
<tr>
<td>Birth weight (kg)</td>
<td>3.2±0.4</td>
<td>3.0±0.4</td>
<td>0.228</td>
</tr>
<tr>
<td>Surgical weight (kg)</td>
<td>3.2±0.4</td>
<td>3.1±0.4</td>
<td>0.511</td>
</tr>
<tr>
<td>EGA* (wks)</td>
<td>38.3±1.2</td>
<td>38.5±1.5</td>
<td>0.184</td>
</tr>
<tr>
<td>Asc aorta† (mm)</td>
<td>3.1±1.3</td>
<td>3.6±1.3</td>
<td>0.256</td>
</tr>
</tbody>
</table>

EGA* = estimated gestational age.
Asc aorta = ascending aorta.

Follow-up data were obtained from all 47 hospital survivors. This information was obtained directly from the patients’ cardiologists during a 2-month period ending September 30, 2002. We examined morbidity, mortality and survival to second stage.

Statistical Methods

Comparisons were made based on source of pulmonary blood flow (RV to PA conduit versus systemic to pulmonary artery shunt). Patient and operative variables were evaluated for their influence on patient outcome. Data analysis included chi-square, t-tests, Mann-Whitney test, bivariate correlation and repeated measures ANOVA.

Results

Means and standard deviations for the continuous preoperative dependent variables analyzed are shown in Table 1. There were no significant differences by independent samples t-test for birth weight, surgical weight, gestational age or ascending aortic diameter between groups. Although there was a difference in the mean age between the 2 groups (4.5±3.6 versus 9.0±8.6, t=2.20, df=54, P=0.032), this was largely due to the referral pattern and preoperative management practice in the subgroup of patients from Poland, who commonly had to be transported from long distances. However, no age difference was observed in the subgroup of patients from the US (mean age 2.7 versus 4 days). Similarly, there was no significant difference by chi-square analysis for the independent variables: prenatal diagnosis, associated cardiac and noncardiac diagnosis, HLHS variant and diagnosis of aortic atresia between the two groups (Table 2). An associated non cardiac diagnosis or a chromosomal anomaly was present in 9 patients and included meconium aspiration, necrotizing enterocolitis with Gram-negative sepsis, omphalocele, club feet, cleft palate, renal hypoplasia, pes equine and Turner’s syndrome. Also there were no differences between

TABLE 2. Preoperative Variables (categorical)

<table>
<thead>
<tr>
<th>Preoperative Variables</th>
<th>BTS</th>
<th>RV/PA</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>n=</td>
<td>20</td>
<td>36</td>
<td></td>
</tr>
<tr>
<td>Prenatal dx*</td>
<td>14</td>
<td>18</td>
<td>0.14</td>
</tr>
<tr>
<td>Assoc† cardiac dx</td>
<td>7</td>
<td>9</td>
<td>0.43</td>
</tr>
<tr>
<td>Assoc noncardiac dx</td>
<td>4</td>
<td>8</td>
<td>0.24</td>
</tr>
<tr>
<td>Ao‡ atresia</td>
<td>11</td>
<td>20</td>
<td>0.86</td>
</tr>
</tbody>
</table>

*dx=diagnosis.
†Assoc=associated.
‡Ao=aortic.
the groups for right ventricular shortening fraction, atrio-ventricular valve function and pulmonary venous obstruction.

Eleven patients had aortic atresia with mitral atresia, 8 had aortic atresia with mitral hypoplasia, 8 had aortic hypoplasia with mitral hypoplasia, and 2 had aortic hypoplasia with mitral atresia. Four patients had unbalanced complete common atroventricular canal defect, 2 had double outlet right ventricle with mitral atresia and 1 patient had aortic hypoplasia with moderate-severe left ventricular hypoplasia and endocardial fibroelastosis. The size of the ascending aorta ranged between 1.5 and 5 mm with a median value of 3.0 mm.

Analysis of the perfusion data revealed no difference for the total duration of CPB (95.1±26 minutes versus 102.8±27.2 minutes, t-test P=0.34) between the two groups. The duration of dhca time was shorter in the RV/PA group (49.0±15.9 minutes versus 61.2±8.2 minutes t=-3.8, DF [51] P=0.00), because of the shorter dhca time in the subgroup of patients from Poland. These patients often had the distal pulmonary artery patch sewn during the period of cooling and commonly had the RV/PA conduit anastomosis to the ventricle during the period of warming. This difference was not observed in the subgroup of patients from the US, who had a similar duration of the period of dhca for the BTS and the RV/PA conduit (61.4±8.2 minutes and 57.2±7.3 minutes t-test P=0.15).

The postoperative hemodynamic profile for the entire cohort of patients is shown in Figure 2. Systolic and diastolic blood pressure measurements were obtained 2 hours before surgery, 1, 8, 24, 48 hours postoperatively and at the time of discharge. Analysis of variance with repeated measures demonstrated a significant group by time interaction for both the diastolic pressure (F=4.08, df [4,37] P=0.008) and pulse pressure (F=3.63, df [4,37] P=0.014), showing that the two surgical groups had a significant difference for the dependent variables diastolic blood pressure and pulse pressure at different time points. Although both groups had a similar preoperative systolic and diastolic pressure, the RV/PA group exhibited a higher mean diastolic pressure, in excess of 40 mm Hg, associated with a narrower pulse pressure in the postoperative period. Conversely, only a time effect was shown for systolic blood pressure, without any group interaction.

Echocardiographic assessment of time-velocity integrals measured by pulse wave Doppler interrogation using a sagittal view of the distal aortic arch revealed no retrograde flow in the patients who received a RV/PA conduit, compared with the significant holodiastolic flow reversal in the patients who received a modified Blalock shunt. The mean values for the DFR (time-velocity integral of retrograde flow/ antegrade flow) were 0 for the RV/PA group compared with 0.064±0.02 for the BTS. Similarly, the value for the antegrade flow component was lower in the RV/PA group compared with the BTS (0.064 v/s 0.123 t-test P=0.0013) (Figure 3). Moreover, Doppler interrogation of the RV/PA conduit showed no significant diastolic retrograde flow into the right ventricular cavity.

Analysis of variance with repeated measures for perioperative partial pressure of arterial oxygen (Pa02) and arterial oxygen saturation (Sa02) measured 2 hours preoperatively, 1, 8, 24, 48 hours postoperatively and at the time of discharge, demonstrated a significant group by time interaction for Pa02 (F=4.97, df [3,84] P=0.003). Although both surgical groups had similar preoperative values for Pa02 and Sa02, in the postoperative period the RV/PA group exhibited a lower mean Pa02 generally below 35 mm Hg in the first 48 hours, associated with a Sa02 between 60 and 65%. This difference reached the highest significance for the measurement at 8 hours postoperatively (Pa02 30.7±7.1 versus 41.7±5.5 mm Hg; F=6.0, df [1,28] P=0.021). These Pa02 values, although lower than the ones observed in patients who received a modified Blalock-Taussig shunt were appropriate to meet the metabolic requirements and were associated with signs of excellent peripheral perfusion, brisk urine output, and metabolic alkalosis.

This is likely to be a reflection of a lower Qp/Qs secondary to the reduced amount of diastolic run off into the pulmonary circulation. Although this difference was significant in the early postoperative period, it became nonsignificant for Pa02 (34.1±0.79 versus 34.0±1.1 mm Hg) or Sa02 (75.1±6.0 versus 71.0±7.2%) after the first 48 hours in the postoperative period.

Comparison of postoperative management end points using the chi-square test is shown in Table 3. There were significant differences in the use of ventilatory manipulations to reduce pulmonary blood flow, use of extracorporeal circulatory support and delayed sternal closure between the two surgical groups; a reflection of the increased circulatory stability demonstrated by the patients who received a RV/PA conduit. All these parameters reached high statistical significance. Conversely, no significant differences were detected by unpaired t-test for the postoperative variables duration of mechanical ventilatory support (48.3±55.4 versus 69.0±69.7 hours), intensive care unit stay (6.2±3.9 versus 6.1±4.1 days), or hospital stay (12.0±5.5 versus 10.6±5.7 days) between the 2 groups.

The comparisons for hospital survival and interim mortality by chi-square are shown in Table 4. There was a significant increase in hospital survival for patients who received a RV/PA conduit during the Norwood procedure. The likelihood ratio for this analysis was 4.89, making the subjects in the RV/PA group over 4 times less likely to die compared with the patients who received a BTS. Moreover, although there was a trend toward reduced interim mortality
for the RV/PA group this did not reach statistical significance ($P=0.184$) possibly because of the small patient sample.

Finally, we examined the relative contribution of the independent variables on outcome. All independent variables were recorded using a binary code to assure equal variances. Correlations were calculated using phi ($\phi$) coefficients. The variables which predicted worse outcome included: use of ecss, requirement of ventilatory manipulations, delayed sternal closure, a PaO$_2$ $>45$ mm Hg in the first 48 hours postoperatively, a diastolic blood pressure $<40$ mm Hg in the first 24 hours, total cpb $>120$ minutes and use of a BTS as the source of pulmonary blood flow.

When considering suitability for further palliation toward a Fontan, all 6-month survivors in the BTS (12/12) and RV to PA conduit (32/32) group underwent the second stage (hemi-Fontan) successfully.

**Figure 3.** Pulsed Doppler spectral display of the waveforms generated when sampling the distal arch/proximal descending aorta after Stage I Norwood with a RV to PA conduit and BTS. Flow below the baseline represents antegrade flow and flow above the baseline represents retrograde flow. Electrocardiographic tracing provides relationship with the cardiac cycle. (A) Corresponds to a patient to a patient after Stage I Norwood with a BTS. (B) Demonstrates a minimal amount of flow reversal during early diastole in a patient after Norwood procedure with a RV/PA conduit.

**TABLE 3.** Postoperative Management

<table>
<thead>
<tr>
<th>Postoperative Management</th>
<th>BTS</th>
<th>RV/PA</th>
<th>$P$ value</th>
</tr>
</thead>
<tbody>
<tr>
<td>n</td>
<td>20</td>
<td>36</td>
<td></td>
</tr>
<tr>
<td>Ventilatory manipulation</td>
<td>8</td>
<td>1</td>
<td>0.001</td>
</tr>
<tr>
<td>ECCS*</td>
<td>7</td>
<td>5</td>
<td>0.01</td>
</tr>
<tr>
<td>Open chest</td>
<td>7</td>
<td>6</td>
<td>0.001</td>
</tr>
</tbody>
</table>

*ECCS = extracorporeal circulatory support.

**TABLE 4.** Hospital Survival

<table>
<thead>
<tr>
<th>Survival</th>
<th>BTS</th>
<th>RV/PA</th>
<th>$P$ value</th>
</tr>
</thead>
<tbody>
<tr>
<td>n</td>
<td>20</td>
<td>36</td>
<td></td>
</tr>
<tr>
<td>Hospital survival</td>
<td>14  (70%)</td>
<td>33 (91.7%)</td>
<td>0.034</td>
</tr>
<tr>
<td>Interim mortality</td>
<td>2/14</td>
<td>1/33</td>
<td>0.16</td>
</tr>
</tbody>
</table>
Discussion

Since the initial efforts to develop a strategy for the management of patients with hypoplastic left heart syndrome by Norwood and colleagues, the progressive improvement in perioperative management has lead to a hospital survival close to 90%. It has been the cumulative experience of managing a large number of these patients which has allowed us to understand why the resulting physiology, characterized by a delicate equilibrium between systemic pulmonary and coronary circulation, has made further improvement in survival difficult to achieve.

The initial surgical procedures in the late seventies and early eighties included a 12 mm valved Dacron conduit between the right ventricle and the pulmonary artery that was narrowed to provide a controlled amount of pulmonary blood flow. However, large size of available valved conduits and concerns of the effect of a ventriculotomy on right ventricular function, quickly led to the adoption of a modified Blalock-Taussig systemic to pulmonary artery shunt. This seemingly simple technical modification connected both arterial circuits in parallel resulting in a non-trivial physiological effect, characterized by the potential for continuous flow from the systemic to the pulmonary circulation during the cardiac cycle. Because of the unequal, and more importantly highly variable vascular resistance ratio, a common net effect is significant runoff from the systemic into the pulmonary bed during diastole, a lower diastolic blood pressure, a wider pulse pressure and a change in the pattern of coronary perfusion.

To neutralize this adverse physiology a number of strategies including, the use of a smaller shunt or manipulation of vascular resistances using inspired carbon dioxide, nitrogen or sodium nitroprusside, have been developed to aid in the perioperative management with relative success. However, perioperative mortality has not been eliminated and the issue of interim sudden death before the second stage remains unsolved.

Patients with HLHS generally show signs of a large Qp/Qs in the preoperative period, often precipitating some form of ventilatory and/or pharmacologic intervention. The striking feature in this study was the improvement in circulatory stability exhibited since very early in the postoperative period by the group of patients who received a RV/PA conduit.

This circulatory stability was clearly reflected on the blood pressure comparison between the two groups. Although the blood pressure characteristics were similar for both surgical groups in the preoperative period, the RV/PA group showed a higher diastolic blood pressure which was consistently over 40 mm Hg throughout the entire postoperative period, in association with a narrower pulse pressure compared with the BTS group. This observation is also validated by the similarities in blood pressure data between the BTS group and the previously reported hemodynamic characteristics of a group of neonates who underwent a Norwood procedure with a modified Blalock-Taussig shunt. In this published data the blood pressure measurements in the first 72 hours revealed a diastolic blood pressure <40 mm Hg associated with a wide pulse pressure despite the use of inotropes in all patients.

Furthermore, a significant difference was detected between the 2 surgical groups when comparing the diastolic flow reversal ratio by echocardiographic pulse wave Doppler sampling in the distal aortic arch. This data demonstrated a complete elimination of diastolic flow reversal in the distal aortic arch, in the patients with a RV/PA conduit. Additionally, there was trivial reversal of flow across the RV/PA conduit into the right ventricle. Moreover, the patients in the RV/PA group showed a lower value for the time-velocity integral representing antegrade flow compared with the patients who received a BTS. Although the patients with a RV/PA conduit had the pulmonary and systemic circulations connected in parallel, the elimination of the systemic to pulmonary connection at the arterial level provided the added benefits of avoiding the diastolic runoff away from coronary perfusion, and reduced the amount of volume load on the single ventricle. This preliminary data provides an attractive explanation for the beneficial circulatory effect observed, however, further characterization of the physiology of the coronary circulation will be necessary to make a definitive statement about the influence of the RV to PA conduit on coronary perfusion.

The challenging physiology provided by the presence of a BTS in patients who undergo a Norwood procedure has prompted the use of several strategies, namely eccs, delayed sternal closure, manipulations of Qp/Qs etc, aimed at reducing its negative impact on hospital survival.

In this study, the beneficial effects of the physiology provided by the RV/PA conduit were clinically evident by a significant decrease in the use of some of these strategies, in contradistinction to the patients who received a BTS. These observations represent direct evidence of the beneficial impact provided by the use of a RV/PA conduit. In fact, ventilatory manipulations to balance Qp/Qs were only used at the beginning of our experience in a 2.6-kg neonate born at 35 weeks of gestation who received a 5-mm RV/PA conduit. This resulted in a large Qp/Qs prompting intervention. Since then a 4 mm conduit has been used in patients under 3 kgs, resulting in a well-balanced Qp/Qs without any need for intervention. Additionally, the decrease in the use of eccs in the RV/PA group is a reflection of the lower number of patients who received eccs because of circulatory instability in the postoperative period.

The comparisons for duration of mechanical ventilation and length of stay intensive care unit did not show a statistical significant difference between groups, probably because of the large data dispersion and the sample size. If we only consider the data available for the subgroup of patients form the US, effectively reducing the range of dispersion, the slight trend toward longer mechanical ventilatory support observed, is due to the significantly larger proportion of patients who received eccs in the BTS group.

In addition, evidence of the favorable physiology contributed by an RV/PA conduit is provided by the negative influence of the independent variables: use of eccs, ventilatory manipulations, delayed sternal closure, PaO2>45 mm Hg, diastolic blood pressure <40 mm Hg and use of a BTS as the source of pulmonary blood flow, on patient outcome. All these variables were significantly more prevalent in the presence of
a Blalock-Taussig shunt, and reflect the deleterious impact of the diastolic run off into the pulmonary circulation afforded by these patients. In fact, patients who received a RV/PA conduit, rarely received ventilatory manipulations, minimized the use of ecgs and always had a PaO2 < 45 mm Hg and a diastolic blood pressure > 40 mm Hg in the first 48 hours after Stage I Norwood.

In view of our preliminary observations, it seems reasonable to believe that the potential change in physiology and most importantly coronary perfusion introduced by use of the RV to PA conduit as part of Stage I Norwood reconstruction could improve the underlying physiology and decrease hospital and interim mortality.

The use of a RV to PA conduit has resulted in appropriate protection of the pulmonary vascular bed during early infancy, allowing for pulmonary vascular maturation to occur before the hemifontan procedure.

There are several limitations to this study. Although the cohort of patients expands over two years only, and perioperative management strategy was no different between the two groups, the fact that the groups are not contemporary makes the conclusions susceptible to errors. Also, the lack of randomization and the retrospective nature of the study introduce threats that may affect the validity of the analysis performed.

In conclusion, these data suggest that a RV to PA conduit eliminates the diastolic run off into the pulmonary circulation and results in a higher diastolic blood pressure. This physiology seems to be associated with a more stable postoperative course and improved hospital survival. Furthermore, it is possible this improved physiology may have a beneficial impact on the interim mortality before hemifontan procedure.

Acknowledgments

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References


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