Homograft Valved Right Ventricle to Pulmonary Artery Conduit as a Modification of the Norwood Procedure

Olaf Reinhartz, MD; V. Mohan Reddy, MD; Edwin Petrossian, MD; Malcolm MacDonald, MD; John J. Lamberti, MD; Stephen J. Roth, MD, MPH; Gail E. Wright, MD; Stanton B. Perry, MD; Sam Suleman, BS; Frank L. Hanley, MD

Background—The use of a right ventricle to pulmonary artery (RV-PA) conduit in the Norwood procedure has been proposed to increase postoperative hemodynamic stability. A valve within the conduit should further decrease RV volume load. We report our clinical experience with this modification.

Methods and Results—From February 2002 through August 2005, we performed 88 consecutive Norwood procedures using RV-PA conduits. We used composite valved conduits made from cryopreserved homograft and polytetrafluoroethylene (PTFE) in 66 cases (54 pulmonary, 12 aortic homografts), other valved conduits in 14, and unvalved PTFE in 8 cases. Hospital survival was 88.6% overall and increased to 93.1% after the initial year. Early interventions were required in 18 patients (16 for cyanosis). Prestage II cardiac catheterization was performed at a mean age of 126 days. Mean Qp/Qs was 1, with mean aortic saturation 71%, mean O₂ extraction 24%, and mean right ventricular end-diastolic pressure 9 mm Hg. Patient weight, use of an aortic homograft valve in the conduit, stage I palliation within the first year of our experience, and low O₂ extraction and high transpulmonary gradient prestage II were risk factors for overall death. Early interventions were more frequent in aortic valve conduits compared with all other conduits.

Conclusions—The valved RV-PA conduit was associated with low early mortality after the Norwood procedure. The majority of these patients had normal cardiac output and well-maintained RV function. There may be a higher risk for early conduit interventions and death when aortic valve homografts are used in the RV-PA conduit. (Circulation. 2006; 114[suppl I]:I-594–I-599.)

Key Words: congenital heart defects surgery survival

Over the past few years, the use of a conduit from the right ventricle to the pulmonary artery (RV-PA) as an alternative to the modified Blalock-Taussig (BT) shunt in the stage I Norwood procedure has gained popularity.1 Some groups reported decreased surgical and/or interstage mortality using this modification,2–4 whereas others did not find any difference.5 The RV-PA conduit is thought to favorably change some aspects of the poststage I hemodynamics. It is proposed to lead to more reliable coronary flow by way of increased diastolic aortic pressures, because it limits pulmonary blood flow to systole. It may possibly also result in reduced ventricular volume load, through secondary mechanisms.6–11 Potential concerns are earlier onset of postoperative cyanosis and the possibility of ventricular dysfunction and dysrhythmias over time caused by the RV infundibulotomy.12 Two of the early reports from Japan about the RV-PA conduit modification described integrating a valve into the pathway. Kishimoto made a bicuspid valve from xenopericardium,13 and Murakami used a valved saphenous vein homograft.14 Eliminating diastolic regurgitation into the right ventricle should further reduce volume load and increase hemodynamic efficiency. We have considered these potential advantages and recently pursued a routine policy of using valved composite conduits in all our stage I Norwood palliations.

Methods

Study Design
We provide a retrospective analysis of all patients undergoing stage I Norwood palliation between January 2002 and August 2005 by the 6-surgeon Stanford pediatric cardiac surgery group. Procedures were performed at Lucille Packard Children’s Hospital (Stanford, Calif), Children’s Hospital of Central California (Madera, Calif), and Children’s Hospital and Research Center Oakland (Oakland, Calif). All data were collected from existing sources (patient files and clinical databases). The study was approved by the Stanford Administrative Panel on Human Subjects. The authors had full access to the data and take responsibility for their integrity. All authors have read and agree to the manuscript as written.

Operative Technique
Details of the operative management were consistent across the time period and between surgeons. For stage I surgery, cardiopulmonary

From the Divisions of Pediatric Cardiothoracic Surgery and Pediatric Cardiology, Stanford University School of Medicine, Stanford, Calif. Presented at the American Heart Association Scientific Sessions, Dallas, Tex, November 13–16, 2005. Correspondence to Olaf Reinhartz, Cardiothoracic Surgery, Stanford University, 300 Pasteur Drive, Stanford, CA 94305. E-mail orx@stanford.edu © 2006 American Heart Association, Inc. Circulation is available at http://www.circulationaha.org DOI: 10.1161/CIRCULATIONAHA.105.001438
bypass was established by cannulation of the innominate artery and right atrial appendage. Patients were cooled to 18°C and perfusion was maintained at a minimum of 30 mL/kg per minute. A brief period of sucker bypass was used during the atrial septectomy. No deep hypothermic circulatory arrest was employed.

Arch reconstruction was performed using a pulmonary artery homograft patch. In the majority of patients, a composite conduit was fashioned from polytetrafluoroethylene (PTFE) tubing and an aortic or pulmonary homograft valve (if available) before sternotomy and inserted between a right ventricular infundibulotomy and the pulmonary artery bifurcation on the left side of the neo-aorta (Figure 1). Patient weight generally determined the choice of PTFE diameter: <2 kg, 4 mm; 2 to 3.5 kg, 5 mm; >3.5 kg, 6 mm. The sternum was routinely closed in a delayed fashion. For stage II palliation, patients underwent a bidirectional Glenn procedure, which was performed without cardiopulmonary bypass utilizing a passive superior-vena-cava to right-atrium shunt whenever feasible.

Definitions
Surgical or early mortality was defined as death after stage I Norwood palliation within 30 days or before hospital discharge. If patients were transferred back to referring centers, the date of transfer was considered to be the time of discharge. Interstage mortality was defined as death between discharge after stage I and time of stage II palliation. Early intervention for cyanosis was defined as any surgical or transcatheter intervention required urgently for cyanosis before planned evaluation for stage II.

Statistical Analysis
Descriptive data are presented as means±standard deviations of the mean. For Kaplan-Meier survival analysis, a composite endpoint of any failure of the procedure resulting in either death or transplant was used. Univariate risk analysis for categorical variables was performed producing odds ratios with 95% confidence intervals. Student t test was used for univariate analysis of continuous variables. P≤0.05 was considered significant. Multivariate analysis of risk factors was performed using logistic regression. Statistical analyses were conducted with Stata 8.0 (StataCorp LP, College Station, Tex).

Results
Patient Population
Eighty-eight consecutive patients (56 male, 32 female) with hypoplastic left heart syndrome or variants of single ventricle with aortic arch obstruction underwent stage I palliation within the time period. Mean age was 6.0±4.3 days and mean weight was 3.1±0.5 kg. Table 1 provides a list of the morphological cardiac diagnoses as well as concomitant noncardiac diagnoses. Preoperative echocardiographic RV function was qualitatively assessed as normal in 80 patients, mildly decreased in 4, and moderately decreased in 4. Three patients had more than mild tricuspid regurgitation. Seven patients with severely restrictive atrial septal defects underwent emergent preoperative balloon septostomy or stent placement.

RV-PA Conduits
When small aortic or pulmonary homografts were not available, other valved or occasionally nonvalved conduits were used between the RV and the PA. A list of all conduits used is provided in Table 2.
Survival and Follow-Up
Complete follow-up information was available for all patients. Survival in the first 30 days was 94.3%. It was increased to 98.6% after 2002. Survival to discharge was 88.6% overall and increased to 93.1% after 2002. Of the patients discharged, 5 died before stage II palliation, for an interstage mortality of 7%.

A bidirectional Glenn procedure was performed in 64 patients at a mean age of 151 days; 64% of Glenn procedures could be performed without cardiopulmonary bypass. In those who underwent bypass, 10 tricuspid valve repairs and 11 pulmonary artery augmentations were performed concomitantly. Hospital survival after stage II was 97%. Two patients died late after stage II, 1 suddenly at home and 1 from fungal sepsis after readmission for pneumonia. Two others required cardiac transplantation late after Glenn surgery at ages 9 and 21 months for severe right ventricular dysfunction. One patient had a biventricular repair instead of a Glenn procedure (aortic atresia with multiple ventricular septal defects). Another patient was considered not to be a candidate for stage II palliation because of severe neurologic dysfunction related to cri-du-chat syndrome; this patient died from progressive cyanosis.

The incidence of recurrent aortic coarctation was 14%. Seven patients required balloon dilatations of the aortic arch and 2 others surgical patch augmentation.

Figure 2 shows Kaplan-Meier estimated survival for the entire patient cohort. Mean follow-up was 15 months (2.5 to 40 months). Estimated 1-year survival was 73.4% and estimated 2-year survival 70.8%.

Conduit Interventions Before Stage II Palliation
Eighteen patients (20%) required early unplanned interventions to the RV-PA conduit before the bidirectional Glenn procedure. Sixteen of these interventions were performed for early cyanosis and included 11 stent placements, 3 balloon dilations, 1 RV myectomy, and 1 PTFE graft exchange (from 4 mm to 5 mm). Two interventions were indicated for pulmonary overcirculation and included 1 placement of a covered stent in the conduit and 1 surgical conduit banding.

Evaluation Before Stage II
Cardiac catheterization was performed in all stage II candidates. The hemodynamic data are provided in Table 3. On echocardiography at the time of prestage II evaluation, RV function was moderately decreased in 8% of patients and severely decreased in none. At this time, moderate tricuspid regurgitation was present in 16% of patients and severe cyanosis.

### Table 3. Hemodynamics Before Bidirectional Glenn

<table>
<thead>
<tr>
<th>Catheterization data</th>
<th>Mean ± SD</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (days)</td>
<td>126 ± 46</td>
</tr>
<tr>
<td>Qp/Qs</td>
<td>1.0 ± 0.5</td>
</tr>
<tr>
<td>Aortic saturation (%)</td>
<td>71 ± 7</td>
</tr>
<tr>
<td>SVC saturation (%)</td>
<td>47 ± 7</td>
</tr>
<tr>
<td>O₂ extraction (%)</td>
<td>24 ± 5</td>
</tr>
<tr>
<td>PAp (mm Hg)</td>
<td>13.8 ± 3.7</td>
</tr>
<tr>
<td>RVEDP (mm Hg)</td>
<td>9 ± 2.6</td>
</tr>
</tbody>
</table>

Qp indicates pulmonary blood flow; Qs, systemic blood flow; SVC, superior vena cava; PAp, mean pulmonary artery pressure; RVEDP, right ventricular end-diastolic pressure.

### Table 4. Analysis of Risk Factors for Death

<table>
<thead>
<tr>
<th>Preoperative Risk Factors</th>
<th>OR, Early Death</th>
<th>95% CI</th>
<th>OR, Overall Death</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Weight &lt;2.5 kg</td>
<td>7.93</td>
<td>0.93–56.13</td>
<td>7.63*</td>
<td>1.11–83.56</td>
</tr>
<tr>
<td>Age &gt;14 days</td>
<td>0</td>
<td>0–4.24</td>
<td>1.01</td>
<td>0.09–6.72</td>
</tr>
<tr>
<td>Ascending aorta &lt;2 mm</td>
<td>0.32</td>
<td>0.01–2.68</td>
<td>0.77</td>
<td>0.19–2.69</td>
</tr>
<tr>
<td>Restrictive ASD</td>
<td>2.57</td>
<td>0.37–13.43</td>
<td>1.58</td>
<td>0.37–6.04</td>
</tr>
<tr>
<td>Pulmonary venous anomaly</td>
<td>1.62</td>
<td>0.03–17.04</td>
<td>5.81</td>
<td>0.75–66.96</td>
</tr>
<tr>
<td>Noncardiac risk factor</td>
<td>1.62</td>
<td>0.03–17.04</td>
<td>5.81</td>
<td>0.75–66.96</td>
</tr>
<tr>
<td>Operative Risk Factors</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Stage I in 2002</td>
<td>6.09*</td>
<td>1.16–30.64</td>
<td>6.33*</td>
<td>1.72–83.56</td>
</tr>
<tr>
<td>Homograft valve: aortic vs pulmonary</td>
<td>1.34</td>
<td>0.12–8.61</td>
<td>6.71*</td>
<td>1.76–25.65</td>
</tr>
<tr>
<td>Postoperative Risk Factors</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mechanical support (n=6)</td>
<td>10.71*</td>
<td>1.14–91.62</td>
<td>5.81</td>
<td>0.75–66.96</td>
</tr>
<tr>
<td>Early intervention for cyanosis</td>
<td>n/a</td>
<td>1.49</td>
<td>0.39–5.15</td>
<td></td>
</tr>
</tbody>
</table>

ASD indicates atrial septal defect; OR, odds ratio.
*Statistically significant.
tricuspid regurgitation in 2% (all patients with valved conduits). All others had mild tricuspid regurgitation or none.

**Risk Analysis for Death**

Several preoperative, operative, and postoperative variables were analyzed for their predictive value for both early and overall death (Table 4). Of the preoperative factors, only patient weight <2.5 kg was a significant predictor for late death. Of the operative factors, stage I procedure during the first year was a significant predictor for both early and overall death. Homograft size was not a significant risk factor. However, the use of an aortic valve was a significant predictor for overall death, but not for early death. Neither the operating surgeon nor the hospital site (not in table) was a predictor for death. Of the postoperative risk factors, mechanical support was a significant predictor for early death.

**Prestage II Predictors for Death**

We analyzed hemodynamic variables obtained at the pre-Glenn catheterization for their predictive value for death at any time after stage II palliation. Variables that were significant or approached significance are listed in Table 5.

**Risk Analysis for Types of Conduits Used**

Because the use of an aortic valve in the RV-PA conduit was determined to be a predictor for overall death in the univariate analysis, we performed logistic regression to rule out confounding risk factors. Even after adjusting for other variables that had been significant in the univariate analysis, aortic valve was still a significant predictor for overall death when compared with pulmonary valve or all other groups combined (Table 6).

**Discussion**

We also compared the 4 main groups of conduits used with regard to different complications (Table 7). There was a substantially higher rate of early interventions for cyanosis in the aortic valve group than in all others, but it was not statistically significant. There were no differences between conduits for low aortic saturations at the pre-Glenn evaluation or for the need for pulmonary artery augmentations. All conduits without a valve (PTFE only) were moderately or severely insufficient by echocardiogram, compared with one-quarter of the pulmonary valves and cryoveins. All aortic valves remained competent until stage II.

**Early Mortality**

Early surgical mortality during the hospitalization after stage I surgery can often be attributed to one of the following

**TABLE 5. Pre-Glenn Catheterization Predictors for Death**

<table>
<thead>
<tr>
<th></th>
<th>Survivors</th>
<th>Nonsurvivors</th>
<th>P*</th>
</tr>
</thead>
<tbody>
<tr>
<td>n</td>
<td>Mean (SD)</td>
<td>n</td>
<td>Mean (SD)</td>
</tr>
<tr>
<td>O₂ extraction (%)</td>
<td>46</td>
<td>24.1 (5.5)</td>
<td>10</td>
</tr>
<tr>
<td>PAP (mm Hg)</td>
<td>47</td>
<td>13.3 (3.8)</td>
<td>10</td>
</tr>
<tr>
<td>TPG (mm Hg)</td>
<td>42</td>
<td>4.6 (2.9)</td>
<td>10</td>
</tr>
</tbody>
</table>

PAP indicates mean pulmonary artery pressure; SD, standard deviation; TPG, transpulmonary gradient.

*P as determined by Student t test.

**TABLE 6. Multivariate Risk Analysis (Logistic Regression) of Valves Used in the RV-PA Conduit**

<table>
<thead>
<tr>
<th></th>
<th>OR (CI) Unadjusted</th>
<th>OR (CI) Adjusted for Weight &lt;2.5 kg and Year of Stage I</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>A0 vs PV</td>
<td>6.71* (1.76–25.65)</td>
<td>6.25* (1.25–31.32)</td>
</tr>
<tr>
<td>A0 vs cryovein</td>
<td>6.0* (1.02–35.37)</td>
<td>4.8 (0.63–6.82)</td>
</tr>
<tr>
<td>A0 vs all other groups</td>
<td>6.6* (1.8–24.6)</td>
<td>6.3* (1.4–27.3)</td>
</tr>
</tbody>
</table>

A0 indicates aortic valve homograft; PV, pulmonary valve homograft.

*Statistically significant.

**TABLE 7. Comparison of Types of Conduits Used**

<table>
<thead>
<tr>
<th></th>
<th>PTFE Only</th>
<th>Aortic Valve + PTFE</th>
<th>Pulmonary Valve + PTFE</th>
<th>Cryovein</th>
</tr>
</thead>
<tbody>
<tr>
<td>Early intervention for cyanosis</td>
<td>1/6</td>
<td>5/9</td>
<td>9/42</td>
<td>1/10</td>
</tr>
<tr>
<td></td>
<td>16.7%</td>
<td>55.6%</td>
<td>21.4%</td>
<td>10%</td>
</tr>
<tr>
<td>Aortic saturation &lt;70% before Glenn</td>
<td>3/6</td>
<td>4/9</td>
<td>15/42</td>
<td>6/10</td>
</tr>
<tr>
<td></td>
<td>50%</td>
<td>44.4%</td>
<td>19%</td>
<td>60%</td>
</tr>
<tr>
<td>Pulmonary artery augmentation at Glenn</td>
<td>1/6</td>
<td>1/9</td>
<td>8/42</td>
<td>1/10</td>
</tr>
<tr>
<td></td>
<td>16.7%</td>
<td>11.1%</td>
<td>19%</td>
<td>10%</td>
</tr>
<tr>
<td>Conduit insufficiency moderate or severe before Glenn</td>
<td>6/6</td>
<td>0/6</td>
<td>7/31</td>
<td>2/8</td>
</tr>
<tr>
<td></td>
<td>100%</td>
<td>0%</td>
<td>22.6%</td>
<td>25%</td>
</tr>
</tbody>
</table>
problems: (1) technical shortcomings leading to hemodynamic instability and low cardiac output, which typically occurs intraoperatively and/or within the first few postoperative days; (2) complications in the intensive care unit such as infection or iatrogenic adverse events; and (3) organ failure caused by severe pre-existing noncardiac conditions. In many instances, death is related to a combination of these factors. A reduction in this early mortality can therefore be achieved either through: (1) improvements in surgical technique that increase early hemodynamic stability; (2) improvements in ICU management; and (3) exclusion of certain high-risk patients. The RV-PA conduit is believed by some to be such a technical improvement. Therefore, it has been proposed to lead to reduced early mortality in some studies when compared with BT shunt cohorts. However, because these studies use historical cohorts as controls, other factors may also contribute to improved outcomes.

The only published report comparing contemporaneous groups of BT shunt and RV-PA conduit patients did not find differences in outcomes between the 2 techniques. However, that study also has some limitations, in that it is retrospective, and bias between individual surgeons and a difference in risk profile between the groups cannot be excluded. Only a large, prospective, randomized trial might be able to answer this question. A prospective, randomized trial sponsored by the National Institute of Health to compare these 2 techniques has, in fact, been initiated.

In our risk analysis, patient weight was the only significant preoperative predictor of early mortality. The fact that other variables such as restrictive atrial septal defects, small ascending aorta, or severe comorbidities did not predict death as they have in other studies could suggest that some high-risk patients survive with an RV-PA conduit who would otherwise die early because of additive risk factors. At some institutions, this modification is being performed primarily on high-risk patients. The RV-PA conduit is believed by some to be such a technical improvement. Therefore, it has been proposed to lead to reduced early mortality in some studies when compared with BT shunt cohorts. However, because these studies use historical cohorts as controls, other factors may also contribute to improved outcomes.

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**Interstage Mortality**

The second distinct time period is referred to as the “interstage” period. Stage I palliated patients appear to have a uniquely high risk for death during this time period, and the cause of death remains largely unknown. It has been proposed to be preventable by a home surveillance program. There has been some evidence that the RV-PA conduit might decrease interstage death, both in individual studies and in a recent metaanalysis. Again, a prospective trial should help to determine if the risk of death is reduced.

In our series, we were not able to identify risk factors for interstage death because of the small number of events.

**Late Mortality**

During the third time period, the “late death” period beginning after stage II palliation, chronic right ventricular failure is the predominant cause of death or transplantation. Because of the requirement for long term follow-up, this time period is obviously the most difficult one to analyze and will take additional time. There is theoretical concern that the valved homograft valve in the conduit versus a pulmonary valve or all other conduit materials to be significantly associated with late death. In conjunction with the finding of an increased rate of early interventions in the aortic valve group, one could conclude that aortic valves lead to earlier conduit narrowing. A possible mechanism for this could be early calcification as has been noted when valved aortic homograft is used for other indications, such as repair of pulmonary atresia. Therefore, it would be an inferior conduit material and not recommended. However, the results in this analysis are not conclusive. We used far fewer aortic than pulmonary homografts, limiting the statistical power of the analysis. If aortic valve is a risk factor for death, and this risk is largely caused by early interventions, then one would expect that early intervention would be a risk factor for death. However, our analysis did not lead to this result. Finally, not all deaths in the aortic valve group were clearly attributable to early cyanosis or were sudden in nature. Still, some suspicion remains, and we will...
have to follow our patients carefully, particularly when aortic homografts are used.

Valved Versus Nonvalved Conduits

Because of small patient numbers, our study cannot determine survival differences between patients with conduits containing valves and those with nonvalved grafts. However, not surprisingly, we could show that nonvalved conduits lead to a higher rate of “pulmonary” insufficiency by color Doppler echocardiography. In this retrospective study, we did not quantify regurgitant fractions. Echocardiography is limited in its ability to measure regurgitation quantitatively. To evaluate the differences between valved and nonvalved conduits, one would have to design a prospective study comparing both groups, preferably using magnetic resonance imaging, at different time intervals and assess RV function, ventricular volumes, and regurgitant fraction from the conduit. We are currently debating the feasibility of such a study.

Conclusions

Our preliminary experience with valved RV-PA conduits in the stage I Norwood procedure shows low early mortality, with well-maintained RV function in most patients. This encourages us to continue to use this modification. There is a potential concern with using aortic valve conduits because of an observed higher risk for early conduit interventions and death. More data and longer follow-up are needed to address this issue.

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Disclosures

None.

References

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