Hypoplastic Left Heart Syndrome: Hemodynamic and Angiographic Assessment After Initial Reconstructive Surgery and Relevance to Modified Fontan Procedure

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After undergoing initial reconstructive surgery for hypoplastic left heart syndrome performed between August 1985 and March 1989, 59 patients (age range 3 to 27 months, mean 13.8 ± 4.5) underwent elective cardiac catheterization in anticipation of a modified Fontan procedure. Five important hemodynamic and anatomic features considered to be components of successful reconstructive surgery were specifically addressed. 1) Interatrial communication: Only two patients had a measured pressure difference of >4 mm Hg across the atrial septum. 2) Tricuspid valve function: Angiography demonstrated significant tricuspid valve regurgitation in only five patients (moderate in two and severe in three). 3) Aortic arch: Pressure tracings from the right ventricle to the descending aorta revealed a gradient >25 mm Hg in only two patients. 4) Pulmonary vasculature: Ten patients had a calculated pulmonary vascular resistance >4 U·m²; 51 (86%) of the 59 patients had no evidence of distortion (stenosis or hypoplasia) of either the left or the right pulmonary artery. 5) Right ventricular function: Five patients had an end-diastolic pressure in the right ventricle >12 mm Hg and two patients had qualitative assessment of decreased ventricular function.

Comparison of catheterization data between survivors and nonsurvivors of the subsequent modified Fontan procedure showed that only significant tricuspid regurgitation is a possible predictor of poor outcome. After first stage reconstructive surgery for hypoplastic left heart syndrome, most survivors have favorable anatomy and hemodynamics at follow-up cardiac catheterization for a subsequent Fontan procedure.

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any possible differences in anatomic or physiologic variables.

Methods

Study patients. Between August 1985 and March 1989, 200 patients with hypoplastic left heart syndrome underwent stage I reconstructive surgery (Norwood operation). The procedures consisted of 1) atrial septectomy, 2) pulmonary homograft augmentation of the ascending aorta and the aortic arch with anastomosis of the transected proximal pulmonary artery to the augmented aorta, 3) ligation of the ductus arteriosus, and 4) placement of a 4 mm polytetrafluoroethylene modified Blalock-Taussig (28 patients) or central (172 patients) shunt. Postoperative survival (>30 days) was 66% (135 patients).

Of the survivors of the initial reconstructive surgery, 59 had elective cardiac catheterization in preparation for a modified Fontan procedure. We reviewed the hemodynamic and angiographic data for all of these patients. In addition, the following information was collected: primary anatomy; gender; age at the time of the initial reconstructive surgery, cardiac catheterization and subsequent Fontan procedure and any additional surgery during the interval between reconstructive surgery and Fontan procedure.

Fifty of these 59 study patients have subsequently undergone a modified Fontan procedure consisting of: 1) an intraatrial baffle of inferior vena cava return to an augmented anastomosis between the right atrium, superior vena cava and right pulmonary artery; and 2) central pulmonary artery augmentation. Since May 1989, our strategy for patients with hypoplastic left heart syndrome has included a superior cavopulmonary anastomosis (with pulmonary artery augmentation) before the Fontan procedure. The remaining 9 of 59 patients have all undergone this intermediate procedure.

Cardiac catheterization. Patients were sedated with either 0.1 mg/kg body weight of morphine sulfate and 2 mg/kg of pentobarbital intramuscularly or 3 mg/kg of pentobarbital and 2 mg/kg of meperidine orally for the procedure.

Pressure and oxygen saturation measurements were obtained in the right and left atria, right ventricle and proximal and distal reconstructed aortic arch. Direct measurements of pulmonary artery pressure were obtained in 38 of the 59 patients (right pulmonary artery, n = 17; left pulmonary artery, n = 26; both pulmonary arteries, n = 5) by advancing a catheter (3F or 4F thin-walled catheter guided over a tip deflecting wire) into the branch pulmonary arteries through either the modified Blalock-Taussig or the central shunt. Pulmonary artery oxygen saturation was assumed to be equivalent to the measured aortic oxygen saturation in the hemodynamic calculations because the aorta was the only source of pulmonary blood flow. Pulmonary venous wedge pressures were obtained in 47 of the 59 patients and were utilized in the calculation of pulmonary vascular resistance when a direct pulmonary artery pressure measurement was not available (21 patients). Utilization of pulmonary venous wedge pressure in the calculation of pulmonary vascular resistance was considered valid in these patients given the range of measurements obtained. Oxygen consumption was measured by using a Waters oximeter.

Angiography was performed in the right ventricle (in the anteroposterior and lateral projections) using a pigtail catheter passed retrogradely through the reconstructed aortic arch for the assessment of ventricular function and tricuspid valve competence. In addition, angiography was also performed (in the anteroposterior and lateral projections) with use of a pigtail catheter in the midportion of the reconstructed arch in proximity to the shunt orifice to assess the patency of the shunt, the anatomy of the branch pulmonary arteries and the anatomy of the reconstructed arch; 1 to 2 ml/kg of contrast agent (diatrizoate [Hypaque-76]) was injected in <1 s.

Tricuspid valve regurgitation was assessed according to the method of Nagel et al. (5) (for mitral regurgitation). In
Table 1. Cardiac Catheterization Data for 59 Patients Before the Fontan Procedure

<table>
<thead>
<tr>
<th>Measured hemodynamic variable (mm Hg)</th>
<th>Range (mean ± SD)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Right atrium</td>
<td>0-13 (6.2 ± 2.9)</td>
</tr>
<tr>
<td>Left atrium</td>
<td>2-16 (7.2 ± 3.2)</td>
</tr>
<tr>
<td>RV end-diastolic pressure</td>
<td>3-19 (8.9 ± 3.3)</td>
</tr>
<tr>
<td>Right pulmonary artery pressure</td>
<td>8-35 (16.2 ± 8.2)</td>
</tr>
<tr>
<td>Left pulmonary artery pressure</td>
<td>3-31 (16.1 ± 6.3)</td>
</tr>
<tr>
<td>Right pulmonary venous wedge pressure</td>
<td>6-20 (13.2 ± 4.0)</td>
</tr>
<tr>
<td>Left pulmonary venous wedge pressure</td>
<td>7-27 (13.5 ± 4.2)</td>
</tr>
<tr>
<td>RV systolic pressure</td>
<td>75-189 (113.8 ± 19.1)</td>
</tr>
<tr>
<td>Ascending aorta</td>
<td></td>
</tr>
<tr>
<td>Systolic pressure</td>
<td>75-180 (113.4 ± 19.5)</td>
</tr>
<tr>
<td>Diastolic pressure</td>
<td>32-70 (49.1 ± 8.9)</td>
</tr>
<tr>
<td>Mean pressure</td>
<td>54-100 (73.8 ± 11.6)</td>
</tr>
<tr>
<td>Descending aorta</td>
<td></td>
</tr>
<tr>
<td>Systolic pressure</td>
<td>75-144 (110.2 ± 16.3)</td>
</tr>
<tr>
<td>Diastolic pressure</td>
<td>32-70 (48.5 ± 8.4)</td>
</tr>
<tr>
<td>Mean pressure</td>
<td>54-96 (72.4 ± 10.3)</td>
</tr>
<tr>
<td>Calculated hemodynamic variable</td>
<td></td>
</tr>
<tr>
<td>Systemic vascular resistance (U·m²)</td>
<td>7.9-33.2 (20.5 ± 6.8)</td>
</tr>
<tr>
<td>Pulmonary vascular resistance (U·m²)</td>
<td>0.4-7.4 (2.6 ± 1.8)</td>
</tr>
<tr>
<td>Systemic blood flow (Qs) (liters/min per m²)</td>
<td>1.7-7.0 (3.5 ± 1.2)</td>
</tr>
<tr>
<td>Pulmonary blood flow (Qp) (liters/min per m²)</td>
<td>1.5-6.9 (3.6 ± 1.1)</td>
</tr>
<tr>
<td>Qp/Qs</td>
<td>0.5-3.3 (1.1 ± 0.5)</td>
</tr>
</tbody>
</table>

RV = right ventricular.

Results

Patient characteristics. There were 36 male and 23 female patients whose age at catheterization ranged from 3 to 27 months (mean 13.8 ± 4.5, median 12.5). Their weight ranged from 3.4 to 11.4 kg (mean 7.8 ± 1.4).

The preoperative anatomic subtypes for the 59 patients were aortic and mitral atresia in 25, aortic atresia and mitral stenosis in 13, aortic stenosis and mitral stenosis in 10, malaligned atrioventricular (AV) canal in 6, double outlet right ventricle with aortic atresia in 3 and other complex lesions with hypoplastic left ventricle in 2.

mild regurgitation, there is minimal dye refluxing into the atrium. In moderate regurgitation, dye fills the atrium but to a density less than that of the ventricle. In severe regurgitation, dye fills an enlarged atrium or a smaller atrium to a density equal to that of the ventricle.

Statistical analysis. The mean value, SD and SE for all hemodynamic variables were calculated. All hemodynamic variables for the survivors and nonsurvivors of the Fontan procedure were compared by two-tailed, nonpaired Student's t test. To assess possible effect of risk factors on survival, Fisher's exact test was used between the Fontan survivor and non survivor subgroups to examine the following: 1) mean pulmonary artery pressure > 15 mm Hg; 2) pulmonary vascular resistance >4 U·m²; 3) right ventricular end-diastolic pressure >12 mm Hg; 4) presence of pulmonary artery distortion from a previous shunt; and 5) presence of significant tricuspid valve regurgitation.

All 59 patients had reconstructive surgery that included either a modified Blalock-Taussig (n = 12) or central (n = 47) shunt. Of these 59 patients, 18 (31%) had 19 additional procedures after initial reconstructive surgery and before their cardiac catheterization (median interval from initial reconstructive surgery to additional procedure 4.4 months, range 0.5 to 14.7). These additional procedures included shunt revision in 11, arch reconstruction for proximal arch stenosis in 3, balloon angioplasty of distal arch obstruction in 4 and atrial septectomy in 1.

All patients had normal sinus rhythm at the time of the cardiac catheterization, with a heart rate ranging from 80 to 142 beats/min (mean 111 ± 17). The hemoglobin ranged from 13.7 to 20.4 g/dl (mean 17.4 ± 1.6) and aortic oxygen saturation ranged from 68% to 90% (mean 78 ± 4%).

Hemodynamic Data and Angiographic Findings Before the Fontan Procedure (Table 1)

Interatrial communication. Of the 59 patients who underwent cardiac catheterization, 51 (86%) had no gradient...
between the right and left atria. In the remaining eight patients, the measured pressure differences (mm Hg) by pullback from the left to the right atrium were: 3 (n = 3), 4 (n = 3), 6 (n = 1) and 10 (n = 1).

Of the two patients with a pressure gradient >4 mm Hg, both had a pulmonary vascular resistance of <2 U·m². Both patients had an atrial septectomy as part of their subsequent surgery. Although the patient with the 6 mm Hg gradient is doing well after a cavopulmonary anastomosis, the patient with the 10 mm Hg gradient (Fig. 2) died of respiratory insufficiency 24 days after the Fontan procedure, but without any evidence of pulmonary venous obstruction.

Tricuspid valve function. On angiography, 10 patients had mild tricuspid valve regurgitation and 5 had significant tricuspid valve regurgitation (2 with moderate and 3 with severe regurgitation). Although one of the two patients with moderate tricuspid regurgitation survived the subsequent Fontan procedure, all three patients with severe regurgitation died after the Fontan operation. Two of these three patients died in the 1st postoperative week despite tricuspid valvoplasty. The third patient, who had a 29 mm St. Jude valve replacement at the time of the Fontan procedure, died of sepsis 8 months later while awaiting cardiac transplantation (Fig. 3).

Aortic arch. None of the 59 patients had a systolic pressure gradient between the right ventricle and the ascending portion of the reconstructed aorta. Of the 59 patients, 53 (88%) had a normal appearance of the reconstructed aortic arch; the remaining 6 patients had angiographic evidence of distal arch narrowing (all had a measured gradient ≥25 mm Hg [25 mm Hg in 4, 30 mm Hg in 1 and 40 mm Hg in 1]) (Fig. 4). The two patients with a gradient of 30 and 40 mm Hg, respectively, underwent balloon angioplasty before the Fontan procedure, with obliteration of the gradient.

Pulmonary vasculature. Although the ratio of pulmonary to systemic blood flow (Qp/Qs) ranged from 0.5 to 3.5, 46 (78%) of the 59 patients had a Qp/Qs ratio between 0.8 and 1.5. Pulmonary vascular resistance in the entire study group ranged from 0.4 to 7.4 U·m² (mean 2.6 ± 1.8); 10 patients (17%) had a calculated pulmonary vascular resistance >4 U·m².

Angiographically, 51 (86%) of the 59 patients had normal pulmonary artery anatomy without any evidence of stenosis or hypoplasia of either pulmonary artery branch (Fig. 5). Seven patients were found to have a discrete stenosis of either pulmonary artery branch. In addition, two patients had angiographic evidence of hypoplasia of the left pulmonary artery.

Right ventricular function. Right ventricular end-diastolic pressure in these patients ranged from 3 to 19 mm Hg (mean 8.9 ± 3.3); in five patients, it was >12 mm Hg (two of these five patients survived the subsequent Fontan procedure).

On angiography, two patients had qualitative evidence of poor systolic ventricular function. One patient (previously mentioned) with a right ventricular end-diastolic pressure of 16 mm Hg and severe tricuspid valve regurgitation died of sepsis 8 months after the Fontan procedure while awaiting cardiac transplantation. The other patient (also with a right ventricular end-diastolic pressure of 16 mm Hg) underwent cardiac transplantation and is alive and well.

Comparison of Survivors and Nonsurvivors of the Fontan Procedure

There were nine patients in the study group who underwent superior cavopulmonary anastomosis (at a mean age of 17.7 months) and all are alive and doing well. Six of these nine patients have subsequently had a Fontan procedure (at
a mean interval of 8 months after superior cavopulmonary anastomosis; all six patients survived.

Among the 50 patients who underwent a Fontan procedure (at a mean age of 17.1 ± 5.1 months) without intermediate superior cavopulmonary anastomosis, there were eight early deaths (<30 days) for an early survival rate of 84% and an additional 13 late deaths for an overall survival rate of 58% after the modified Fontan procedure. The interval from the Fontan procedure to death ranged from 1 day to 10 months (median interval 36 days). We separated this group of 50 patients into survivor (n = 29) and nonsurvivor (n = 21) groups.

**Non-age-related risk factors.** Several traditional non-age-related risk factors for the Fontan procedure, including 1) mean pulmonary artery pressure >15 mm Hg; 2) pulmonary vascular resistance >4 U·m⁻²; 3) right ventricular end-
diastolic pressure >12 mm Hg; 4) presence of pulmonary artery distortion from a previous shunt; and 5) presence of significant tricuspid valve regurgitation, were examined. The results show that there is no statistically significant difference in percent mortality for any of these risk factors. There is, however, a statistical trend for poor outcome in the presence of significant tricuspid valve regurgitation (Table 2).

Clinical and hemodynamic risk factors. There was no statistically significant difference between survivors and nonsurvivors of the Fontan operation when compared by 1) age, 2) body surface area, 3) hemoglobin, 4) aortic saturation, or 5) any of the measured or calculated hemodynamic variables (including atrial pressures, left atrium-right atrium pressure gradient, right ventricular and aortic systolic, diastolic and mean pressures and pressure gradients and systemic and pulmonary blood flow and vascular resistance).

Discussion

Initial reconstructive surgery. In an analysis of potential anatomic and physiologic determinants of the outcome of stage I reconstructive surgery for hypoplastic left heart syndrome, Helton et al. (6) demonstrated that preoperative atrial septal anatomy, right ventricular wall thickness, right ventricular systolic performance, ascending aorta size and presence or absence of coarctation were not predictive of survival. Barber et al. (7), however, subsequently demonstrated that a large proportion of patients with hypoplastic left heart syndrome had evidence of tricuspid regurgitation preoperatively (mild, 37%; moderate, 13%; severe, 3%) and that the degree of tricuspid regurgitation remained relatively constant from the preoperative period to the late postoperative period. In their study (7), significant (moderate or severe) AV valve regurgitation was a factor in long-term survival after initial reconstructive surgery.

For a patient to be an optimal candidate for a subsequent Fontan procedure, several components of initial reconstructive surgery for hypoplastic left heart syndrome must be present. 1) The interatrial communication should be unrestrictive for unimpeded pulmonary venous return to the right ventricle. A restrictive interatrial communication can eventually lead to pulmonary venous hypertension and possibly adversely affect survival after Fontan repair. In addition, prompt recognition of the anatomic diagnosis of anomalous attachment of the septum primum in some of these patients has led to a decreased incidence of incomplete resection and restrictive interatrial communication (8). 2) Tricuspid valve competence is crucial because tricuspid regurgitation adds an additional volume load to the right ventricle. We attempted to reduce significant regurgitation of the tricuspid valve either by valvoplasty or by valve replacement; however, long-term survival in patients with moderate or significant tricuspid regurgitation remains poor. 3) An unobstructed aortic arch is necessary to avoid an additional pressure load on the right ventricle. We consider any gradient >25 mm Hg at either the proximal or distal anastomosis to be significant and thus warranting surgical reconstruction or balloon dilation. Modifications in the surgical reconstruction of the aortic arch, such as extending the arch reconstruction to the area beyond where the ductus arteriosus inserts, have decreased the incidence of distal arch obstruction (unpublished observations).

4) It is essential to establish pulmonary blood flow to maintain oxygenation while protecting the pulmonary vascular bed for a subsequent Fontan procedure. Pulmonary blood flow, provided by an aortopulmonary shunt during initial reconstructive surgery, resulted in a pulmonary/systemic blood flow (Qp/Qs) ratio ranging from 0.5 to 3.5 (and aortic oxygen saturation ranging from 68% to 90%); however, the majority of the patients had a Qp/Qs ratio between 0.8 to 1.5 and thus maintained adequate oxygenation while being protected from pulmonary overcirculation. There was a very low incidence of pulmonary artery distortion in our patients. 5) Lastly, preservation of right ventricular function is obviously necessary for long-term survival. In the small subset of patients with right ventricular dysfunction in our study group, elevated right ventricular end-diastolic pressure failed to predict which patients would do poorly after a Fontan procedure. One of our patients with qualitative assessment of right ventricular systolic dysfunction by angiography was considered to be a poor candidate for a Fontan procedure and was referred for cardiac transplantation.

With this strategy of initial reconstructive surgery, patient survival continues to improve (9). Failure to accomplish these hemodynamic and anatomic conditions can result in increased morbidity and mortality (10).

The Fontan procedure. After successful reconstructive surgery for hypoplastic left heart syndrome, subsequent management involves the application of Fontan’s principle as in any other single ventricle complex. Traditional “risk factors” for the Fontan operation candidate included: young age, abnormal rhythm, anomalous venous drainage, mean pulmonary artery pressure >15 mm Hg, pulmonary vascular resistance >4 U·m⁻², right ventricular end-diastolic pressure >12 mm Hg, presence of pulmonary artery distortion as a sequela of shunt insertion and presence of significant AV
valve regurgitation (11). A Fontan procedure performed on patients without these risk factors has been shown to have good late results (12).

Several of these risk factors affected our patients uniformly. Because all of our patients underwent a Fontan procedure at <4 years of age, they shared the same risk factor of young age. Conversely, because none of our patients had anomalous venous drainage or abnormal rhythm, they all lacked these risk factors. Although there was no statistical difference between the Fontan survivor and nonsurvivor subgroups when the other risk factors were separately examined, the small number of patients in both groups used in the comparative analysis may mask potential differences in survival.

Although elevated pulmonary artery pressure and pulmonary vascular resistance have been implicated as independent risk factors in the Fontan procedure (13), we did not find these variables to discriminate survivors from nonsurvivors in our patients. There is also disagreement (14) on the relative importance of pulmonary artery distortion as a risk factor. Pulmonary artery distortion was not a risk factor in our group of patients because routine bilateral pulmonary artery augmentation is part of the modified Fontan procedure at our institution. Augmentation of the pulmonary arteries may abolish any negative influence that discrete central stenosis of the pulmonary arteries would have on eventual outcome. This observation is consistent with an earlier report (15) of the lack of predictive value of pulmonary artery size on outcome of the Fontan procedure in our patients.

In our study, there was a statistical trend for poor outcome in patients with moderate or severe tricuspid regurgitation. The small sample size may account for lack of true statistical difference between survivors and nonsurvivors in examining significant AV valve regurgitation as an independent risk factor. After a Fontan procedure, significant tricuspid valve regurgitation can be detrimental because it results in elevated pressure in the pulmonary venous atrium, effectively impeding anterograde pulmonary blood flow, especially during systole. Our observation agrees with a recent report (16) on the Fontan procedure performed in patients <4 years of age, which revealed that moderate AV valve regurgitation and the need to repair the systemic AV valve were significant risk factors in this young group of patients.

Superior cavopulmonary anastomosis. Since May 1989, we have modified our strategy for patients with hypoplastic left heart syndrome to include a superior cavopulmonary anastomosis before performing the Fontan procedure. This intermediate procedure consists of ligation of the systemic to pulmonary shunt and anastomosis of the superior vena cava to the augmented pulmonary arteries. This method of allowing bidirectional pulmonary arterial flow has been previously reported (16) in other univentricular lesions.

The rationale for this intermediate step is to reduce the volume overload imposed on the right ventricle at an earlier stage and avoid an acute change in the ventricular volume and mass interrelation occasionally seen after the Fontan operation. Although all six patients who had a superior cavopulmonary anastomosis followed by a Fontan procedure in our study group survived, the potential benefit of this intermediate procedure remains to be investigated.

Conclusions. Most survivors of stage I reconstructive surgery (Norwood operation) for hypoplastic left heart syndrome had excellent hemodynamic and angiographic findings at the time of their postoperative elective cardiac catheterization, reflecting a successful strategy of initial reconstruction. Moderate or severe tricuspid valve regurgitation appeared to be the only factor that may influence outcome after a modified Fontan procedure. We speculate that the performance of superior cavopulmonary anastomosis before the Fontan procedure may improve eventual outcome in these patients.

References