Unifocalization of Major Aortopulmonary Collaterals in Single-Ventricle Patients

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Background. Unifocalization of major aortopulmonary collateral arteries (MAPCAs) in pulmonary atresia with ventricular septal defect and intracardiac repair has become the standard of care. However, there are no reports addressing unifocalization of MAPCAs in single-ventricle patients. It is unknown whether their pulmonary vascular bed can be reconstructed and low enough pulmonary vascular resistance achieved to allow for superior or total cavopulmonary connections.

Methods. We reviewed data on all patients with functional single ventricles and unifocalization procedures of MAPCAs. From 1997 to 2005, 14 consecutive children with various single-ventricle anatomies were operated on.

Results. Patients had a median of three surgical procedures (range, 1 to 5). Two patients had absent, all others diminutive central pulmonary arteries, with an average of 3.5 ± 1.2 MAPCAs. Seven patients (50%) had bidirectional Glenn procedures, and 3 of these had Fontan procedures. Median postoperative pulmonary artery pressures measured 12.5 mm Hg (Glenn) and 14 mm Hg (Fontan), respectively. Six patients are alive today (46%), with 1 patient lost to follow-up. Three patients died early and 3 late after initial unifocalization to shunts. One other patient survived unifocalization, but was not considered a candidate for a Glenn procedure and died after high-risk two-ventricle repair. Another patient with right-ventricle–dependent coronary circulation died of sepsis late after Glenn.

Conclusions. In selected patients with functional single ventricles and MAPCAs, the pulmonary vascular bed can be reconstructed sufficiently to allow for cavopulmonary connections. Venous flow to the pulmonary vasculature decreases cardiac volume load and is likely to increase life expectancy and quality of life for these patients.

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The surgical treatment of pulmonary atresia with ventricular septal defect (VSD) and major aortopulmonary collaterals (MAPCAs) in pulmonary atresia has evolved substantially over the last 2 decades [1–7]. In the early 1990s, our group started a protocol of early unifocalization of MAPCAs and intracardiac repair in these patients. We follow these general principles: (1) early single-stage complete unifocalization of all sources of pulmonary blood flow and intracardiac repair whenever feasible [8, 9]; (2) complete unifocalization to a shunt if intracardiac repair can not yet be accomplished; (3) creation of an aortopulmonary (AP) window to the true pulmonary arteries (PAs) in appropriate cases of very small PAs with normal arborization [10]; and (4) staged unifocalization through thoracotomies in unfavorable cases of severe segmental level stenoses of MAPCAs. This protocol has been successful in achieving a high rate of early complete repair with low right ventricular pressures [11].

Even though the vast majority of patients with MAPCAs express the intracardiac anatomy of tetralogy of Fallot with pulmonary atresia, there are some rare exceptions. There are case reports in the literature of MAPCAs in association with pulmonary atresia with intact septum (PA/IVS) [12, 13] and with right isomerism [14, 15]. We have also seen MAPCAs with a variety of other defects with biventricular and univentricular morphology. Single-ventricle patients account for 4.1% of the patients undergoing unifocalizations in our experience. This study focuses on the surgical treatment of patients with MAPCAs and single-ventricle physiology, including both true single-ventricle morphology such as PA/IVS, tricuspid atresia, or severely unbalanced common atroventricular canal (CAVC), and complicated two-ventricle morphology that is deemed unsuitable. We describe our experience with this challenging group of patients.

Patients and Methods

All patients with MAPCAs and single-ventricle physiology referred to our surgical group at Stanford University or one of our associated hospitals were retrospectively reviewed. Current follow-up was obtained by facsimile
from the patients’ pediatric cardiologists. The study was approved by the Administrative Panel on Human Subjects at Stanford University on January 5, 2006. Individual patient consent was waived owing to the retrospective nature of the study.

**Pulmonary Blood Supply**

MAPCAs were defined as major collateral arteries arising from the arterial circulation in the setting of pulmonary atresia. Typically, these vessels arise from the proximal descending aorta; however, frequently also from supraaortic branches or other aortic segments. True pulmonary arteries were either absent or diminutive and supplied only by MAPCAs. Patients with discontinuous pulmonary arteries such as those due to closure of a persistent ductus arteriosus or iatrogenically (that did not have true MAPCAs) were excluded, as well as patients with acquired aortopulmonary collaterals only, such as they frequently occur in cyanotic heart disease.

**Intracardiac Morphology**

Only patients with pulmonary atresia were included. Patients had either true single-ventricle cardiac morphology or two-ventricle hearts that could not be surgically septated and therefore had to be palliated like single ventricles. Patients with forms of tetralogy or balanced double-outlet right ventricle (DORV) as well as all other septatable hearts were excluded. In fact, the majority of patients referred to us with MAPCAs and complex biventricular morphology such as corrected transposition had unifocalizations along with intracardiac repairs and are consequently not included in this study.

**Surgical Protocol**

In general, we applied similar treatment principles to this patient population as to those with pulmonary atresia/VSD as mentioned in the introduction section. All patients were completely unifocalized to shunts as early as possible. In selected cases, AP windows or staged thoracotomy unifocalizations were performed initially.

In addition, we applied other generally accepted concepts of single-ventricle palliation. We performed bidirectional Glenn shunts for volume unloading as early as possible, and we completed total cavopulmonary connection (Fontan circulation) whenever appropriate. Both these procedures were preferably done avoiding cardiopulmonary bypass, using passive shunts intraoperatively. Concomitant abnormalities such as total anomalous pulmonary venous return were corrected early as well.

**Statistics**

Owing to the small number of patients, no complex statistical analyses were performed.

**Results**

Between 1997 and 2005, 14 consecutive patients with MAPCAs and single ventricles (6 male, 8 female) presented to our institution. Median age at first operation was 3 months (range, 5 days to 9 years). Eight of these patients were referred from other states.

**Morphology and Additional Morbidities**

Patients had an average of 3.5 ± 1.2 MAPCAs. The average number of MAPCAs was similar in survivors (3.3 ± 1.0) and nonsurvivors (3.7 ± 1.5). Two patients had completely absent intrapericardial PAs; 1 of these 2 had a Fontan connection and survived, the other died late after a Glenn procedure. All other patients had diminutive PAs. Figure 1 shows a preoperative angiogram of a 3-months old infant with complex, nonseptatable L-transposition and pulmonary atresia who underwent aortopulmonary window, right thoracotomy unifocalization of major aortopulmonary collateral arteries, and bidirectional Glenn shunt. (A) Multiple aortopulmonary collateral arteries arising from different levels of the descending aorta. (B) Diminutive true pulmonary arteries connecting to a right upper lobe collateral.

**Surgical Procedures**

A total of 40 surgical procedures were performed in these patients. The median number of operations per patient...
was 3. Table 2 shows a chronologic overview of all procedures in all 14 patients, illustrating that all patients had initial shunt or AP window procedures with or without unifocalizations, except for 2 patients with previously undiagnosed MAPCAs that underwent initial mediastinal explorations.

Survival

Six patients are alive today, for an overall survival of 46% (with 1 patient lost to follow-up). Time of follow-up ranges from 2 months to 5.5 years (median, 33 months).

Table 1. Spectrum of Intracardiac Morphology and Concomitant Cardiac Defects

<table>
<thead>
<tr>
<th>Spectrum of Intracardiac Morphology and Concomitant Cardiac Defects</th>
<th>Number</th>
</tr>
</thead>
<tbody>
<tr>
<td>Atrioventricular septal defect (of these, severely unbalanced)</td>
<td>5 (4)</td>
</tr>
<tr>
<td>Single left ventricle</td>
<td>3</td>
</tr>
<tr>
<td>Pulmonary atresia/intact ventricular septum/RV-dependent coronary circulation</td>
<td>2</td>
</tr>
<tr>
<td>Tricuspid atresia</td>
<td>2</td>
</tr>
<tr>
<td>Double-outlet right ventricle/severely hypoplastic left ventricle</td>
<td>1</td>
</tr>
<tr>
<td>Complex, nonseptatable L transposition</td>
<td>1</td>
</tr>
<tr>
<td>Supracardiac total anomalous pulmonary venous return</td>
<td>2</td>
</tr>
<tr>
<td>Partial anomalous pulmonary venous return of the right upper lobe</td>
<td>1</td>
</tr>
<tr>
<td>Cor triatriatum</td>
<td>2</td>
</tr>
</tbody>
</table>

Early Deaths

Three patients died early after unifocalization procedures to a central shunt. Two of these deaths were sudden deaths: a patient with PA/IVS and RV-dependent coronary circulation arrested suddenly on postoperative day 1; another died of refractory arrhythmia on postoperative day 2. The third patient was not considered a candidate for cavopulmonary anastomosis owing to high pulmonary artery pressures. Two-ventricle repair was attempted but failed, and he died the next day.

Late Deaths

Four patients died late postoperatively: One patient died 2 months after repair of total anomalous pulmonary venous return from recurrent pulmonary vein stenosis. Two other patients with tracheobronchomalacia were discharged after unifocalizations to shunts, but they died after acute respiratory events 3 and 6 months postoperatively, respectively. One patient with PA/IVS and RV-dependent coronary circulation died of sepsis and subsequent myocardial ischemia 7 months after bidirectional Glenn shunt.

Bidirectional Glenn Shunt

A superior cavopulmonary anastomosis could be achieved in 7 patients (50%). It was performed without cardiopulmonary bypass in 5 of these cases. Patient ages at operation were 4, 5, 6, 20, 21, 66, and 112 months (median, 20). The shunt was divided in 5 cases and banded in 2 cases. Glenn (PA) pressure after the proce-

Table 2. Surgical Procedures

<table>
<thead>
<tr>
<th>Patient Number</th>
<th>Intracardiac Morphology</th>
<th>1st Procedure</th>
<th>2nd Procedure</th>
<th>3rd Procedure</th>
<th>4th Procedure</th>
<th>5th Procedure</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Tricuspid atresia</td>
<td>Uni shunt</td>
<td>Shunt</td>
<td>Glenn</td>
<td>Fontan</td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>CAVC</td>
<td>Uni shunt</td>
<td>Glenn</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>PA/IVS</td>
<td>APW</td>
<td>Uni Th</td>
<td>Shunt</td>
<td></td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>PA/IVS</td>
<td>Expl</td>
<td>Uni shunt</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>5</td>
<td>DORV, hypoplastic LV</td>
<td>APW</td>
<td>Uni shunt</td>
<td>Glenn</td>
<td>Taked. Coll.</td>
<td></td>
</tr>
<tr>
<td>6</td>
<td>Single LV</td>
<td>Uni shunt</td>
<td>Glenn</td>
<td>Fontan</td>
<td></td>
<td></td>
</tr>
<tr>
<td>7</td>
<td>Tricuspid atresia</td>
<td>APW</td>
<td>Uni Shunt</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>8</td>
<td>CAVC</td>
<td>Uni Th</td>
<td>Uni Th</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>9</td>
<td>CAVC</td>
<td>Expl</td>
<td>Shunt</td>
<td>Glenn</td>
<td>Uni + Fontan</td>
<td></td>
</tr>
<tr>
<td>10</td>
<td>CAVC</td>
<td>Shunt</td>
<td>Uni Th</td>
<td>Uni Th</td>
<td>TAPVR repair</td>
<td></td>
</tr>
<tr>
<td>11</td>
<td>Complex transposition</td>
<td>APW</td>
<td>Uni Th</td>
<td>Glenn</td>
<td>Shunt</td>
<td></td>
</tr>
<tr>
<td>12</td>
<td>Single LV</td>
<td>Uni shunt</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>13</td>
<td>Single LV</td>
<td>Uni shunt</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>14</td>
<td>CAVC</td>
<td>APW</td>
<td></td>
<td></td>
<td>TAPVR repair</td>
<td></td>
</tr>
</tbody>
</table>

* Patient died.  b Patient lost to follow-up.

APW = aortopulmonary window; CAVC = common atrioventricular canal; DORV = double-outlet right ventricle; Expl = mediastinal explanation; LV = left ventricle; PA/IVS = pulmonary atresia with intact ventricular septum; Taked. Coll. = takedown of acquired collaterals; TAPVR = total anomalous pulmonary venous return; Uni Shunt = unifocalization to a shunt; Uni Th = unifocalization through thoracotomy.
dure ranged from 9 to 17 mm Hg, with a median of 12.5 mm Hg. Six of these 7 patients are alive today (37 to 63 months postoperatively), and all survivors are in New York Heart Association (NYHA) class I to II. Three have achieved a Fontan connection, 2 are currently awaiting Fontan palliation, and 1 is not considered a candidate for Fontan owing to high PA pressures (17 mm Hg).

**Fontan Procedure**

Total cavopulmonary connections were achieved in 3 patients. Extracardiac conduits from polytetrafluoroethylene (PTFE) with diameters of 20 mm (2 patients) and 18 mm (1 patient) were used. Two of these procedures were done off bypass. Fontan pressures (central venous pressures) postoperatively were 10, 14, and 14 mm Hg, respectively. All 3 patients are alive and in NYHA class I at a follow-up period of 2, 24, and 29 months.

Figure 2A shows the pre-unifocalization angiogram and Figure 2B shows the post-Glenn (pre-Fontan) angiogram of a 9-year-old patient. This patient (the oldest in the series) had a PA reconstruction using a 14-mm ringed PTFE graft to centrally connect three MAPCAs remote from each other. The extracardiac conduit was then connected to the underside of this graft.

**Comment**

The combination of pulmonary atresia with major aortopulmonary collaterals and single-ventricle physiology is extremely rare. These patients account for only a small percentage of all patients with MAPCAs, an abnormality that is already considered infrequent. Our literature search revealed only a few case studies of patients with single ventricle and MAPCAs.

According to a study by morphologists, MAPCAs are present in 3% of patients with right isomerism [16]. However, in the surgical literature, we found only a single case report of a patient with heterotaxy/asplenia/unbalanced atrioventricular canal, good-sized central PAs, and MAPCAs who was unifocalized and achieved a Fontan circulation [14]. Another report from Japan describes a patient with heterotaxy and unbalanced atrioventricular canal with a single MAPCA who was unifocalized and eventually had a cavopulmonary shunt [17]. These are the only reports in the literature of single-ventricle patients with MAPCAs achieving cavopulmonary anastomosis.

We can assume that most of these patients have traditionally been considered inoperable. The mortality in our series of 54% confirms that they are obviously a very high risk group. On the other hand, we were able to recruit enough pulmonary vascular bed and achieve a low enough pulmonary vascular resistance in the surviving patients to perform bidirectional Glenn shunts or even Fontan connections. These patients will have to be followed up to confirm long-term survival, but we believe that our preliminary experience justifies the enormous effort spent on their care and the high number of procedures that they had to undergo.

Even though the small size of our series does not allow for statistical risk analysis, it may reveal some factors to be associated with particularly poor prognosis. With regard to pulmonary artery anatomy, the number of MAPCAs or the presence of absence of intrapericardial PAs did not appear to be associated with outcome. It is obviously difficult to quantify how favorable for unifocalization any individual MAPCAs morphology is, and we did not attempt to do that in this series. With regard to other risk factors, PA/IVS is generally considered a high-risk lesion even with normal pulmonary artery anatomy, presumably because of frequent RV-dependent coronary circulation [18]. No patient with PA/IVS in our series survived, even though we were able to reconstruct a low resistance pulmonary vascular bed in...
both, and 1 of them even had a bidirectional Glenn shunt. This experience and the case reports cited earlier characterize PA/IVS with MAPCAs as an extremely high risk combination.

The presence of anomalies of pulmonary venous return may represent another risk factor, since only 1 of 4 patients with total anomalous pulmonary venous return or cor triatriatum survived (the patient with PAPVR is lost to follow-up). Finally, tracheobronchomalacia appears to be another risk factor, since both of our patients with this condition expired. Heterotaxy with asplenia may not carry a substantial additional risk, as 3 of 5 patients survived long term.

All patients who had Glenn or Fontan connections are alive today, except for 1 with PA/IVS and RV-dependent coronaries. On the other hand, no patient who did not achieve cavopulmonary anastomosis survived. Even more so, as in the general single-ventricle population, cavopulmonary anastomoses appear to be protective in these patients, presumably because they provide obligatory pulmonary blood flow, have a low risk of thrombosis compared with aortopulmonary shunts, and reduce volume load and heart failure [19, 20]. All our patients with Glenn or Fontan physiology are clinically doing well.

We therefore conclude from this experience that in patients with single ventricle and MAPCAs, all efforts should be undertaken to recruit all collateral vessels and optimize the pulmonary vascular bed to achieve cavopulmonary anastomoses, as this improves patient survival and clinical status.

References


DISCUSSION

DR MARSHALL L. JACOBS (Philadelphia, PA): This is a very, very challenging group of patients, and the success with even a fracture of them represents a tremendous accomplishment.

I want to address only your final comment about the pulmonary atresia intact septum with presumed right ventricular coronary dependence, and I guess I didn’t focus on it throughout the course of the talk and did only at the end.

I have 1 such patient who presented at about 5 months of age as a very cyanotic infant, pulmonary atresia, intact septum, RV-dependent coronaries; and in fact his very diminutive true pulmonary arteries arose from the right coronary. And he had MAPCAs. And we took the pulmonary arteries off the right coronary and perfused him with a shunt, and then did a unifocalization of the largest of the MAPCAs into the true pulmonary arteries associated with a Glenn. But then moved ahead very quickly afterwards with the completion Fontan,
despite the borderline nature of his pulmonary vascular bed, and did so on the supposition that completing the Fontan was really the only way to get maximally saturated blood into the coronaries.

So I wondered, with respect to your recommendation that they may be a group particularly at high risk, had you reached the Glenn stage with those? Was it after the Glenn stage? And if you’re faced with another, might you move ahead more quickly to complete the Fontan in order to at least oxygenate that abnormal coronary circulation?

DR REINHARTZ: Thank you for your comments. That is a good point. One of these PA-IVS patients died early after a shunt, so we never made it out that far. But I agree with your comment, because in the other patient, in retrospect, we could have thought about that, because that is the patient who died about 6 months after Glenn. Since we generally do extracardiac Fontans, we would not be able to do this operation in this particular patient, but we probably could have considered earlier lateral tunnel Fontan completion in this patient.

DR FORBESS: As for the 1 patient with the high PA pressures, if cyanosis were to develop, would that patient be considered for transplantation then?

DR REINHARTZ: Either that, or that is actually a patient with two ventricles that we have just not deemed septatable, so we might consider high-risk septation.

DR CHARLES D. FRASER, JR (Houston, TX): This is obviously courageous work in a very challenging group of patients, and you are to be congratulated for taking this on and presenting these data. I wonder, since you all have so much experience unifocalizing pulmonary arteries, could you share with us what insight you might have about which patients did well and which ones didn’t—in terms of, could you now look back retrospectively and say for a certain pulmonary arterial anatomy, probably we wouldn’t tackle again? For example, did you try to separate the good outcomes and the bad outcomes in terms of the number of bronchopulmonary segments that were originally supplied by native pulmonary arteries? What benefit did unifocalizing really have on the patient outcome long term?

DR REINHARTZ: This is in regard to this patient group?

DR FRASER: Correct, this patient group.

DR REINHARTZ: I did not do that, and I think the patient group is too small to do that. That would probably be something to analyze in the whole population, because I wouldn’t assume that that would be any different between tetralogy patients and other kinds of MAPCAs patients. No, I did not specifically look at segment numbers in this patient group.

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