Primary Arterial Switch Operation for Transposition of the Great Arteries With Intact Ventricular Septum in Infants Older Than 21 Days

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Objectives. The aim of this study was to assess the surgical outcome of the primary arterial switch operation (ASO) in infants 3 weeks to 2 months old.

Background. The surgical management of transposition of the great arteries and intact ventricular septum (TGA/IVS) beyond 2 to 3 weeks of age is controversial. Concern that regression of the left ventricular (LV) myocardial mass will render the left ventricle incapable of coping with the acutely increased work of systemic perfusion has been considered a contraindication to a primary ASO.

Methods. We used retrospective analysis of 37 patients 3 weeks to 2 months old and 156 patients <3 weeks old who underwent primary ASO with TGA/IVS to determine the surgical outcomes.

Results. Between January 1990 and December 1996, primary ASO was performed in 37 patients 21 to 61 days old (late ASO group) and 156 patients <21 days old (early ASO group) with TGA/IVS. One (2.7%, 95% confidence interval [CI] 0.07% to 14.2%) of 37 patients and 13 (8.3%, 95% CI 4.5% to 13.8%) of 156 patients died. One late death occurred in each group. Mechanical LV support was required in 1 (2.7%, 95% CI 0.07% to 14.2%) of 37 late ASO and 6 (3.8%, 95% CI 1.4% to 8.2%) of 156 early ASO group patients postoperatively. Neither death nor the need for mechanical LV support in the late ASO group patients could be attributed to LV failure. In the late ASO group, age, LV geometry, LV mass index, LV posterior wall thickness index, LV volume index, LV mass/volume ratio, patent arterial duct or pattern of coronary anatomy did not predict death, duration of postoperative ventilation or inotropic support or time in intensive care. Moreover, there was no difference in duration of ventilation, duration of inotropic support or the time spent in intensive care in comparison to a random sample of 37 neonates from the early ASO group.

Conclusions. Primary ASO may be appropriate treatment for infants with TGA/IVS <2 months old, regardless of preoperative echocardiographic variables. The upper age limit for which primary ASO is indicated in TGA/IVS is not yet defined.

The usual current surgical management of transposition of the great arteries with intact ventricular septum (TGA/IVS) involves an arterial switch operation (ASO) within the first 2 to 3 weeks of age (1). Beyond this age, surgical management is controversial. This is because of concern that regression of the left ventricular (LV) mass might render the left ventricle incapable of coping with the acutely increased work of systemic perfusion that occurs following ASO. Consequently, either an atrial switch operation (Senning or Mustard), or a two-stage procedure involving the use of a pulmonary artery band to prepare the left ventricle for a later ASO, has been advocated in infants with TGA/IVS beyond the neonatal period (2,3). In 1990, we adopted a policy of primary ASO in infants with TGA/IVS presenting to our institution between the ages of 3 weeks and 2 months in the belief that this might provide a better outcome than that obtained with either our then existing Senning protocol (4) or by adoption of a rapid two-stage ASO protocol (3). We report our experience with this group of patients.

Methods

Patients. Between January 1990 and December 1996, 193 patients ≤2 months old underwent ASO for TGA/IVS. Patients with even a small ventricular septal defect not subsequently requiring surgical closure were excluded from this group. The 37 patients who underwent ASO between 21 and 61 days of age (late ASO group) are the subject of this study. In most of these cases, the diagnosis had been made in the neonatal period, but many were transferred to our hospital from overseas, resulting in an unavoidable delay between diagnosis and the opportunity for surgery. From the 156 patients who underwent ASO before 21 days (early ASO group), 37 were randomly selected for detailed comparison.
Echocardiography. Transthoracic echocardiography was performed using an Acuson 128 XP machine (Acuson, Mountain View, California). Oral sedation was used when necessary. All studies included two-dimensional imaging of the left ventricle from subcostal, apical and parasternal views and were recorded on half inch videotape in the S-VHS format. Frozen end-diastolic images of the left ventricle in the subcostal or parasternal short axis and subcostal or apical long axis were used to measure LV end-diastolic and epicardial volumes using the bullet formula (3,5). The LV myocardial mass was determined by subtraction of the end-diastolic volume from the epicardial volume, and multiplying the product by myocardial density (1.05 g/cm^3) to obtain mass. The LV posterior wall thickness was measured at end-diastole at the midcavity level. These values were indexed to body surface area. LV cavity shape was assessed from subcostal short axis views of the heart at end-systole (6,7). LV geometry was classified as “favorable” or type I if the lateral/anteroposterior dimension ratio was <2; “acceptable” or type II if the ratio was between 2 and 3; and “unfavorable” or type III if the ratio was >3. Patients with the higher ratios had crescent-shaped LV cavities (Fig. 1). The presence of a patent arterial duct was considered significant if it measured >2 mm at its narrowest point. The pattern of coronary artery anatomy was determined using echocardiography and confirmed at surgery.

Preoperative management. In the late ASO group patients, balloon atrial septostomy was performed, often before transfer to our hospital, in all but three patients who had good-size atrial communications demonstrated on echocardiography. Patients were fed enterally until the time of surgery. None was receiving prostaglandin at the time of surgery.

Surgical technique. Surgical correction was performed on cardiopulmonary bypass under profound hypothermia with periods of reduced flow to improve exposure where necessary. In most patients a single atrial cannula was used and the atrial septostomy was closed during a brief period of circulatory arrest. Cold crystalloid cardioplegia was used in all patients. The coronary arteries were excised from the aortic sinuses together with a variable amount of sinus wall. In some patients the proximal portions of the coronary arteries were dissected free of the epicardial surface of the heart to facilitate transfer to the pulmonary artery, whereas in most a “trap-door” modification to the neoaorta facilitated coronary transfer with the benefit of minimal epicardial dissection (8). A Lecompte maneuver (9) was performed in most patients. Ultrafiltration was used to obtain satisfactory fluid balance and hemococoncentration before transfer to the cardiac intensive care unit.

Postoperative care. Ventilatory support with anesthesia or heavy sedation was continued for at least the first postoperative night. Intravenous inotropic and vasodilator support was used in all patients. Extracorporeal membrane oxygenation (ECMO) was available for mechanical support of the circulation when necessary. The duration of ventilatory support and the duration of intravenous inotropic and vasodilator administration, as well as the total time spent on the cardiac intensive care unit, was recorded.

Statistical analysis. Normally distributed continuous variables are expressed as mean value ± 1 SD. Nonparametric variables are expressed as the median value with a range. Data from subgroups were compared using the chi-square test or 95% confidence interval (CI) for discrete variables or the nonpaired Student t test for continuous variables. A two-tailed p value < 0.05 was considered significant. The size of the study group provided power of approximately 80% to detect a hypothetical 50% prolongation of the duration of postoperative assisted ventilation, inotropic or vasodilator drug support or intensive care stay at this level of significance (10). Similarly, the study group size provided power of approximately 80% at this level of significance to detect a hypothetical threefold

**Figure 1.** Schematic representation of the three patterns of LV geometry in patients with TGA: A, “Favorable” (type I). B, “Acceptable” (type II). C, “Unfavorable” (type III). These three diagrams represent the end-systolic subcostal short-axis echocardiographic projections of the left and right ventricles at the level of the tips of the LV papillary muscles. The minor axis ratio is calculated as v/h (see text). RV = right ventricle; LV = left ventricle; v = superoinferior minor transverse axis; h = anteroposterior minor transverse axis.
increase in operative mortality in the late ASO group patients. Univariate regression analysis was used to explore whether potential preoperative predictors of risk were associated with measures of postoperative morbidity.

Results

Surgical outcome. The baseline characteristics of all patients are shown in Table 1. The median age of the patients in the late ASO group at the time of surgery was 28 days, with the range extending to 61 days. One (2.7%, 95% CI 0.07% to 14.2%) of 37 infants in the late ASO group died in-hospital, whereas 13 (8.3%, 95% CI 4.5% to 13.8%) of 156 patients in the early ASO group died. The one hospital death in the late ASO group occurred in a male infant 57 days old and weighing 2.1 kg at surgery. He also had a cleft lip and palate, severe respiratory failure and systemic pulmonary artery pressure at the time of operation related to the presence of a large arterial duct. “Favorable” (type I) LV geometry was present preoperatively, and his coronary artery anatomy was normal. An apparently satisfactory surgical repair was performed. Postoperatively, he was stable for 3 h before the onset of systemic oxygen desaturation and bradycardia, which rapidly progressed to electromechanical dissociation and asystole. No specific cause of death was identified at the postmortem examination. It was thought that death was most likely the result of a pulmonary hypertensive crisis, although LV failure could not be excluded. One patient in the late ASO group required ECMO and was 41 days old when the median age at ASO was 28 days. Patients receiving PGE after BAS had a peak LV outflow tract velocity of (30%) and “unfavorable” in the remaining 9 (24%) of 37 patients. No patient had a peak LV outflow tract velocity of >2 m/s. An atrial septal defect was present in 15 (41%) of 37 patients. Of these 15 patients, LV geometry was “favorable” in 12 (80%) and “acceptable” in 3 (20%) patients. Most patients (27 of 37, 73%) in the late ASO group of patients were transferred to our unit from another country and this was the predominant reason for late surgical repair. A small number of patients had their surgery delayed due to concomitant medical problems.

Preoperative data. Clinical and anatomic characteristics of the late ASO group of patients are shown in Table 2. Balloon atrial septostomy was not required in three patients due to the presence of preexistent secundum atrial septal defects. LV geometry was “favorable” in 17 (46%), “acceptable” in 11 (30%) and “unfavorable” in the remaining 9 (24%) of 37 patients. No patient had a peak LV outflow tract velocity of >2 m/s. An atrial septal defect was present in 15 (41%) of 37 patients. Of these 15 patients, LV geometry was “favorable” in 12 (80%) and “acceptable” in 3 (20%) patients. Most patients (27 of 37, 73%) in the late ASO group of patients were transferred to our unit from another country and this was the predominant reason for late surgical repair. A small number of patients had their surgery delayed due to concomitant medical problems.

Preoperative two-dimensional echocardiographic data (mass, mass index, volume, volume index, mass/volume ratio and diastolic LV posterior wall thickness and its index) from the late ASO group patients are shown in Table 3. Subgroup analysis of mass, volume and these variables indexed to body surface area versus the pattern of LV geometry is shown in Figure 2. It can be seen that patients with an “unfavorable” or type III LV geometry had the lowest values for LV mass and volume. Mass/volume ratios were similar in all three groups. Patients with a significant arterial duct (n = 15) possessed higher LV volume indexes when compared with the rest of the group (n = 22), 49.8 ± 19.7 versus 34.7 ± 12.5 ml/m², respectively, p = 0.007.

The distribution of coronary artery anatomy in the late
ASO group patients and in the 37 randomly selected patients from the early ASO group was similar, \( p = 0.20 \) (Fig. 3).

**Postoperative data.** Postoperatively, there was no significant difference between patients in the late and early ASO groups in terms of ventilation requirements, duration of intravenous inotropic or vasodilator support or the time spent in the cardiac intensive care unit (Table 4). When the pattern of LV geometry in the late ASO group of patients was compared with these same postoperative outcome measures, again no significant differences were found (Table 5). Age, LV mass index, LV posterior wall thickness index, LV volume index, LV mass/volume ratio, pattern of LV geometry, presence of an arterial duct and pattern of coronary artery anatomy did not allow prediction of an adverse outcome in terms of mortality, the duration of ventilation, the duration of inotropic or vasodilator support or the time spent on the intensive care unit.

The change in the diastolic LV posterior wall thickness index measured preoperatively and that measured before hospital discharge is depicted in Figure 4. There were similar significant increases in patients in both the late and early ASO groups. There was no significant difference between the two groups (Pearson chi-square = 4.647 with 3 degrees of freedom, \( p = 0.1995 \)).

There was a late death in the late ASO group of patients in a patient first seen at 18 days of age with “favorable” LV geometry who underwent ASO when 21 days old. The pulmonary artery pressures were elevated but less than systemic at the time of operation. The postoperative course was prolonged and complicated by early His bundle tachycardia and pneumonia. This patient remained in the hospital for 43 days and was discharged on a combination of diuretic, digoxin and vasodilator therapy. She returned 3 weeks later with RV failure. Cardiac catheterization revealed an unobstructed neopulmonary anastomosis and normal pulmonary venous drainage, but a high mean transpulmonary gradient of 50 mm Hg. She died shortly after readmission and a postmortem examination confirmed severe pulmonary vascular obstructive disease.

**Discussion**

**Background.** When successful neonatal ASO for TGA/IVS was demonstrated in the 1980s (11,12), the procedure was embraced enthusiastically, despite the excellent operative survival after atrial switch repairs being obtained at that time (13). This was because of the intuitive appeal of using the morphologic left ventricle as the systemic ventricle and, it was hoped, thereby avoiding late systemic ventricular and atrioventricular valve dysfunction and arrhythmias that had become apparent.

**Table 3. Echocardiographic Results of Mass, Volume and Wall Thickness Indexed to Body Surface Area in the Patients Undergoing Late Arterial Switch Operation (n = 37)**

<table>
<thead>
<tr>
<th></th>
<th>Mean Value ± SD</th>
<th>Range</th>
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<tbody>
<tr>
<td>LV mass index (g/m²)</td>
<td>59 ± 23</td>
<td>28–117</td>
</tr>
<tr>
<td>LV volume index (m³/m²)</td>
<td>41 ± 17</td>
<td>18–98</td>
</tr>
<tr>
<td>Mass/volume ratio</td>
<td>1.5 ± 0.3</td>
<td>0.9–2.1</td>
</tr>
<tr>
<td>LV PW[d] index (mm/m²)</td>
<td>17 ± 3</td>
<td>13–26</td>
</tr>
</tbody>
</table>

LV = left ventricular; LVPW[d] = diastolic left ventricular posterior wall thickness.

**Figure 3. Distribution of coronary artery anatomy for patients in the early and late ASO groups.** There was no significant difference between the two groups (Pearson chi-square = 4.647 with 3 degrees of freedom, \( p = 0.1995 \)). LAD = left anterior descending coronary artery; LCx = left circumflex coronary artery; RCA = right coronary artery.

**Table 4. Postoperative Outcome Measurements in the Early and Late Arterial Switch Operation Group Patients**

<table>
<thead>
<tr>
<th></th>
<th>Late ASO Group (≥21 days old; ( n = 37 ))</th>
<th>Early ASO Group (&lt;21 days old; ( n = 37 ))</th>
<th>( p ) Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ventilation (days)</td>
<td>5.6 ± 3.8</td>
<td>5.3 ± 4.4</td>
<td>0.75</td>
</tr>
<tr>
<td>INO/VOD Rx (days)</td>
<td>5.2 ± 3.1</td>
<td>5.1 ± 5.8</td>
<td>0.93</td>
</tr>
<tr>
<td>ECMO</td>
<td>1</td>
<td>2</td>
<td>1.0</td>
</tr>
<tr>
<td>Delayed sternal closure</td>
<td>12</td>
<td>14</td>
<td>0.81</td>
</tr>
<tr>
<td>ICU (days)</td>
<td>7.3 ± 4.4</td>
<td>6.6 ± 5.1</td>
<td>0.53</td>
</tr>
</tbody>
</table>

Data presented are mean value ± SD or number of patients. ASO = arterial switch operation; ECMO = extracorporeal membrane oxygenator support; ICU = intensive care unit; INO/VOD Rx = intravenous inotropic/vasodilator therapy.
during late follow-up of atrial switch repairs (14,15). By contrast, ASO for transposition with a significant ventricular septal defect (TGA/VSD) was already established, both because of poor results with atrial switch repair (11,16) and the presence of a pressure and volume loaded left ventricle that could cope with the work of systemic perfusion following an ASO beyond the neonatal period.

The upper age limit for a primary ASO in TGA/IVS remains contentious. A multi-institution study suggested that the risk of death increased rapidly after the age of 14 days (17). As early as 1977, a two-stage approach with preparatory pulmonary artery banding, together with a systemic to pulmonary shunt, followed by later ASO, was proposed for older patients with TGA/IVS (2). However, this did not achieve widespread use, partly because of the demonstration of postoperative abnormalities of LV function, to which older age at pulmonary artery banding and a longer pulmonary artery banding to ASO interval were thought to be important contributory factors (18,19). LV hypertrophy was shown to occur rapidly after the imposition of a pressure load by banding the pulmonary trunk and a rapid two-stage arterial switch protocol, with an interval of only about 1 week between banding and ASO, demonstrated low operative mortality and normal LV function in the early postoperative period (3). At this time in the late 1980s, many institutions, including our own (4), continued to employ an atrial switch repair for infants with TGA/IVS older than 2 to 3 weeks of age. However, increasing experience in surgical techniques and postoperative care in neonates with TGA/IVS, and knowledge of early success with surgical ventricular septal defect closure as having a virtually intact ventricular septum (16,20,22). We excluded all patients with an identified ventricular septal defect, however small, because of concern that we might underestimate the LV thickness.

A postmortem study of 61 infants with unoperated TGA/IVS has shown that normal or near normal LV wall thickness is maintained up to at least 2 months of age (21). As expected, patients with a significant (>2 mm diameter) arterial duct had increased LV mass and volume preoperatively, but this did not favourably influence the postoperative course.

We cannot exclude a selection bias in the 27 of 37 infants who were referred to our institution from overseas. However, we believe this is unlikely, as we are unaware of a selection process for referral of patients with TGA/IVS <2 months old when first seen at any of the referring centers. If “selection” had been undertaken by local physicians, it would very likely have been on the basis of an unfavorable LV geometric appearance on echocardiography and our data demonstrate that this was not a risk factor for an adverse outcome after ASO in this study group. By definition, infants with TGA/IVS first seen beyond the age of 3 weeks must have survived the early newborn period and factors such as persistence of the arterial duct and slower than usual involution of the pulmonary arterial resistance may be features that contribute to survival and enable this late presentation. The designation of a minimal duct diameter >2 mm at last preoperative assessment as “significant” was arbitrary, and smaller size persistent ducts may also have had a role in maintaining a LV volume and pressure load. Certainly, persistence of a duct beyond the first week of life may have contributed to preoperative survival in some of these patients, but the same would apply to any other group of infants with TGA/IVS who are first diagnosed beyond the immediate newborn period. However, the relatively long interval (17 ± 6 days) between balloon atrial septostomy and ASO did not compromise the ability of the “decompressed” LV to cope after ASO in this study group.

Most reports of surgery for transposition categorize patients who have a ventricular septal defect but do not undergo surgical ventricular septal defect closure as having a virtually intact ventricular septum (16,20,22). We excluded all patients with an identified ventricular septal defect, however small, because of concern that we might underestimate the LV

### Table 5. Postoperative Outcome Measurements in Relation to the Pattern of Preoperative Left Ventricular Geometry in the Late Arterial Switch Operation Group (n = 37)

<table>
<thead>
<tr>
<th></th>
<th>“Favorable” or Type I (n = 17)</th>
<th>“Acceptable” or Type II (n = 11)</th>
<th>“Unfavorable” or Type III (n = 9)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ventilation (days)</td>
<td>5.9 ± 4.3</td>
<td>5.7 ± 3.9</td>
<td>4.9 ± 2.7</td>
</tr>
<tr>
<td>INO/VD Rx (days)</td>
<td>4.8 ± 3.1</td>
<td>5.4 ± 2.9</td>
<td>5.6 ± 3.4</td>
</tr>
<tr>
<td>ICU (days)</td>
<td>7.2 ± 4.3</td>
<td>7.6 ± 3.9</td>
<td>6.9 ± 5.6</td>
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</tbody>
</table>

Data presented are mean value ± SD. ICU = intensive care unit; INO/VD Rx = intravenous inotropic/vasodilator therapy.
pressure and volume load that this provided preoperatively, and reach a falsely optimistic view of surgical outcome after primary ASO in these patients. It was notable, however, that the three adverse surgical outcomes in this series (1 early death, 1 late death and 1 patient requiring ECMO) could not be attributed to inadequacy of postoperative LV performance. The patient who died early after ASO was known to have systemic LV systolic pressure preoperatively in the presence of a large arterial duct and airway abnormality. The patient who died late had RV failure secondary to rapidly progressive pulmonary vascular occlusive disease. The patient who required ECMO had high risk coronary anatomy (16,22) and required ECMO because of RV failure from an evolving acute inferior myocardial infarction; LV performance was satisfactory throughout the postoperative period.

Older age at repair is a risk factor for death after neonatal ASO (1,22). However, factors other than regression of LV myocardial mass preoperatively may be important: although the risk of increasing age was more pronounced in patients with TGA/IVS, a similar relation existed for patients with TGA/VSD, leading to the recommendation that TGA/VSD be repaired as early in life as possible. The TGA/VSD group excluded patients with small VSDs, who were categorized as having a virtually intact ventricular septum, and thus almost certainly had LV pressure and volume loading up to the time of the ASO.

Surgical options. The surgical options for an infant with TGA/IVS present beyond the age of 2 to 3 weeks include a primary ASO as in this series, a two-stage approach with preliminary banding of the pulmonary trunk, or an atrial switch procedure. The rapid two-stage ASO has several advantages over the delayed two-stage approach, including the demonstration of normal LV function in the early postoperative period (3). However, there are longer term concerns. This approach is associated with reduced LV contractility and increased LV end-systolic stress, and also an increased incidence of aortic regurgitation, compared with patients who have undergone a one-stage ASO (23,24). With the limited follow-up period available, LV contractility did not seem to deteriorate with time after the procedure, but there may have been a progressive increase in LV end-systolic stress (23). In addition, the rapid two-stage ASO results in a higher incidence of important RV outflow tract obstruction (22). These factors diminish the attractiveness of an approach that is employed because of concerns about late postoperative systemic ventricular dysfunction after atrial switch repairs. In a careful analysis of patients who underwent rapid two-stage ASO, measures of LV shortening and contractility at late follow-up were inversely correlated with the peak rate of the development of LV hypertrophy after banding of the pulmonary trunk, and directly correlated with the left ventricle/right ventricle pressure ratio and the minimum LV ejection fraction before ASO (23). This indicates that a tight pulmonary artery band leading to the rapid development of LV hypertrophy and a hypertensive left ventricle before ASO results in impaired LV systolic performance at late follow-up. It could be argued that optimal postoperative management after a primary ASO, especially maintenance of vasodilation and avoidance of excessive LV filling pressure by accepting a relatively low systemic blood pressure in the immediate postoperative period, may actually impose a less acute increase in LV work than the placement of a tight pulmonary artery band. All survivors in this series had normal LV shortening but the possibility of a late deterioration

Figure 5. Subcostal short-axis echocardiograms of the left ventricle at end-diastole (left) and end-systole (right) from (A) a patient with “unfavorable” (type III) LV geometry preoperatively who (B) developed a normal LV geometry postoperatively, associated with normal systolic function. See text for details.
in LV performance such as is observed after the rapid two-stage ASO cannot be excluded.

At present, we believe it may be appropriate to cautiously extend the age limit for primary ASO in infants with TGA/IVS beyond the age of 2 months, especially in the presence of LV outflow tract obstruction, whether this is dynamic or fixed (25). However, a Senning operation remains a very reasonable alternative for older infants with TGA/IVS, provided that RV and tricuspid valve function is satisfactory, especially as the infants have already survived the period of major preoperative attrition in early infancy that occurred when patients with TGA/IVS were all entered into a Senning protocol (4).

**Conclusions.** This study confirms the feasibility of primary ASO in TGA/IVS beyond the neonatal period, and this may be the optimal surgical treatment for infants <2 months old. In a series of consecutive patients undergoing surgery 21 to 61 days old, preoperative variables defined by echocardiography could not predict an adverse outcome when compared with patients having ASO within the first 3 weeks of age. The upper age limit for which primary ASO is indicated in TGA/IVS is not yet defined.

### References