Extending the Boundaries of the Primary Arterial Switch Operation in Patients With Transposition of the Great Arteries and Intact Ventricular Septum

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***Background*—**We have previously suggested that the primary arterial switch operation is a feasible strategy for patients with transposition of the great arteries and intact ventricular septum (TGA-IVS) up to age 2 months. This study reports our current results with this approach and examines whether this policy could be extended beyond age 2 months.

***Methods and Results*—**380 patients who underwent arterial switch for TGA-IVS were reviewed. 275 patients were younger than 3 weeks at the time of surgery (early switch group); 105 patients were 3 weeks or older (range, 21 to 185 days) (late switch group). There was no difference in outcome in terms of in-hospital mortality (5.5% versus 3.8%) or need for mechanical circulatory support (3.6% versus 5.7%) between early and late switch groups. However, duration of postoperative ventilation (4.9 versus 7.1 days, $P=0.012$) and length of postoperative stay (12.5 versus 18.9 days, $P<0.001$) were significantly prolonged in the late switch group. Primary left ventricular failure resulting in death occurred in 2 patients in the late switch group, with no deaths in 9 patients aged 2 to 6 months.

***Conclusions*—**This experience confirms that in TGA-IVS, the left ventricle maintains the potential for systemic work well beyond the first month of life. Consequently, neonates at high risk or late referrals can benefit from delayed arterial switch, even beyond age 2 months. However, the need for mechanical support in some of the older patients may limit the widespread adoption of such a strategy. **(*Circulation*. 2004;110[suppl II]:II-123–II-127.)**

Key Words: transposition of great vessels ■ heart defects ■ congenital ■ surgery

Patients with transposition of the great arteries and intact ventricular septum (TGA-IVS) presenting for surgery beyond the first few weeks of life have been considered at high risk for the arterial switch operation because of concern over the ability of the left ventricle (LV) to support the systemic circulation.[1] In many parts of the world, however, late diagnosis of congenital heart disease is a significant issue, and up to 95% of infants go untreated (K. S. Iyer, MCh, unpublished data, 2001). In older patients with TGA-IVS who do reach medical care, alternative strategies such as the atrial switch or rapid 2-stage arterial switch have generally been used.

In 1998 we published our experience with 37 patients undergoing "late" arterial switch (age 3 weeks to 2 months) during the period 1990 to 1996.[2] We demonstrated at that time that preoperative echocardiographic parameters (LV geometry, mass index, wall thickness, volume index, and mass/volume ratio) were not predictive of outcome and therefore concluded that "unfavorable" echocardiographic features could not be used to exclude patients from primary arterial switch, at least up to age 2 months. On the basis of these initial data, we have continued to use this strategy and to cautiously extend the upper age limit of patients selected for surgery.

This study reports the results of our current experience with this group of patients. We examine the incidence of postoperative LV failure and its relationship to age at operation using this approach. Based on these data, we offer guidelines for the surgical management of TGA-IVS presenting at varying ages.

Methods

A retrospective study of arterial switch operations performed from May 1986 to January 2003 was undertaken. Patients undergoing concomitant procedures (eg, closure of ventricular septal defect) and those with previous surgical palliation (eg, pulmonary artery banding or systemic to pulmonary shunt) were excluded. Patients were analyzed in 2 groups: those younger than 3 weeks and those 3 weeks of age or older. Outcomes were compared in terms of in-hospital mortality and need for mechanical circulatory support. When exam-

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ining duration of postoperative ventilation and postoperative length of stay, survivors from the late switch group were compared with a matched sample of survivors from the early switch group. The matching was performed on the basis of nearest date of operation to eliminate the effect of changes in intensive care and ward practices over the 17-year study period.

Surgical Technique and Postoperative Care

Surgery was performed with cardiopulmonary bypass using profound hypothermia. In most cases, single venous cannulation was used and the interatrial communication closed during a brief period of circulatory arrest. Early in the series, cold crystalloid cardioplegia was used. More recently, cold blood cardioplegia has been used. The technique of coronary transfer most often involved the use of medially hinged trapdoor incisions in the neo-aorta. The Lecompte maneuver[3] was used in almost all cases. Ultrafiltration on bypass and modified ultrafiltration after bypass was used. A left atrial pressure monitoring line and peritoneal dialysis catheter were inserted intraoperatively. The chest was left open at the end of surgery at the discretion of the surgeon.

Postoperative care included inotropic support and liberal use of vasodilators or inodilators, with the aim of maximally reducing afterload. Our current preferred regime is a combination of adrenaline (0.05 to 0.20 μg/kg per minute) and milrinone (0.25 to 0.75 μg/kg per minute). Glyceryl trinitrate (0.5 to 1.0 μg/kg per minute) is added if tolerated. Excessive volume loading is avoided. Lower than usual systemic blood pressure is accepted provided adequate peripheral perfusion is maintained. In cases of low cardiac output not responding to inotropic vasodilator therapy, core cooling, paralysis, and peritoneal dialysis are used. Mechanical support with extracorporeal membrane oxygenation (ECMO) is used if conventional measures fail.

Statistical Analysis

Values for normally distributed continuous variables are expressed as mean±1 SD. Nonparametric variables are expressed as the median value and range. Discrete variables are expressed as percentages. Outcomes between groups were compared using a nonpaired heteroscedastic *t* test for continuous variables. A 2-tailed $P<0.05$ was considered significant. Discrete variables were compared using the χ^2 test. Univariate linear regression using the least squares method was used to analyze the association between age at operation and (1) duration of postoperative ventilation and (2) postoperative length of stay.

Results

Three hundred eighty patients were identified. There were 275 in the "early" switch group (aged younger than 3 weeks) and 105 in the "late" switch group (aged 3 weeks or older). The predominant reason for delayed surgery in the late switch group was late referral of patients from overseas. Other reasons included prematurity or severe intercurrent illness. The demographic and intraoperative data for the late switch group are summarized in Table 1.

TABLE 1. Preoperative and Operative Data for Late Arterial Switch Group

Median age	28 d (21–185)
Weight	3.4±0.68 kg
Sex	68% male
Preoperative balloon atrial septostomy	89%
Coronary pattern	
Sinus 1 LAD, LCx; sinus 2 RCA	70%
Sinus 1 LAD; sinus 2 LCx, RCA	15%
Sinus 1 RCA, LAD; sinus 2 LCx	6%
Intramural LCA	5%
Other	4%
Bypass time	129.9±34.2 min
Cross-clamp time	69.3±12.3 min
Circulatory arrest time	9.5±10.7 min
Lowest temperature on bypass	18.0±2.3°C
Delayed sternal closure	37%

LAD indicates left anterior descending coronary artery; LCA, left coronary artery; LCx, circumflex coronary artery; RCA right coronary artery.

Postoperative Outcomes

Four patients in the late switch group died in hospital postoperatively (3.8%). Of these, 2 were believed to have died as a result of primary LV failure, whereas 2 were thought to have died for other reasons. These 4 deaths are detailed here.

In patient 1 (aged 28 days), preoperative echocardiogram revealed a squashed ("banana-shaped") LV and a gradient of 64 mm Hg across a small duct, suggesting low LV pressure. Coronary pattern was usual and a technically satisfactory repair performed. However, left atrial pressure was high and quite labile in response to volume, despite the heart appearing well perfused in all territories. In contrast, right atrial (central venous) pressure remained low. Significant inotropic support was required in the postoperative period and a low cardiac output state with metabolic acidosis ensued, which progressed to cardiac arrest within 2 to 3 hours. ECMO support was not available in this era and the patient could not be resuscitated.

In patient 2 (aged 49 days), preoperative echocardiogram suggested low LV pressure with no duct but a good-size atrial septostomy. Coronary pattern was usual and a technically satisfactory repair performed with no evidence of ischemia. However, left atrial pressure was high, with signs of low cardiac output and increasing inotrope requirement. ECMO was instituted after 3 to 4 hours. However, the patient had a large intracerebral hemorrhage and by day 2 had an isoelectric electroencephalogram. ECMO was therefore withdrawn and the patient died soon thereafter.

In patient 3 (aged 23 days), preoperative echocardiogram suggested favorable LV geometry with a large duct. At operation there was evident regional ischemia related to transfer of an intramural left coronary, with poor perfusion of the left coronary territory and electrocardiographic changes. The left anterior descending coronary artery was subsequently grafted using the left internal mammary artery, but the patient could not be weaned from bypass and died intraoperatively.

In patient 4 (aged 57 days), preoperative respiratory failure and systemic pulmonary artery pressure were related to a large duct. Echocardiogram demonstrated favorable LV geometry and usual coronary pattern. Surgery was technically uncomplicated with stable hemodynamics and low left atrial pressure. However, there was a sudden episode of desaturation and bradycardia 3 hours postoperatively, progressing to electromechanical dissociation and asystole. No specific cause of death was identified at postmortem examination. It

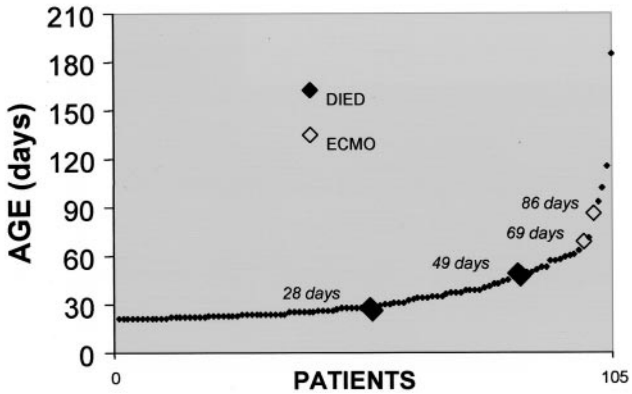

Figure 1. Patients in the late switch group who died or required extracorporeal membrane oxygenation because of primary left ventricular failure. Note that all 4 patients are aged 28 days or older.

was felt the most likely explanation was a pulmonary hypertensive crisis, although primary LV failure cannot be ruled out categorically.

Five other patients survived but required ECMO. Of these, 3 had coronary anastomotic problems requiring revision and had documented perioperative myocardial infarction, whereas 2 (aged 69 and 86 days) had primary LV failure. In total, therefore, 4 of 105 late switch patients (3.8%) had primary LV failure resulting in death or need for mechanical circulatory support, all of whom were aged 28 days or older at surgery (Figure 1).

There was no significant difference in terms of in-hospital mortality or use of ECMO between the early and late switch groups (Table 2). In fact, mortality was slightly higher in the early switch group, which may simply reflect the fact that more "late switch" operations were performed in the latter part of the series, when operative mortality overall improved. Conversely, the use of ECMO was slightly higher in the late switch group, reflecting increasing familiarity with mechanical support during the study period.

Comparing survivors in the 2 groups, the late switch group remained ventilated an average of 2.2 days longer and spent an additional 6.4 days in hospital (Table 3). Linear regression analysis demonstrated a significant association between age at operation and both these outcomes (Figures 2 and 3).

Preoperative and Postoperative Echocardiography

Twenty-six patients (25%) in the late switch group were noted on preoperative echocardiogram to have displacement of the interventricular septum toward the left at end-systole in the subcostal short-axis view, resulting in a "squashed" or "banana-shaped" LV, suggestive of low LV systolic pressure.[4] The mortality, need for ECMO, and mean duration of ventilation in this subset of patients was not significantly different from the remaining 79 patients in the late switch group (Table 4). All survivors in the late switch group except 2 had normal LV systolic function on echocardiogram at the time of discharge. The first exception was a patient aged 31 days in whom perioperative myocardial infarct developed related to transfer of an intramural left coronary artery and required ECMO to separate from bypass. She was discharged from hospital after 72 days, with echocardiogram revealing global biventricular dysfunction and calcification. The other patient was a 69-day-old infant who required 6 days of ECMO support for primary LV failure. At discharge on postoperative day 32, echocardiogram demonstrated moderately impaired LV function.

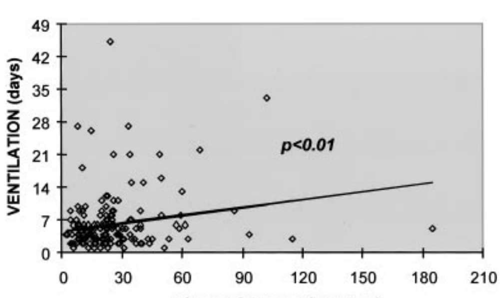

Figure 2. Duration of postoperative ventilation versus age at operation.

TABLE 2. Preoperative and Operative Data for Late Arterial Switch Group

	Early Switch Group (n=275), %	Late Switch Group (n=105), %	P
Mortality	5.5	3.8	0.51
ECMO (all cases)	3.6	5.7	0.37
ECMO (survived)	2.5	4.8	0.27

ECMO indicates extracorporeal membrane oxygenation.

Patients Older Than 2 Months

Nine patients were aged 2 months or older at operation, of whom 4 were older than 3 months. All survived to discharge, although 2 (aged 69 and 86 days) required ECMO for primary LV failure. The oldest patient was 185 days. Diagnosis was made at 3 months of age and he experienced further delay before to referral to our institution. Systemic arterial oxygen saturation was 40% to 60% on arrival. Echocardiogram confirmed TGA-IVS and revealed a restrictive atrial septal defect with small patent duct. Balloon septostomy was performed during cardiac catheterization, which documented LV systolic pressure of 50 mm Hg versus right ventricular systolic pressure of 65 mm Hg. Surgery was uneventful and the sternum was electively stented for 48 hours. He was extubated on day 5 and discharged on day 10 without significant complication. Echocardiogram before discharge demonstrated good LV function.

Late Follow-Up

Because many of these patients were referred from centers overseas, most have returned abroad for ongoing medical

TABLE 3. Outcome in Survivors of the Late Switch Group Compared With a Matched Sample of Survivors From the Early Switch Group

	Early Switch Group (n=101), d	Late Switch Group (n=101), d	P
Duration of ventilation	4.9±4.3	7.1±7.1	0.012
Length of stay	12.5±6.2	18.9±15.9	0.0003

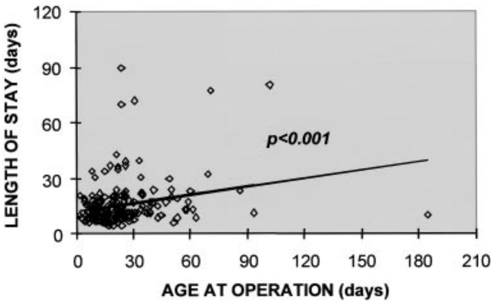

Figure 3. Postoperative length of stay versus age at operation.

follow-up. We are aware of only 1 late death in the late switch group. This patient had surgery at age 21 days. Preoperative echocardiogram suggested "favorable" LV geometry with elevated but subsystemic pulmonary artery pressure. Initial postoperative echocardiogram confirmed good biventricular function, but by 3 weeks postoperatively the right ventricle had become dilated and poorly contractile, whereas LV function was preserved. She was eventually discharged from hospital but returned 3 weeks later with clinical signs of right heart failure. Cardiac catheterization documented a transpulmonary gradient of 50 mm Hg in the absence of right ventricular outflow tract or pulmonary venous obstruction. She died soon afterward and postmortem examination confirmed severe pulmonary vascular disease.

Discussion

The optimal management of a patient presenting with TGA-IVS beyond the first few weeks of life remains contentious. The association between age at operation and risk of death after arterial switch was highlighted in 1988 by the Congenital Heart Surgeons Society,[5] which suggested the risk was increased significantly beyond 14 days of age. This was attributed to failure of the LV to cope with systemic work beyond the first few weeks of life, because of preoperative deconditioning as pulmonary vascular resistance declined.[1,2]

These observations led to the arterial switch being limited to neonates in many centers, whereas the atrial switch (Senning/Mustard operation) continued to be performed in older patients. The 2-stage arterial switch, which had been proposed a decade earlier,[6] and later modified by reducing the interval between stages to ≈1 week,[7] was put forward as a solution to patients presenting for surgery beyond the neonatal period.[8] Although most reports now suggest that the arterial switch provides a superior long-term outcome compared with the atrial switch,[9,10] the same cannot be said for the 2-stage repair. The latter imposes an added early risk,[11] which needs to be balanced against the relatively low operative mortality of the Senning/Mustard operation. Late follow-up of the 2-stage approach has revealed impaired LV systolic performance,[12] and an increased incidence of neoaortic regurgitation[13] and right ventricular outflow tract obstruction[14] compared with the primary arterial switch. The increased use of resources also makes the 2-stage approach less appealing in many parts of the world where economic constraints are paramount (K. S. Iyer, MCh, unpublished data, 2001).

TABLE 4. Outcomes Within the Late Switch Group in Relation to Preoperative Left Ventricular Geometry

	Banana-Shaped LV (n=26)	Normal (n=79)	*P*
Mortality	3.8%	3.8%	0.99
ECMO	3.8%	3.8%	0.99
Duration of ventilation (d)	6.5±5.2	7.3±7.7	0.64

LV indicates left ventricle.

In 1998 we reported our experience with 37 patients with TGA-IVS undergoing primary arterial switch between 3 weeks and 2 months of age.[2] We were unable to demonstrate any difference in outcome between these patients and a control group younger than 3 weeks old. The results of this initial experience led us to continue this strategy, and the facility for mechanical circulatory support permitted us to adopt such an approach in patients, even up to 6 months of age. Our present experience indicates that <4% of patients undergoing "late" arterial switch have primary LV failure resulting in death or the need for mechanical support, and that all such patients are 4 weeks of age or older.

We believe that these results make a case for primary arterial switch as a feasible alternative to the 2-stage arterial switch and atrial switch operations in patients with TGA-IVS within the first few months of life. We have demonstrated that primary arterial switch in these patients can be performed with mortality comparable to that in younger patients. Furthermore, LV function can be expected to return to normal in the majority of cases, given careful perioperative intensive care management. The ability to offer ECMO clearly adds safety in adopting such an approach, especially in the oldest patients. In those who do require mechanical support, the LV can be rested initially and then gradually weaned from support over several days. It can be argued that this is analogous to ventricular "retraining," but with the added advantages of normoxemia and loading conditions that can be adjusted in a controlled manner.

In contrast to our original report, we have now accumulated data to demonstrate an association between increasing age at operation and duration of postoperative ventilation, as well as postoperative length of stay. We suspect that this is a reflection of temporary but reversible LV dysfunction, which is likely to be more pronounced as age increases. Although it seems reasonable to assume that the LV in older patients with TGA-IVS might take longer to adapt to the acutely increased work after arterial switch, there appears to be wide variation in the rate of preoperative LV deconditioning. The size of the interatrial communication and duct clearly influence LV preload and afterload, but other factors, possibly genetically predetermined, might also play a role in dictating the involution of pulmonary vascular resistance and LV performance.

Our practice of primary arterial switch for TGA-IVS has evolved over time. In the early 1990s we continued to perform Senning operations for older patients. However, as our experience with the arterial switch operation grew, the number of Senning operations being performed gradually diminished. Between 1986 and 1990, Senning operations were still performed in neonates. From 1990 to 1997, this approach was limited to patients older than age 2 months and, since 1997, was only performed in patients older than 4 months. Concurrent with this, our experience with ECMO increased, which afforded us greater confidence in pursuing a policy of primary arterial switch for TGA-IVS, initially in patients up to 2 months of age and now up to 6 months of age in selected cases.

Other groups have reported smaller series of primary arterial switch beyond 3 weeks of age. Davis et al[15] in 1993 reported 18 patients aged 21 to 118, with only 1 death, which was attributed to a coronary anastomotic problem. One other patient in their series required an LV assist device for 2 days. Dabritz et al[16] reported 7 patients aged 4 weeks or older undergoing successful arterial switch. Five of these had low LV pressure preoperatively and underwent preliminary pulmonary artery banding for 15 to 30 minutes. All 5 remained hemodynamically stable and therefore proceeded to immediate arterial switch without mortality. The authors suggested that a trial of pulmonary artery banding could be used to select patients who would tolerate primary repair, an approach that we have not tested in our own population.

Some centers, however, consider age older than 3 weeks to be a definite contraindication to primary arterial switch and have adopted the rapid 2-stage approach.[17] Lacour-Gayet et al have also used LV mass index $<35 g/m^2$ as an indication for LV "retraining," even in patients younger than 3 weeks of age.[17] However, they noted frequent LV dysfunction after banding and in 10% of cases the "retraining" needed to be discontinued. In our original series,[2] we could find no association between LV mass index (or other indices) and adverse postoperative outcome. Our data continue to demonstrate no difference in outcome based on preoperative LV geometry. Therefore, we would not currently exclude patients from a primary arterial switch strategy based on echocardiographic features alone, at least up to age 2 months. However, because we have been more selective for patients older than 2 months of age, we do not wish to draw the same conclusions for these older patients.

Conclusions

Our experience supports the notion that the LV in TGA-IVS maintains the potential for systemic work well beyond the neonatal period. Temporary postoperative LV dysfunction appears to be manifest by a prolonged postoperative course, the duration of which is a function of age at surgery. However, such dysfunction is reversible in the majority of cases, even when mechanical circulatory support is required. The conceptual advantages of a 1-stage anatomic correction make this an appealing strategy for patients who present late or in whom postponing surgery might be desirable for reasons such as intercurrent illness or prematurity. However, the need for mechanical support as a rescue strategy may limit the widespread adoption of such an approach.

Recommendations

It should be emphasized that our current policy for patients referred with TGA-IVS is to undertake arterial switch within the first 2 weeks of life when possible. When this is not the case, we would be prepared to offer primary arterial switch up to the age of 3 months, although we are concerned about the possible need for mechanical support with increasing age. Preoperative assessment of LV "preparedness" for operation (as determined by LV geometry, wall thickness and function on echocardiogram, and other evidence of pressure and volume loading related to the size of the duct and interatrial communication) assumes increasing significance as age increases beyond 2 months. In patients aged 3 to 6 months, our experience is favorable but too limited to make firm guidelines. We would be prepared to consider a primary arterial switch in such patients provided there was evidence that the LV was still reasonably conditioned (pressure-loaded and/or volume-loaded). In the absence of such evidence, we would favor an atrial switch as a safer approach.

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