ORIGINAL ARTICLES

Transposition of the great arteries: operative outcome in the current era

J Armishaw, *Paediatrician, Tauranga Hospital*; TL Gentles, *Paediatric Cardiologist*; AL Calder, *Paediatric Cardiologist*; PJ Raudkivi, *Cardiothoracic Surgeon*; AR Kerr, *Cardiothoracic Surgeon, Greenlane Hospital, Auckland.*

Abstract

Aims. To assess the operative outcome, cardiac and neurodevelopmental sequelae in infants with transposition of the great arteries (TGA) undergoing the arterial switch operation (ASO).

Method. Cross-sectional review of the 48 consecutive patients operated on in the calendar years 1995 and 1996 was undertaken to obtain recent cardiac, growth and neurodevelopmental parameters, and the mortality results were compared to the entire cohort of infants who underwent the ASO for definitive repair of TGA and double outlet right ventricle at Greenlane hospital between 1984 and 1998.

Results. Between January 1995 and December 1996, 48 patients underwent the ASO. 96% were alive, and 88% alive and free from reoperation or significant neurological sequelae at a mean followup interval of sixteen months. Six (13%) had important residual cardiac lesions, of which supra valvular pulmonary stenosis was the most common. Growth parameters at follow-up were normal, as was the neurodevelopmental progress of all but two survivors (96%).

Conclusion. In the current era, the ASO is a relatively safe procedure with excellent cardiac and neurodevelopmental outcome in the majority of infants.

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Transposition of the great arteries (TGA) is the commonest cause of cyanotic heart disease in the newborn period. Because the aorta arises from the right ventricle and the pulmonary artery from the left ventricle, the systemic and pulmonary circulations function as two separate circuits. Postnatal survival is dependent on mixing of oxygenated and deoxygenated blood via the ductus arteriosus and foramen ovale. Those infants with TGA and no ventricular septal defect develop life-threatening hypoxaemia as the ductus arteriosus closes. Without treatment, most die during early infancy.[1] Early attempts at physiological repair using the intra-atrial baffling procedures of Mustard and Senning significantly reduced mortality.[2] However, atrial baffle procedures were associated with important late sequelae including atrial dysrryhthmia, stenosis of the interatrial pathways[3] and systemic right ventricular dysfunction.[3,4]

Anatomic correction involving relocation of the great arteries and translocation of the coronary arteries to the neoaorta was reported by Jatene in 1976.[5] Initial attempts at the arterial switch operation (ASO) were associated with high mortality, but modifications in the surgical technique, and introduction of repair in early infancy have resulted in a marked decrease in operative risk. Since the mid 1980s, the ASO has replaced the atrial baffle procedure as the operation of choice in repair of TGA with intact ventricular septum, ventricular septal defect (VSD) and double outlet right ventricle with subpulmonary VSD.[6]

At Green Lane Hospital, the ASO was attempted in the late 1970's in a small number of patients. The operation was used in a more routine way from 1984 onward, initially in the subgroup with TGA and VSD, who appeared at greater risk of developing tricuspid valve and right ventricular dysfunction after the atrial switch operation, and later in patients with TGA and an intact ventricular septum.

The ASO is associated with a lower incidence of arrhythmias than the atrial baffle procedure, and with normal post operative systemic ventricular and atrioventricular valvular function.[6] The most common late cardiac complications for survivors are supravalvular pulmonary stenosis[7] and neoaortic valve dysfunction.[8] In this study, we review the operative outcome, and cardiac and neurodevelopmental sequelae in infants undergoing the ASO at our institution between 1995 and 1996.

Methods

Patient selection and data collection. A cross-sectional review was undertaken in a subset of patients who had an ASO between January 1995 and December 1996. Demographic, operative and postoperative data were obtained from a retrospective chart review, and the most recent cardiac, growth and neurodevelopmental parameters were obtained, either during routine review at our hospital, or by letter and phone call to the patient's cardiologist or paediatrician. In addition, early mortality data were collected for patients who had undergone the ASO for primary treatment of TGA and double outlet right ventricle at Green Lane Hospital between 1984 and 1998. Patients who underwent ASO as palliation for single ventricle circulation (n=five), or were converted from an atrial switch (n=two) were not included.

End points. Early mortality was defined as death within 30 days of operation, or during the hospital admission. These data were ascertained from the records of the Departments of Cardiothoracic Surgery and Cardiology.

Operative technique. Cardiopulmonary bypass was instituted through a median sternotomy, excising most of the thymus for exposure and using a single venous cannula in the right atrium. Infants with intact ventricular septum were cooled to 18-22°C. Following aortic cross clamping, a single dose of cold blood cardioplegia was given and the heart cooled with ice slush. Perfusion flows were reduced to 1.2 L/m²/min during coronary transfer and neo-aortic reconstruction. The atrial septum was repaired during a five to ten minute period of circulatory arrest. Substrate enriched (glutamate and aspartate) warm cardioplegia was then infused and following de-airing, the aortic clamp was released. The neo-pulmonary artery was constructed during rewarming with full bypass flows. Infants with VSDs require somewhat long periods of circulatory arrest for repair, but these rarely exceed 30 minutes. Extra cerebral protection was achieved by cooling to 15°C, combined with head cooling with ice.

Peritoneal dialysis catheters were placed for post-operative use. Conventional ultrafiltration during bypass and modified ultrafiltration bypass are now routinely used to improve haematocrit and remove inflammatory mediators.

Statistical analysis. Kaplan Meier survival analysis was used to predict freedom from death and from death and reoperation. Dichotomous variables were compared by t-test, with a p value of < 0.05 considered significant. All results are expressed as a mean ± 1 standard deviation unless otherwise stated.

Results

Patient characteristics. Of the 48 infants operated on between 1995 and 1996, 28 had TGA with intact ventricular septum. Nineteen had TGA with VSD; two of these also had hypoplasia of the aortic arch not requiring surgical correction, one had coarctation of the aorta and one had associated pulmonary stenosis. One patient had double

outlet right ventricle, a subpulmonary VSD and coarctation of the aorta (Taussig-Bing anomaly).

Ventricular septal defects were multiple in two patients. Morphology included subpulmonary (13) and muscular defects (7). The usual pattern of coronary arteries in TGA, with the left anterior descending and the circumflex arising from the left-facing sinus, and the right coronary artery arising from the right-facing sinus, was found in 36 (75%), the circumflex arose from the right facing sinus in five patients (10%), the coronary pattern was inverted in six patients (13%), and there was a single origin of the right, left anterior descending, and circumflex coronary arteries in one (2%). No patient had an intramural coronary artery course.

The mean birthweight of the 48 patients was 3457 ± 508 gm (range 2620-4500 gm). One was born prematurely at 35 weeks gestation, weighing 2620 gm. Important non-cardiac comorbidities included left renal agenesis in one infant, and meconium aspiration syndrome in another. In addition, there were two infants with significant ventricular hypertrophy. Both were infants of diabetic mothers.

Perioperative management. Surgery was undertaken between the first and 367th day of life (median, day nine), with 69% undergoing ASO by day fourteen (Figure 1).
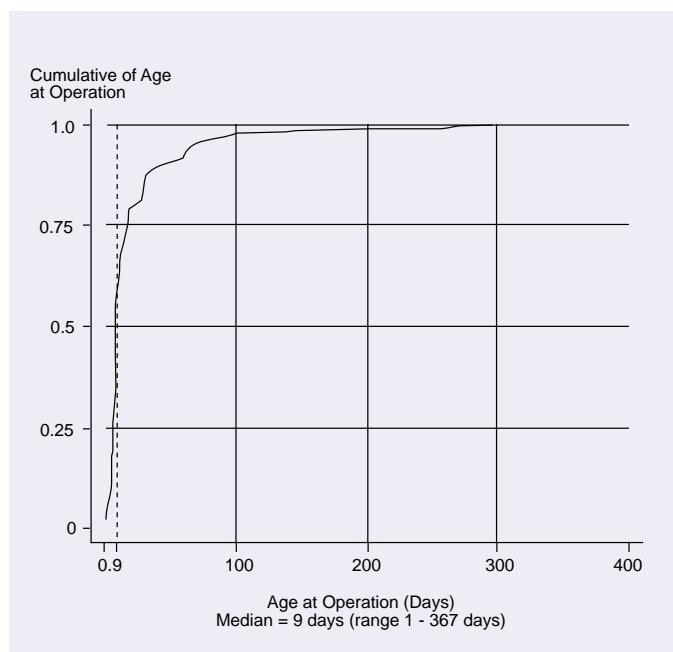

Figure 1. Cumulative age at arterial switch operation in 1995 and 1996.

Preoperative balloon atrial septostomy was undertaken in 33 (69%) infants. Of the remaining patients, twelve had a VSD and one with an intact ventricular septum had an unusually thick atrial septum; balloon atrial septostomy was not attempted and he proceeded to an emergency ASO. A further two infants with TGA and intact ventricular septum were maintained on a prostaglandin E₁ infusion and proceeded to surgery without preoperative balloon atrial septostomy.

Operative and early postoperative results. Early mortality in 1995 and 1996 was one of 48 (2.0%). This is comparable to the early mortality experienced in 1997 and 1998 (one of 37 (2.7%)), and significantly improved, compared to our experience in previous years (Figure 2).

The early death in the 1995 to 1996 cohort occurred in a term 2.8 kg female who died on the second postoperative day with severe hypoxic ischaemic encephalopathy. She was delivered by emergency caesarean section for foetal distress and remained acidotic and difficult to ventilate preoperatively despite a prostaglandin E₁ infusion and balloon atrial septostomy. Operation was uneventful; perinatal asphyxia may have contributed significantly to her poor outcome, although an intra-operative event may also have been responsible. There were a total of 26 other events in the immediate post operative period, affecting 20 infants (Table 1). Operative parameters are detailed in Table 2. Five (10%) infants required greater than seven days ICU care, and six (12%) infants were hospitalised for more than 21 days after operation (Table 3).
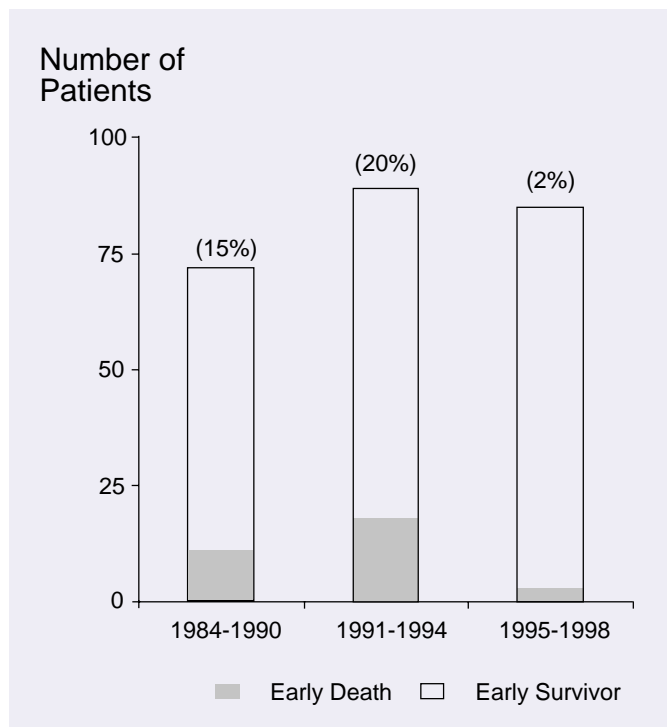

Figure 2. Early mortality grouped by four yearly intervals, excepting 1984 to 1990 where numbers were small. Numbers in brackets indicate the percentage of early deaths.

Table 1. Early postoperative events (1995 and 1996; n=47).

Event	Number
Tamponade*	5 (11%)
Arrythmia†	6 (13%)
Sepsis	8 (17%)
Seizures	4 (9%)
Acute renal failure	2 (4%)
Chylothorax	1 (2%)

* Requiring sternotomy
† Requiring anti-arrhythmic treatment or electrical cardioversion
Several patients had more than one event.

Table 2. Operative parameters (1995 and 1996).

	Time (mean ± 1 SD)
Total bypass time	155 ± 47 min
Cross clamp	80 ± 19 min

SD = standard deviation

Table 3. Post operative parameters (1995 and 1996).

	Median (days)	Range (days)
Intensive care stay	4	1-28
Inotropes	3	0-13
Ventilation	3	1-21
Total postoperative hospital stay	12	8-40

Late Complications. In the 47 survivors, there were a total of 783 months of clinical follow-up (16.1 ± 7.4 months, range 2.5-31 months). At the time of cross sectional review, 46 patients (96% of the study cohort) were alive and accounted for, and 42 (88%) had not required reoperation and were neurologically normal (Figure 3). Two years after operation, the actuarial probability of survival was 94% and the probability of freedom from death and reoperation was 88% (Figure 4).
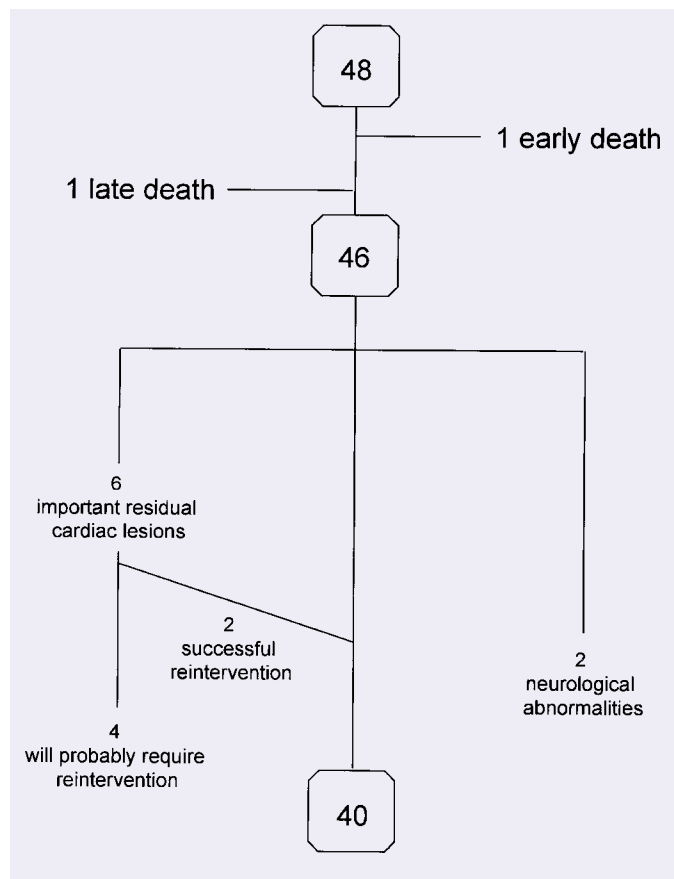

Figure 3. Summary of clinical outcome in the 1995 and 1996 cohort. 40 patients were neurologically normal with no significant cardiac residua at the time of the review.
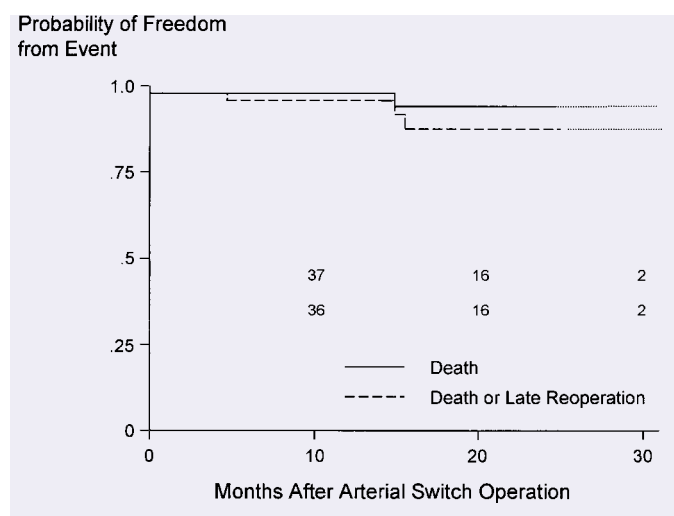

Figure 4. Actuarial plot showing probability of freedom from event (death and late reoperation) in the 1995 and 1996 cohort.

There was one late death. This occurred in a fifteen-month-old male, who underwent uneventful ASO and closure of his VSD at one week of age. An echocardiogram at eleven months of age suggested pulmonary artery hypertension. At cardiac catheterisation, pulmonary vascular resistance was markedly elevated and there was thrombosis of the right jugular vein. Of the remaining 46 patients, six have significant cardiac residua. Two infants have required re-intervention. The first has undergone repair of a false aneurysm of the right ventricular outflow tract, four months after repair of TGA and a VSD. At nineteen months of age, she is asymptomatic with no significant residual cardiac anomaly. A second infant required balloon angioplasty of her right pulmonary artery at seventeen months of age. At the time of cross-sectional follow-up, she was asymptomatic with moderate right pulmonary artery and mild left pulmonary artery stenosis. There are four patients with significant supra valvular pulmonary stenosis (right ventricular outflow tract maximum instantaneous gradient > 50 mmHg) who will likely require further intervention. One of these infants also developed severe left main coronary artery stenosis and severe left ventricular dysfunction, several months after the ASO operation. Intervention was not attempted; ventricular function improved over a twelve month period and is now normal.

In addition, one infant has left main bronchus compression. He is now 30 months old, and has had recurrent respiratory tract infections, but growth and development are normal.

Growth and neurodevelopmental outcome. Height and weight of the 46 patients alive at the time of cross-sectional follow-up are similar to those of the normal population (weight z-score 0 ± 1.2, height z-score 0.3 ± 1.2 percentile, p = not significant for both). 44 patients were assessed by their paediatrician or cardiologist as having normal developmental milestones. The other two patients have significant neurological sequelae.

The first is now seven months of age and has cerebral palsy with spastic quadriplegia. He had significant birth asphyxia, having been born by emergency caesarean section for foetal distress at term. Meconium was present during delivery, scalp pH indicated significant acidosis and Apgars were one and four at one and five minutes. He required ventilation preoperatively and operation was unremarkable. Abnormal neurological behaviour was evident in the post-operative period and a CT scan demonstrated widespread cerebral and brain stem ischaemic changes.

The second child has mild right arm hemiplegia and expressive speech delay at sixteen months of age. He presented aged nine days with marked cyanosis and congestive cardiac failure. He had several focal right-sided seizures in the preoperative period. Internal cardiac massage was required during the immediate postoperative period, and recovery involved a one month stay in intensive care.

Discussion

Medium term survival after the ASO in 1995 and 1996 was excellent, with 96% survival at a mean follow-up interval of sixteen months. This compares favourably with results from other centres. Wernovsky and associates reported a ten year survival rate of 91%.[6] Survival rates at one month and eight years among 470 patients were 93% and 91% respectively. The hazard function for death declined rapidly in the first postoperative year and approached zero by twelve months,[6] indicating little risk in the longer term. Earlier studies of the ASO in TGA reported a mortality as high as 35% in the first three years of institutional experience,[9-11] consistent with the early mortality demonstrated in our earlier experience. This phenomenon is indicative of the steep surgical and

institutional learning curve necessary to master a technically demanding operation, and to manage the critically ill infant in the immediate postoperative period. In addition to absolute numbers, annualised case volume is probably also important; a recent report from smaller institutions in North American indicates a mortality approaching 15%, even in the current era.[12] The reduction in mortality is most likely reflective of cumulative surgical and institutional experience, and coincided with a trend toward subspecialisation within the team of medical, nursing and technical staff responsible for the care of these infants. A detailed analysis of factors responsible for this trend is currently underway.

In our cohort, 12% of infants had important residual cardiac defects. Two of these infants have required reoperation, and another four, with supravalvar pulmonary stenosis, may do so in the coming years. Supravalvular pulmonary stenosis is a commonly recognised complication following the arterial switch operations. The pulmonary arteries are moved anterior to the neoaorta, and tension, particularly during the time of rapid growth in infancy and early childhood, can result in narrowing of the main pulmonary artery and proximal branch pulmonary arteries. Because the mechanism of the stenosis is usually tension, transcatheter balloon pulmonary angioplasty is frequently unsuccessful, and reoperation is required. In our experience, the incidence of this complication has decreased following more aggressive augmentation of the pulmonary anastomosis with pericardium, and is similar to that reported elsewhere.[13]

Coronary artery stenosis or occlusion is rare after the ASO,[14,15] and left ventricular size and function are almost always normal.[16] One patient in our series had severe proximal left coronary arterial stenosis, presumably a consequence of tension on the coronary artery after reimplantation. Left ventricular function was severely impaired, but progressively recovered. Earlier in our experience, another patient had a similar clinical course with severe heart failure and then a gradual recovery of function. Others have reported cases of asymptomatic coronary occlusion detected late after ASO in patients with normal ventricular function.[15] It appears that coronary artery collateral formation is rapid in young hearts, and that severe myocardial ischaemia may be associated with myocardial stunning, rather than necrosis. Although late sudden death has been reported after the ASO, late coronary complications are rare.

The one late death in our series occurred as a result of progressive and intractable pulmonary hypertension. The reason for this is not clear. There was jugular vein thrombosis, probably secondary to central line placement, and recurrent pulmonary microthrombi may have been responsible. Pulmonary vascular disease was not an uncommon late sequelae in patients with TGA and VSD in the era of the atrial switch operation, when definitive surgery was postponed until later in infancy.[17] This infant's ASO and VSD closure were undertaken at one week of age; pulmonary vascular disease in response to increased pulmonary blood flow and cyanosis in these circumstances would be extraordinarily unusual.

Despite a presentation that is frequently associated with significant hypoxia and major cardiac surgery in early infancy, height and weight were normal at follow-up. Furthermore, the majority of late survivors (96%) are neurodevelopmentally normal. Neurological outcome is an important endpoint that has recently been linked to the duration of circulatory arrest.[18] Because of this, we have limited the use of circulatory arrest as far as is possible. Importantly, all three of the infants with major neurological complications had pre-operative risk factors for an adverse neurologic outcome. It is likely that improved recognition of cyanotic heart disease and more rapid treatment with prostaglandin E_1 will reduce the incidence of neurological deficit in these children.

In conclusion, the ASO has been used for the definitive repair of TGA at Green Lane Hospital for more than a decade. During our initial experience, this operation was associated with significant early mortality, but in the current era, early mortality has been low. At a mean follow-up interval of sixteen months, 96% of patients operated on in 1995 and 1996 are alive and 88% are free from death, reoperation and significant neurological sequelae. These results indicate that the ASO is a relatively safe procedure, with an excellent cardiac and neurodevelopmental outcome in the majority of infants. Further improvements in outcome will, to a large part, be dependent on an increased awareness of cyanotic heart disease, early diagnosis, and early transfer to the paediatric cardiac surgical centre.

Correspondence. Dr Tom Gentles, Cardiology Department, Green Lane Hospital, Greenlane Road, Greenlane West, Auckland. Fax (09) 631-0703; email: tomg@ahsl.co.nz

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One dark rainy night our good friend Walter was called out to see a woman with suspected cholecystitis. Arriving at the house, he was greeted by a large and enthusiastic dog, who rose from a puddle to spatter mud, water, and hair all over W. Door opened in response to frantic knocking. Dog bounded upstairs and leaped on patient's bed - transferring more mud, hair, to patient. Examination was difficult with dog sprawled over patient's abdomen. Finally, in exasperation, W said "Would you mind terribly if we asked your dog to wait outside?" "*My* dog" groaned the patient, "I thought it was *your* dog!"

In England Now - Fifty years of peripatetic correspondence in The Lancet. Hodder & Stoughton, 1989. p86.