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## Outcomes of 829 neonates with complete transposition of the great arteries 12–17 years after repair<sup>☆</sup>

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### Abstract

**Objective:** Between 1985 and 1989, the surgical management of neonates with complete transposition (TGA) underwent a transition from atrial to arterial repair. We sought to examine the intermediate outcomes and their associated risk factors in neonates repaired during the era of transition. **Patients and methods:** Twenty-four institutions entered 829 neonates age less than 15 days in a prospective study. Diagnosis was simple TGA ( $n = 631$ ), TGA with ventricular septal defect (VSD) ( $n = 167$ ), TGA with VSD and pulmonary stenosis (TGA/VSD/PS) ( $n = 30$ ), or TGA with PS ( $n = 1$ ). Repair was by arterial switch ( $n = 516$ ), atrial repair (Senning = 175, Mustard = 110) or Rastelli ( $n = 28$ ). Time-related events were analysed by parametric hazard function modeling and incremental risk factors for mortality, re-intervention, and late functional assessment were sought. **Results:** Survival estimates at 6 months, 5, 10, and 15 years are 85, 83, 83, and 81%, respectively. The hazard function for death after repair has two phases: an early rapidly declining phase and an ongoing constant one. Constant phase mortality is less likely after the arterial switch operation and in children with simple TGA. During follow up, at least one re-intervention was required in 167 children (pacemaker,  $n = 35$ ; percutaneous intervention,  $n = 32$ ; baffle re-intervention,  $n = 27$ ; re-operation,  $n = 125$ ). Freedom from re-intervention at 6 months, 5, 10 and 15 years is 93, 82, 77, and 76%, respectively. Of survivors, 87% have been followed up to the last 3 years, including an assessment of functional ability of 562 children (83%). Functional class 15 years after repair is class I in 76%, II in 22%, III in 2%. The proportion in functional class I decreased over time. Psychosocial deficits, especially learning disorders are prevalent. **Conclusions:** Survival 15 years after TGA repair is good with most children functioning well, and results are best after an arterial switch operation. There is an ongoing risk of death that is less after the arterial switch operation. With the exception of Rastelli patients, the likelihood of survivors needing re-intervention after 5 years is low. There is need for improved neurodevelopmental outcomes.

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**Keywords:** Transposition; Outcome; Functional assessment; Neurodevelopment; Reintervention; Multi-institutional

### 1. Introduction

The management of newborns with complete transposition (TGA) has evolved with the ongoing development of paediatric heart surgery. The outcomes for these infants changed from a natural history of early certain death to a

high probability of long-term survival approaching that for normal children. An important change in the management protocol for most neonates with TGA occurred during the late 1980s from predominantly an atrial type of repair to an arterial repair. The Congenital Heart Surgeon's Society (CHSS) initiated a prospective clinical study in 1985 to study the impact of this change in management strategy. The years of the study encompass what was to become the end of the atrial repair era and the beginning of widespread application of the arterial switch operation (ASO). Six previous reports from the CHSS data center have examined

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risk factors for early outcomes in various cohorts including the importance of an associated ventricular septal defect (VSD) and type of repair (1987,  $n = 245$ ), management of simple TGA (1988,  $n = 187$ ), and intermediate outcome after Mustard and Senning procedures (2000,  $n = 286$ ) [1–3].

In this report we examine the 12–17-year follow-up of all 829 neonates with repair of TGA in the 1985–89 era and entered into the CHSS study. We examine their intermediate survival, prevalence of re-intervention and functional outcomes.

## 2. Materials and methods

Newborns admitted with TGA at age < 15 days to one of 24 CHSS institutions were entered prospectively between January 1, 1985 and March 1, 1989. Treatment was not assigned or randomized but rather was selected by the physicians caring for the children on the basis of their knowledge and experience. Infants with major associated lesions such as univentricular heart, atrioventricular septal defect and atrioventricular discordance were excluded. The present study includes 829 neonates who underwent definitive repair.

### 2.1. Death before repair

Neonates who died prior to definitive repair are excluded from this report ( $n = 34$ ), and this issue was considered in previous publications [1,2]. Among the neonates entering an institution with an arterial switch protocol, there were 13 deaths prior to that repair. These 13 deaths account for a 2.5% mortality prior to repair. The deaths occurred at a median age of 4 days (range 0–31 days). Among neonates admitted to an atrial repair protocol, there were 14 deaths prior to the repair, a mortality rate of 4.7%. Their median age at death was 9.5 days (range 0–155 days) with five of the 13 deaths occurring beyond age one month. Mortality rate prior to repair was higher (15.2%) among those neonates who were candidates for a Rastelli repair. Two deaths prior to repair occurred in patients with important pulmonary stenosis and no ventricular septal defect.

### 2.2. Morphology and repair technique

The diagnostic categories of the 829 neonates included in the study are simple TGA in 631, TGA/VSD in 167, TGA/VSD/pulmonary stenosis (TGA/VSD/PS) in 30, and TGA/PS in one child. The operative management included an arterial switch (ASO) in 516, an atrial repair in 285 (Senning 175, Mustard 110), and a Rastelli operation in 28. Cross-tabulation of diagnosis and operation is shown in Table 1. There were 108 early deaths after repair (within 30 days of repair or prior to hospital discharge), and 43 children died later. Operative mortality for the ASO is

Table 1  
Diagnosis and type of repair for 829 neonates

| Diagnosis  | Repair type |         |         |          | Total |
|------------|-------------|---------|---------|----------|-------|
|            | Arterial    | Senning | Mustard | Rastelli |       |
| Simple TGA | 383         | 150     | 98      |          | 631   |
| TGA/VSD    | 131         | 23      | 10      | 3        | 167   |
| TGA/VSD/PS | 2           | 1       | 2       | 25       | 30    |
| TGA/PS     |             | 1       |         |          | 1     |
| Total      | 516         | 175     | 110     | 28       | 829   |

14.9%, for atrial repair 10.5% (Senning 14.2%, Mustard 3.6%) and for Rastelli, 7.1%.

### 2.3. Follow-up

Cross-sectional follow-up of hospital survivors was attempted annually except between the years 1995 and 1998 when the data centre was in transition from Birmingham to Toronto. The most recent cross-sectional follow-up was between January and March of 2002. During annual follow-up for the 3 years 2000 to 2002, 590 of the known 678 current survivors (87%) were contacted and 562 of them answered a questionnaire. The 13% of the children not contacted after 2000 were followed a median of 7.9 years (range 0.8–11.1 years). Patients who could not be contacted during the cross-sectional follow-up period were censored in the analysis at the last known follow-up date. The median follow-up for the 721 hospital survivors is 13.8 years (range 1 month to 17.2 years).

### 2.4. Informed consent

A parent or the child completed a two-page follow-up questionnaire that included information about medication, functional ability, development, pacing, and any voluntary comments. The form also includes a consent section requesting written permission to include the child in the study and to obtain pertinent medical records. Informed consent had not been requested nor even considered at the inception of this observational study. The institutional review board of the Hospital for Sick Children approved the research application of the CHSS data centre, and each participating institution sought approval for their participation from their own review board. The data centre contacted the majority of the patients (72%) and those institutions that preferred to do their own follow-up did so.

### 2.5. Data collection and analysis

For each patient, pertinent copies of the hospital chart for each admission, including reports of diagnostic and imaging studies, operations and catheter-based interventions, and any autopsy as well summaries of pre- and post-operative

care were forwarded to the CHSS data centre. The data centre staff maintain strict confidentiality and created computerized records for each child.

All analyses were performed using SAS statistical software, version 8 (SAS Institute Inc., Cary, NC). Data are described as frequencies, medians with ranges, or means with standard deviations as appropriate. The number of non-missing values is given for descriptive analyses. Missing data that occurred sporadically and at random were managed in multivariable analysis by non-informative imputation of mean value and formation of an indicator variable that was used in analyses for determining if patients with missing values behaved differently with respect to outcome compared to patients with values present.

Time-related freedom from death and re-intervention focusing on late events was studied by hazard function analysis. Non-risk adjusted non-parametric estimates of time-related outcome events (death and re-operation) were obtained by the Kaplan–Meier method. Parametric estimates were obtained by modelling the hazard function and searching for multiple phases of risk and the characteristic equation for each phase.

Demographic, morphologic, institutional, and surgical risk factors associated with late-phase death or re-intervention including re-operation were sought by multivariable modelling of the parametric hazard function using the variables noted in Appendix A. Variables associated with fewer than five events were eliminated from consideration to minimize the risk of model over-determination. Bootstrap bagging was used for risk factor selection and model validation [4,5]. One thousand bootstrap datasets of the same size as the original dataset were analysed by automated stepwise regression with inclusion criterion of  $P < 0.1$ .

Functional classification was assigned to each child from the annual follow-up questionnaire using the following criteria:

- Class I: asymptomatic on no medication and as much energy as their peers
- Class II: mild limitation, less energy than previously or than their peers or requiring 1 medication
- Class III: moderate symptoms, less energy or  $> 1$  medication
- Class IV: worse than the above

Factors associated with longitudinal changes in functional class were explored initially using ordinal logistic analysis to screen variables for entry into multivariable models, including transformations of time since repair. Candidate variables were then entered into an ordinal logistic repeated-measures regression analysis, and eliminated one by one until only variables with  $P < 0.05$  remained. For significant variables, interactions with time were explored.

Multiple logistic regression analysis was used to identify risk factors for learning deficits.

### 3. Results

#### 3.1. Long-term survival

To date, 151 children have died, including 108 (13.0%) who died in hospital early after repair and 43 that died later. Survival estimates 6 months and 15 years after repair are 85 and 81%, respectively (Fig. 1A). The hazard function illustrates the high and rapidly declining early risk with a lower ongoing constant risk (Fig. 1B).

By univariate stratification of time-related survival by morphology, the 15-year survival for the neonates with TGA/VSD/PS is 93%, for those with simple TGA is 83%, and for those with TGA/VSD is 72% (Wilcoxon  $P = 0.003$ ). By multivariable analysis survival is better for neonates with simple TGA compared to that for other morphology.

Survival estimates stratified by type of operation illustrate significant differences in overall survival at 17 years by univariate analysis (Mustard 94%, Rastelli 89%, Arterial switch 81% and Senning 74%) (Wilcoxon  $P = 0.001$ ). However multivariable analysis for late hazard risk of death revealed that only the Senning operation ( $P < 0.001$ ) and morphology other than simple TGA ( $P = 0.003$ ) is associated with an increased risk of late death

A comparison of all 516 children managed by an arterial switch operation with the 285 managed by an atrial repair reveals an almost identical 15-year survival of 81 and 82%, respectively (Fig. 2A). However, the hazard function illustrates that while the early phase is higher for the arterial switch patients (in that era), the ongoing constant phase risk of death is higher for the atrial repair group. (Fig. 2B) There appears to be a crossover of mortality that will occur soon after 17 years.

#### 3.2. Re-intervention

Following repair, 167 children underwent some type of re-intervention, either catheter-based ( $n = 32$ ), pacemaker ( $n = 35$ ), or surgery ( $n = 125$ ). Freedom from re-intervention at 6 months and 15 years is 93 and 76%, respectively, and is stratified by operative type (Fig. 3).

##### 3.2.1. Re-operations

Important re-operations were more likely to occur in children with a VSD if they had undergone an atrial repair, but not after the arterial switch operation (Table 2). Due to conduit deterioration, the risk of re-operation is much higher after a Rastelli operation than after either an arterial switch or atrial repair. Time-related freedom from re-operation determines that 82% are free of re-operation within 15 years of repair. Incremental risk factors for re-operation are listed in Tables 3 and 4.

##### 3.2.2. Interventional catheterization

All operative groups are experiencing a similar

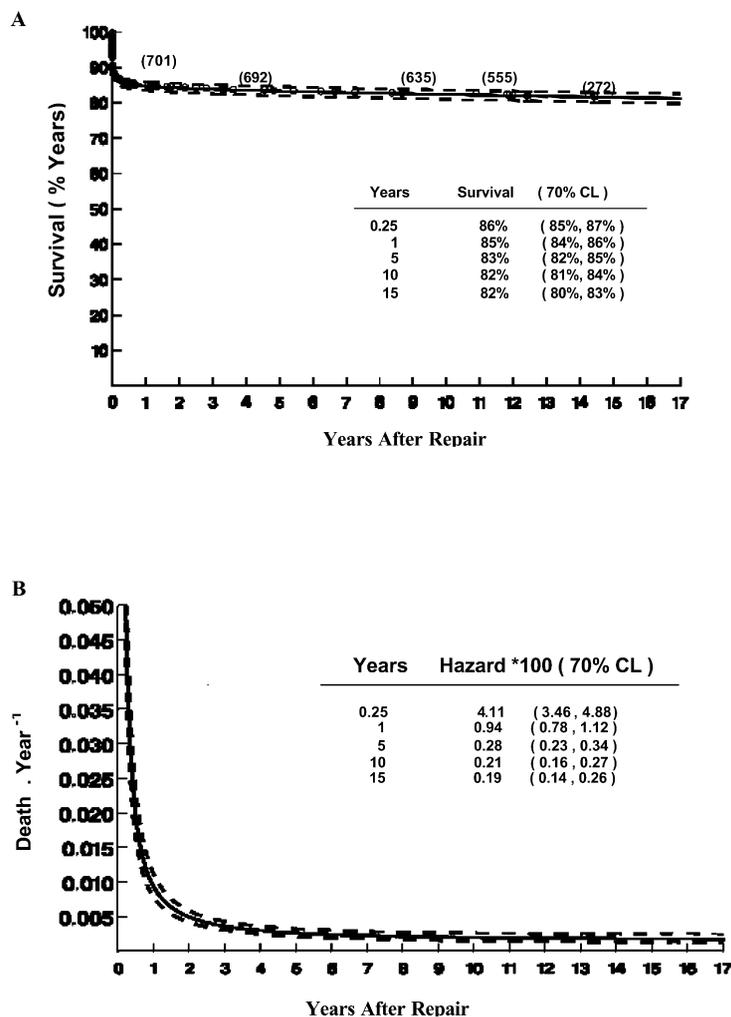


Fig. 1. (A) Overall survival after repair. Each circle represents an actual death, positioned at the time of death along the horizontal axis and actuarially (Kaplan–Meier) along the vertical axis. The vertical bars represent its 70% confidence interval. The numbers in parentheses indicate the numbers of patients still at risk at the time of the estimates. The solid line represents continuous point estimates by the parametric estimate of survival and is enclosed within its dashed 70% confidence intervals. (B) Hazard function representing instantaneous risk of death at each moment in time after repair. Solid line represents the hazard function. Dashed lines enclose the 70% confidence interval.

prevalence of catheter-based re-interventions of 5–10% within 15 years after repair, and along similar time lines. Re-intervention for baffle stenosis or leak after an atrial repair was required in 27 children, 12% of the children followed 15 years after repair. There is no statistically important difference for either type of atrial repair (10% for Mustard patients, 13% for Senning).

### 3.2.3. Pacemaker implant

Freedom from permanent pacing 15 years after repair is 98% for the arterial switch patients and 89% after an atrial repair. A pacemaker implant was more likely among children with a VSD ( $P = 0.019$ ). Pacemaker implant after an arterial switch was required in eight children (1.8% of operative survivors). Seven of these eight had a VSD. Pacemaker implant after an atrial repair was needed in 23 children (9%), and did not occur until after 1 year from

repair, with a steady increase of pacemaker implantations from 1 to 11 years after atrial repair. Incremental risk factors for insertion of permanent pacemaker occurring after repair are a non-arterial type repair ( $P < 0.001$ ) and presence of a VSD ( $P = 0.005$ ).

### 3.3. Functional assessment

Overall changes in functional class are shown in Fig. 4. Multivariable analysis showed a quadratic relationship with time, with functional status slowly decreasing and then improving in the adolescent years ( $P < 0.001$ ). Other significant independent variables affecting functional status include arterial switch repair and the presence of ventricular septal defect. The arterial switch patients had significantly greater functional status throughout compared to all other repair types ( $P < 0.001$ ). There was an interaction with time

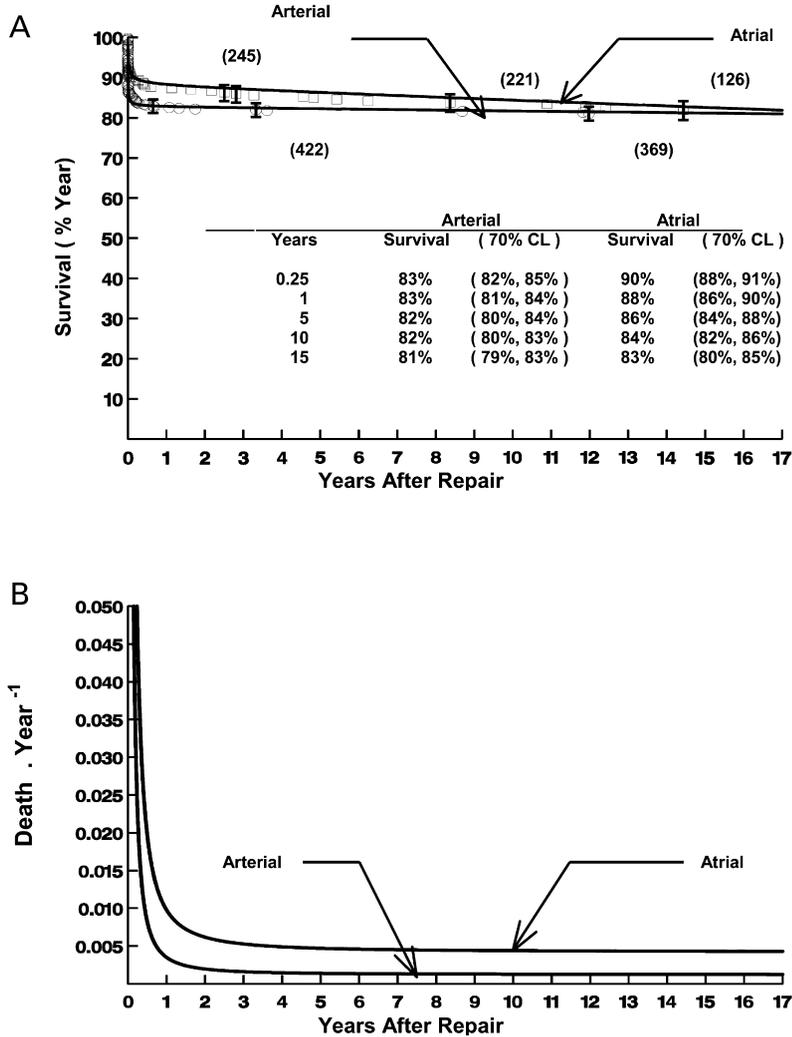


Fig. 2. (A) Survival after repair stratified by arterial or atrial repair. The circles and squares represent deaths and are positioned by Kaplan–Meier estimate stratified according to arterial and atrial repair. Vertical bars represent its 70% confidence interval. The numbers in parentheses indicate the number of patients still at risk at the time of the estimates. Solid lines represent the predicted time-related survival for each group. (B) Hazard function representing instantaneous risk of death at each moment in time after repair. Solid line represents the hazard function. Dashed lines enclose the 70% confidence interval.

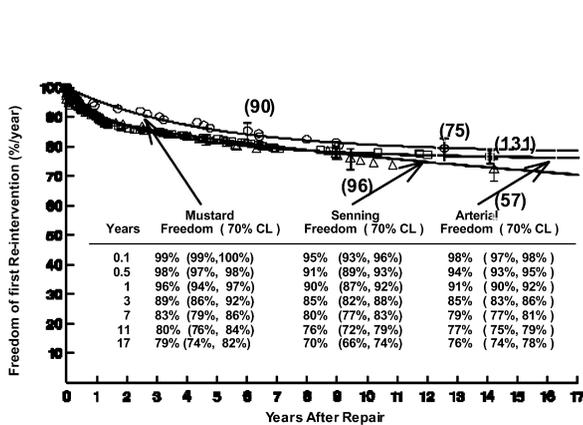


Fig. 3. Freedom from first re-intervention stratified by repair. The squares, circles and triangle represent events that are positioned by Kaplan–Meier estimate stratified according to arterial, Mustard and Senning. Vertical bars represent its 70% confidence interval. The numbers in parentheses indicate the number of patients still at risk at the time of the estimates. The solid lines represent the predicted time-related freedom for each.

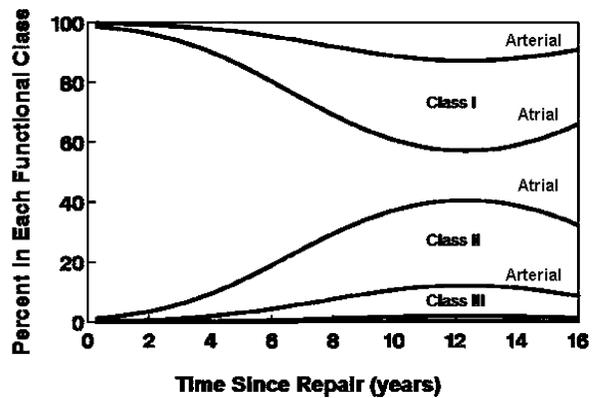


Fig. 4. Time-related change in functional class. Symbols represent the proportion of patients in each functional class in 1-year intervals. Solid lines represent the solution for the ordinal logistic longitudinal repeated measures model with only time as a variable, with the dashed lines representing the 70% confidence interval. The graph illustrates the significant difference in functional class, as reported by their parents, between children having an atrial compared to an arterial repair.

Table 2  
Important re-operations occurring after definitive repair of TGA listed by repair type

|   |    |
|---|----|
| <i>Arterial switch (n = 79):</i>                |    |
| Relief of PS                                    | 58 |
| Closure of ASD                                  | 5  |
| Relief of PS and closure of ASD                 | 4  |
| Repair of recurrent coarctation                 | 3  |
| Closure of VSD                                  | 2  |
| Relief of AS                                    | 2  |
| Relief of AS and PS                             | 2  |
| Relief of subaortic stenosis                    | 1  |
| Repair of pulmonary artery aneurysm             | 1  |
| Aortic valve replacement                        | 1  |
| <i>Senning operation (n = 23):</i>              |    |
| Baffle revision                                 | 12 |
| Takedown  | 2  |
| Relief of sub-PS                                | 2  |
| Repair of recurrent coarctation                 | 2  |
| Relief of PS and mitral valve repair            | 1  |
| Relief of PS                                    | 1  |
| Closure of VSD                                  | 1  |
| SVC thrombectomy and baffle revision            | 1  |
| Heart transplant                                | 1  |
| <i>Mustard operation (n = 11):</i>              |    |
| Baffle revision                                 | 6  |
| Relief of PS                                    | 2  |
| Conversion to arterial switch operation         | 1  |
| Tricuspid valve repair                          | 1  |
| Tricuspid valve replacement and baffle revision | 1  |
| <i>Rastelli operation (n = 12):</i>             |    |
| Conduit replacement                             | 7  |
| Revision of VSD baffle                          | 4  |
| Relief of non-conduit PS                        | 1  |

PS, pulmonary stenosis; ASD, atrial septal defect; VSD, ventricular septal defect

for patients with associated VSD alone, with initially poorer functional status that improved more than for patients with predominately simple TGA ( $P < 0.001$ ).

### 3.4. Psychosocial deficits

In the annual questionnaire for the years 2000–2002 the parents reported that 173 of the children (31%) have

Table 3  
Incremental factors increasing the risk for time-related re-operation

| Risk factor                      | P-value | Frequency (%) |
|----------------------------------|---------|---------------|
| LVOT procedure at initial repair | 0.002   | 79%           |
| Non-simple TGA                   | <0.001  | 82%           |
| Rastelli operation               | 0.058   | 27%           |
| Major non-cardiac anomaly        | 0.074   | 48%           |
| Senning operation                | 0.092   | 24%           |
| Institution 13                   | <0.001  | 93%           |

Table 4  
Incremental risk factors for the presence of learning disorders at latest follow-up

| Risk factors                        | Parameter estimate $\pm$ SE                                   | P-value |
|-------------------------------------|---|---------|
| Presence of post-operative seizures | 1.28 $\pm$ 0.47   | 0.007   |
| Longer TCA duration <sup>a</sup>    | 3 $\times$ 10 <sup>-4</sup> $\pm$ 6 $\times$ 10 <sup>-5</sup> | <0.001  |
| Use of repair other than ASO        | 0.63 $\pm$ 0.20   | 0.002   |
| Institution 7                       | 1.43 $\pm$ 0.47   | 0.003   |
| Not Institution 13                  | 0.78 $\pm$ 0.34   | 0.02    |

TCA, total circulatory arrest; ASO, arterial switch operation. Hosmer–Lemeshow goodness-of-fit test,  $P = 0.56$ .

<sup>a</sup> Entered after square transformation.

learning disabilities. Other deficits reported by the parents are behavioural disorders (13%), hyperactivity (12%), and cerebral palsy (3%).

Independent risk factors identified that increased the likelihood of learning disability are a longer duration of circulatory arrest, the presence of post-operative seizures, repair type other than arterial switch operation, and two specific institutions (one of which was protective).

## 4. Discussion

Our prospective clinical study of neonates with TGA is unique in several ways. Because it is multi-institutional, we were able to accumulate a large cohort of children during a relatively short interval of 4 years. In addition, the study was initiated during an era that a major transition in surgical management occurred.

Neonates born today with simple TGA or TGA/VSD are managed by the arterial switch operation in the neonatal period. The era of this study was the transition away from an atrial type of repair to the arterial switch operation. The follow-up of these children provides a comparison of outcomes for different surgical management protocols from that era. The clinical series includes the initial experience with the arterial switch operation, the so-called learning curve, when the operative risk was 15%, considerably higher than in the present era. In contrast, the techniques of atrial repair were well established and the operative risk lower, especially for the Mustard operation, 3.6%. The early results and risk factors affecting survival have been presented in previous CHSS publications [1,2]. The operative survival of the arterial switch operation for neonates with TGA currently is superior to atrial repair techniques, an outcome that was predicted as early as the 1988 CHSS publication [2].

In comparing the survival outcome of these protocols for neonates born with TGA, it is important to consider deaths prior to an intended repair. Because the ASO is performed in the neonatal period, one would expect lower mortality risk prior to repair. However, even among the ASO group, there were 13 deaths prior to repair, and the mortality risk

compared to the atrial group (2.5 versus 4.7%) is only 2.2% different.

Late survival of these children, 81% at 17 years, is a remarkable improvement over the natural history whereby 80% would die in the first month of life. There is a small immutable risk of late death, and the ongoing constant hazard for death after the arterial switch operation is significantly less than for atrial repair although survival at 17 years is identical either with an arterial or an atrial operation. (Fig. 2A,B).

There is ample literature demonstrating that systemic ventricular dysfunction late after an atrial repair is progressive [6–9]. There is also optimism that ventricular function is preserved late after an arterial switch [10–12]. Late arrhythmia, including sudden unexpected death is also far less prevalent after the arterial switch than after an atrial repair [13]. It is not entirely clear to us why the functional class in our patients, as reported in the questionnaire completed by their parents, improved during adolescence, nor why the improvement was more impressive among the children with a VSD. For the atrial repair patients, the absence of a late rise in hazard for death and the functional improvement observed in adolescence, make it difficult to consider recommending either a switch conversion or a transplant within the first 17 years post repair.

In comparing the two atrial repair operations, early and late survival and the prevalence of re-operation is significantly better in the Mustard patients, either for simple TGA or TGA/VSD as reported previously by Wells [3]. These differences are not surprising given the historical sequence of the operations. Mustard's contribution followed Senning's by 5 years but was technically simpler and reproducible by other surgeons. By multivariable analysis, only the Senning operation and non-simple TGA morphology are identified as risk factors for late phase death. Other comparisons of these two operations from single institutions are confounded by the fact that the operative series were not concurrent.

Neonates with TGA/VSD/PS undergo intra-cardiac repair at an older age, and their mortality risk prior to repair is substantial (15.2%). Repair consists of connecting the left ventricle to the aorta via the VSD and construction of conduit between the right ventricle and pulmonary artery as described by Rastelli and modified by LeCompte and others [14–16]. Only 28 children (3.4%) in our series, including three with VSD but no PS, underwent this type of repair and their survival is excellent. The prevalence of TGA/VSD/PS is under-represented in this series because children with these associated lesions may not present until after age 2 weeks. Pulmonary conduit failure requiring re-operation compromises their late result.

The prevalence of re-intervention is predictably higher for the Rastelli operation, given the necessity of conduit replacement. Baffle-related complications and arrhythmia are the usual indications for re-intervention after an atrial repair, and are more likely after a Senning than a Mustard

repair. After an arterial switch operation, right ventricular outflow stenosis is the most common indication for re-intervention [17]. We have not observed late re-intervention for coronary artery stenosis after the arterial switch, but it may be overlooked without specific investigation including coronary angiography [18,19]. As in other studies, growth of the neo-aortic valve and new left ventricular outflow tract is usually normal [20]. Late neo-aortic valve insufficiency leading to re-operation is also rare and to date has occurred in only one child in our series, in whom a Ross operation 10 years after the TGA repair failed, and led to re-replacement of the aortic valve with an allograft.

In the annual follow-up questionnaire, some parents reported a decrease in their child's functional ability. The change in functional ability is much more evident among the atrial repair group, and by inference from the literature, is probably due to failing systemic ventricular function, arrhythmia and tricuspid valve regurgitation. But a decrease in functional ability is also seen to a lesser extent among the arterial switch patients and the mechanism accounting for this gradual change is not known. These observations parallel a study we conducted using a Child Health Questionnaire that was completed by a cohort of 310 of these children after TGA repair (Culbert et al., in preparation).

An alarming finding in this study is the high prevalence of psychosocial deficits as reported by the parents, especially learning difficulties. Studies from Boston 1 year after the arterial switch identified learning, speech and developmental delay in children who had been randomized to have circulatory arrest or hypothermic bypass with hemodilution to 20% and the alpha stat strategy [21,22]. Bellinger reported that the use of circulatory arrest was associated initially with worse motor coordination, but by 8 years of age, both groups had a lower than anticipated IQ. They correlated lower IQ and academic achievement with worse psychosocial health. Hovels-Gurich studied 33 children 3–4.6 years after an arterial switch and demonstrated that circulatory arrest and low flow bypass is associated with neurologic impairment [23]. Recent studies suggest that higher hematocrit and use of pH-stat perfusion techniques may reduce the incidence of developmental delay after circulatory arrest or continuous hypothermic bypass [24]. In our study, the pH strategy did not correlate with late developmental deficit, although institutional differences, both positive and negative were independent risk factors affecting the prevalence of learning disorders. The duration of circulatory arrest is also a predictor of learning deficit. Forbess found that arrest periods exceeding 39 min were associated with deficits of visual-motor and fine motor skills and possibly with full-scale IQ [24]. We could not identify a 'cut-point' (i.e. a point at which any period of circulatory arrest was either safer or more dangerous) that affected this outcome. The use of circulatory arrest should be limited.

#### 4.1. Limitations of the study

While the advantages of a multi-institutional enrolment of patients is evident in accumulating a large experience during a short interval, the Data Center relies on voluntary institutional patient enrolment. The Data Center did not audit the institutional enrolment but are grateful for the enormous cooperation the participating institutions provided. Once patients were identified, often prior to surgical intervention, all were followed to definitive therapy or death.

The age at admission to a CHSS institution was limited to < 15 days. Therefore we have no information regarding the outcomes for babies with transposition who present later.

Although follow-up data was known by completed questionnaire for 83% of the children, and the recent status of another 4% was known, 13% of the cohort had less complete follow-up albeit a mean of 7.9 years after repair. Unknown events that may have occurred among these children could affect the analysis, although the statistical techniques of adjusting for this group lessen that impact.

Late functional assessment and psycho-social deficits were as reported by the parents of these children ( $n = 562$ ). While this data is not generated by 'objective' testing, we are confident that the parents' annual reports are reliable and we thank them for their cooperation in providing the information.

#### 4.2. Conclusion

The protocol change to the arterial switch operation that occurred in this 1985–89 era for managing neonates with simple TGA or TGA/VSD is clearly supported by our outcomes data for children now 12–17 years after TGA repair. Experience since that time has further improved early survival after the arterial switch. These improvements may also result in fewer long-term complications. Future improvement in care should focus upon protecting these children from neurologic injury during their early management.

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### Appendix A. Demographic, morphologic, and procedural characteristics entered into multivariable analyses for risk factor determination

| Variable                               | n   | Missing | Value                      |
|--|-----|---------|----------------------------|
| <i>Demographic</i>                     |     |         |                            |
| Mean birth weight (SD)                 | 636 | 193     | 3.4 (0.6)                  |
| Gender, male:female                    | 829 | 0       | 581:248                    |
| Major associated cardiac anomalies     | 829 | 0       | 65 (8%)                    |
| Major associated non-cardiac anomalies | 829 | 0       | 15 (2%)                    |
| Number of pre-repair procedures        | 829 | 0       |                            |
| None                                   |     |         | 243 (29%)                  |
| One                                    |     |         | 481 (58%)                  |
| Two                                    |     |         | 91 (11%)                   |
| Three or more                          |     |         | 14 (2%)                    |
| <i>Morphologic</i>                     |     |         |                            |
| Morphologic group                      | 829 | 0       |                            |
| Simple TGA                             |     |         | 631 (76%)                  |
| TGA/VSD                                |     |         | 167 (20%)                  |
| TGA/VSD/PS                             |     |         | 30 (4%)                    |
| TGA/IVS/PS                             |     |         | 1 (0%)                     |
| VSD present                            | 829 | 0       | 291 (35%)                  |
| Small                                  |     |         | 94 (11%)                   |
| Moderate or large                      |     |         | 197 (24%)                  |
| Multiple VSDs                          | 829 | 0       | 40 (5%)                    |
| Pulmonary stenosis                     | 829 | 0       | 68 (8%)                    |
| Mild or moderate                       |     |         | 37 (4%)                    |
| Severe                                 |     |         | 31 (4%)                    |
| History of RVOT obstruction            | 829 | 0       | 37 (4%)                    |
| Coarctation of the aorta               | 829 | 0       | 32 (4%)                    |
| Hypoplastic or interrupted aortic arch | 829 | 0       | 4 (1%)                     |
| Anomaly of atrioventricular valve      | 829 | 0       | 13 (2%)                    |
| Anomaly of systemic venous drainage    | 829 | 0       | 15 (2%)                    |
| Anomalous cardiac position             | 829 | 0       | 13 (2%)                    |
| Juxtaposition of atrial appendages     | 829 | 0       | 14 (2%)                    |
| <i>Procedural</i>                      |     |         |                            |
| Repair type                            | 829 | 0       |                            |
| Arterial switch operation              |     |         | 516 (62%)                  |
| Atrial switch operation                |     |         | 285 (35%)                  |
| Senning operation                      |     |         | 175 (21%)                  |
| Mustard operation                      |     |         | 110 (14%)                  |
| Rastelli operation                     |     |         | 28 (3%)                    |
| Median age at repair (range)           | 829 | 0       | 10 days<br>(1 day–7 years) |
| Use of TCA                             | 738 | 91      | 569 (77%)                  |
| Mean TCA time in min (SD)              | 352 | 217     | 48 (22)                    |
| Mean lowest temperature in C (SD)      | 604 | 225     | 18.4 (3.3)                 |
| Non-cardioplegic cardiac arrest        | 717 | 112     | 21 (3%)                    |
| Mean ischemic time in min (SD)         | 455 | 374     | 69 (26)                    |

### Appendix B. Conference discussion

**Dr F. Haas (Munich, Germany):** I have one question. I was wondering about results of the Senning group and the Mustard group. What do you think is the reason for this difference in mortality and difference in reoperation rate?

**Dr Williams:** Well, I feel somewhat embarrassed presenting this in Europe where the Senning originated, but I don't find it surprising. If you look at the history of the Senning operation, it preceded the Mustard operation by 5 years, and yet I think other surgeons had difficulty duplicating this very elegant operation. I think that the Mustard is a safer, simpler procedure that more surgeons could do. As time evolved and we realized there were problems with the Mustard operation, some surgeons went back to the Senning and got better results, but even during this study period of 1985 to 1989, outcomes are not as optimal as those for the Mustard. And I would stress that this is a multi-institutional study. There is no need for one institution to do one operation or the other. They did the procedure they thought was best, and invariably the people doing the Senning's felt it would be the best operation, but I think the data speaks for itself.

**Dr K. Samir (Marseille, France):** As I was from the new generation where we didn't have many chances to see the atrial switch operation, I want to ask you if there are still indications for the atrial switch operations in some of the transposition of the great arteries, especially for the unique intramural coronary artery.

**Dr Williams:** I think you have pointed out something that's important, and I would stress that this data included only children admitted in the first 14 days of life. I think the quandary of whether to still do atrial switch surgery is based on late presentation, and if we had the exceptional child presenting at a much older age, then the consideration of whether you do an arterial switch or an atrial switch is a different question not addressed by this data. I could give you my personal opinion, but it wouldn't be based on this particular information.

**Dr F. Lacour-Gayet (Hamburg, Germany):** I have a couple of questions. We tried to stratify the complexity of the arterial switch operation and there are many different factors involved. I would like to ask you what you call a non-simple TGA, and if the long-term results are less satisfactory in patients with additional cardiac lesions and associated procedures?

**Dr Williams:** Well, in the interest of time, I didn't show you the data for morphology, but the constant phase mortality for simple TGA is better than for other forms of TGA, that is, VSD, VSD/PS. But I would also stress that these data refer to the constant phase of mortality, not the early mortality. We have addressed that previously. And I think the coronary artery anatomy may well be important in the early survival, but that's not addressed in this analysis. We only looked at the constant or late phase.

**Dr Lacour-Gayet:** I have another question. At Marie-Lannelongue over 1000 arterial switches were followed, and it was absolutely clear that in patients with associated aortic arch obstruction, particularly Taussig-Bing, the risk of late RVOT obstruction was important. I want to ask you if you have seen that in your series.

**Dr Williams:** The prevalence of late RV outflow tract obstruction?

**Dr Lacour-Gayet:** The prevalence of reoperation for RVOT stenosis in patients with Taussig-Bing associated with aortic arch obstruction.

**Dr Williams:** Well, as you saw, the RV outflow tract obstruction was the most common reason for reoperation in the arterial switch group. In this paper we didn't look at the criteria affecting the reoperation for that subgroup. We have in a previous paper, and I think you're quite right, that the downstream obstruction affects outcome.

**Dr C. Schreiber (Munich, Germany):** Could you please clarify this swing in functional classes which you were showing. What were the reasons for that?

**Dr Williams:** A good question, to which the short answer is I don't know. The longer answer is that it did not mean that the children in poorer functional class were dying and therefore the proportion was greater. That didn't seem to be the case. I think one thing we did see was the effect of

treatment. If children were having problems at 10 or 11 years of age and underwent treatment, whatever that might be, they improved and their functional class got better. Beyond that I don't know the explanation for it.

**Dr Schreiber:** They didn't show an impairment of ventricular function maybe due to coronary stenosis or e.g. aortic insufficiency?

**Dr Williams:** No, and we do not have that information about whether these children have coronary artery stenosis and we don't have a direct measurement of their ventricular function.

**Dr G. Sarris (Athens, Greece):** As a result of the data indicating a long-term adverse effect of circulatory arrest in these patients, has the Congenital Heart Surgeons Society come to a recommendation regarding avoidance of circulatory arrest and using full bypass during this operation?

**Dr Williams:** Well, I don't think this society has policies along that line,

but I think management of these infants has evolved to points that we can avoid circulation arrest. Three-quarters of these patients were done with circulation arrest, and it didn't matter whether it was an arterial switch or an atrial repair, and I would think today that probably very few of us would use circulation arrest for an arterial switch operation. I wouldn't want to leave you with the impression that all of our patients or at least 31% of our patients today have learning deficits or will have learning deficits. I think it should be much less than that, but it's probably a long way from zero, and I think we need to focus on that area. We've dealt in the last 15 years with coping with mortality, and I think it's time to look at functional outcome rather than alive or dead basically.