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Current Results of Management in Transposition of the Great Arteries, With Special Emphasis on Patients With Associated Ventricular Septal Defect

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Two hundred forty-five patients <15 days of age with transposition of the great arteries with or without a ventricular septal defect or pulmonary stenosis were entered into an ongoing 20 institution treatment study between January 1, 1985 and June 1, 1986. Complete follow-up is available on all patients. The ventricular septal defect narrowed in only 1 of 36 patients with combined transposition of the great arteries and ventricular septal defect; pulmonary stenosis developed or worsened in 3 of these 36 patients and in 3 of the 187 patients with simple transposition. Twelve month overall survival among the 245 patients was 80%. No morphologic feature of transposition was a risk factor for death but major associated cardiac and noncardiac anomalies (more common in patients with combined transposition and ventricular septal defect) and low birth weight were risk factors.

Neither arterial switch repair (n = 86), atrial switch (Mustard) repair (n = 21) nor atrial switch (Senning) repair (n = 39) was a risk factor for death, but results in all surgical groups were better in the last part of the experience. Death before repair was less frequent late in the study. Possibly, in low birth weight infants, survival was better with the arterial than with the atrial switch repair.

These data suggest that survival at 1 year is similar with either the arterial or the atrial switch repair. The early results of repair of combined transposition of the great arteries and ventricular septal defect are as good as those of simple transposition. Special institutional efforts are required to attain good results with the arterial switch repair and to prevent death before repair.

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Much of the information on which the treatment of patients with transposition of the great arteries is based has been obtained from nonconcurrent studies in individual institutions in an earlier era. The reports often are based on small numbers of patients and include only patients who have undergone repair. This results in overestimation of survival because of the frequency of death before repair (1–3). Many reports fail to include patients with associated cardiac and noncardiac congenital anomalies.

Therefore an ongoing multi-institutional observational study of patients with transposition of the great arteries of all types has been undertaken, entering only individuals admitted to the hospital before 15 days of age to obtain as unselected a group of patients as is possible. This is a report of the early results of the study.

Methods

Definitions. Transposition of the great arteries is defined as an anomaly in which the aorta arises wholly or in large part from the morphologically right ventricle and the pulmonary artery arises wholly or in large part from the morphologically left ventricle. Patients were accepted into the study irrespective of the atrial situs, but were not accepted if the atrioventricular connection was discordant or univentricular.

Study patients. Two hundred forty-five patients with transposition of the great arteries were entered into the study between the starting date of January 1, 1985 and June 1,

See Appendixes A and B for lists of participating institutions and members of the Congenital Heart Surgeons Society and their staff.

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1986. (The rate of acquisition into the study indicates that slightly >500 patients will have been entered into the study by January 1988, the anticipated closing date for entry. Follow-up is programmed to extend to 1998.)

One hundred eighty-seven patients were considered after initial investigation to have simple transposition of the great arteries, with either no ventricular septal defect or only a small one, and no or only mild or moderate pulmonary stenosis (left ventricular outflow tract obstruction). Two other patients had an intact ventricular septum, but on initial investigation had pulmonary stenosis and left ventricular peak pressure equal to or greater than systemic arterial pressure and were categorized separately. Thirty-six patients were found at initial investigation to have a moderate-sized or large ventricular septal defect and are categorized as having transposition of the great arteries and ventricular septal defect. The combination of transposition of the great arteries, ventricular septal defect and pulmonary stenosis, the latter being defined by a gradient of ≥20 mm Hg between the left ventricle and pulmonary artery, was found at initial investigation in 15 patients. The remaining 5 of the total group of 245 patients were entered into the study within 8 weeks of the closing date of June 1, 1986, and could not, with the information available to the data collection center, be placed in any of the morphologic subsets.

Seventy-seven percent of the patients were entered into the study while <48 hours old (Fig. 1); the median age at entry was 1 day. The median birth weight was 3.4 kg and 50% of the patients weighed between 3.0 and 3.7 kg at birth. Six (3%) of the 197 patients with a known birth weight weighed ≤2 kg at birth.

Twenty-two of the 245 patients had at least one major associated cardiac anomaly and 3 had more than one of these (Table 1). In two of the patients with major associated cardiac anomalies, these were not evident until the time of repair. Fifteen patients had one or more minor associated cardiac anomalies, and 4 of these 15 also had one or more major associated cardiac anomalies. Nine patients had important noncardiac congenital anomalies (Table 2), and among these two also had major associated cardiac anomalies.

Institutions. The 20 participating institutions, 3 of which were initially not in the study but joined it on January 1,

Figure 1. Cumulative distribution of age at entry into the study in 245 patients with all types of transposition of the great arteries.

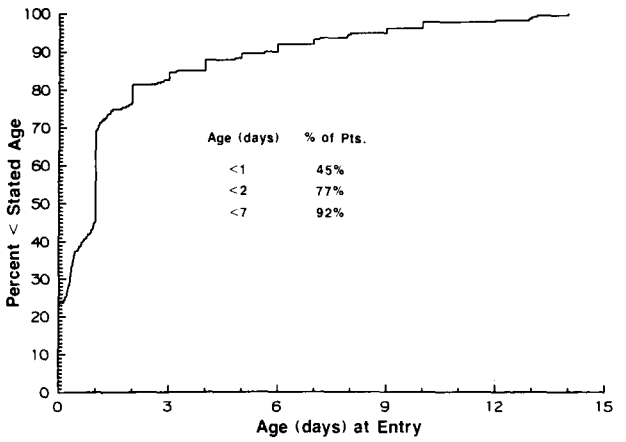


Table 1. Associated Congenital Cardiac Anomalies in 245 Patients With Transposition of the Great Arteries of All Types (CHSS; 1985 to June 1986)

Associated Cardiac Anomalies	No. of Patients
Major (n = 22)	
Coarctation (with or without PDA)	8
Interrupted aortic arch, RV outflow obstruction from VS malalignment	1
TAPVC, infradiaphragmatic	1
PAPVC	1
Unroofed coronary sinus syndrome	3
Severe stenosis, origin LPA	1
Ventricular hypoplasia	
Right	1
Left	1
Overriding tricuspid valve	1
Straddling tricuspid valve	1
Important tricuspid incompetence	1
Dextrocardia with atrial situs solitus	3
Atrial situs inversus	1
Congenital mitral stenosis (parachute valve)	1
RCA to RA fistula	1
Minor (n = 15)	
Superior-inferior ventricles	1
Left superior vena cava	5*
Large AP collateral arteries	5
Aneurysm of membranous septum	1
Juxtaposition of atrial appendages	4

*One was associated with unroofed coronary sinus. AP = aortopulmonary; CHSS = Congenital Heart Surgeons Society; LPA = left pulmonary artery; PAPVC = partial anomalous pulmonary venous connection; PDA = patent ductus arteriosus; RA = right atrium; RCA = right coronary artery; RV = right ventricle; TAPVC = total anomalous pulmonary venous connection; VS = ventricular septum.

Table 2. Associated Major Noncardiac Congenital Anomalies in 245 Patients With Transposition of the Great Arteries of All Types

Associated Major Noncardiac Congenital Anomalies	No. of Patients
Holoprosencephaly	1
Omphalocele	1
Charge association	1
Fetal phenytoin syndrome	1
Mittendorf's spot in left eye	1
Severe thoracic spine scoliosis	1
Pancreatic agenesis	1
Trisomy 13	1
Absent left anterior rib cage	1
Total	9

Table 3. Percent Mortality (death at any time during the study period) in 245 Patients With Transposition of the Great Arteries*

Percent Mortality (overall) (%)		No. of Institutions
≤	<	
	5	3†
5	10	2
10	20	10
20	30	3
30	40	1
40	50	0
50		1
Total		20

*Mortality expressed for each institution as the number of patients who died divided by the number of patients the institution had entered into the study. †In all three institutions, there were no deaths (0% mortality overall). Two of these three institutions entered the study on January 1, 1986; the other entered four patients into the study.

1986, varied as to the number of patients admitted to them and thus through them into the study, and in the overall mortality of their portion of patients in the study (Table 3). They also varied as to the types of surgical repair they performed in their patients (Table 4).

In attempting to determine whether institutional differences in percent mortality were due to chance or to specific institutional risk factors that could be identified and probably then neutralized, and because a number of the deaths occurred after an arterial switch repair, a brief analysis was made of the 87 patients among the total group of 245 with all types of transposition of the great arteries who received an arterial switch repair. Arterial switch repair was performed in 11 of the 20 institutions. In 4 of the 11, the mortality rate after the repair was ≥50%. Among these four institutions, eight deaths (67%; CL 48 to 82%)* occurred in 12 patients, while among the other 7 institutions, nine deaths (12%; CL 8 to 17%)* occurred in 75 patients (p for difference <0.0001). The four institutions together were therefore considered a "high risk for the arterial switch repair group of institutions." The number of patients entered into the study by each of the 4 institutions was not dissimilar to that among the 20 institutions, and as a group the 4 institutions entered into the study 48 of the total of 245 patients. The variable "high risk for arterial switching group of institutions" was entered into several of the multivariate analyses, as well as the individual institutions.

Table 4. Types of Repair Performed by the Institution in 245 Patients With Transposition of the Great Arteries

Type of Repair	No. of Institutions
Arterial switch only	3
Atrial switch only	6
Mustard technique only	4
Senning technique only	2
Atrial switch in early period; arterial switch in later period	1
Both arterial and atrial switch	7*
None	3†
Total	20

*Also, one of the seven institutions performed atrial switch repair by both the Mustard and Senning techniques, one also performed an intraventricular repair and one also a Rastelli repair. †This includes two institutions recently entered into the study, and one institution whose patients were referred for repair to other institutions in the study.

Treatment procedures. The depiction of results according to procedures reflects the actual procedures performed. Because of the potential importance of procedures performed after the patient had been crossed over from one treatment protocol to another, these situations are identified in the presentations.

Data collection. A center was established (Birmingham, Alabama) for collecting and analyzing all the data for each patient entered into the study. In a weekly telephone call to each participating institution, the center received information concerning new patients <15 days of age entering the institution with transposition of the great arteries. During the call, follow-up information was also obtained on patients previously entered and still in the hospital or readmitted later.

Follow-up. During the month of June 1986, a follow-up inquiry was made by a telephone call to each patient's parents, and when indicated, to physicians and hospitals, to identify any interval events and determine the current status of each patient. Follow-up calls were made by the center, except for those concerning the patients in six participating institutions that elected to do their own follow-up calls. The date of closure of the inquiry was July 1, 1986, and events occurring after that date are not included in the analysis. All patients alive at last report were able to be contacted during the formal follow-up, except for three who were known to be alive 5, 5.4 and 13 months, respectively, after entry into the study. The median follow-up period was 7.7 months (range 4 days to 17.2 months).

Statistical analyses. The data were summarized in contingency tables. All events were depicted in a time-related manner using actuarial and parametric methods (4,5). Multivariate analyses were made in the hazard function (parametric) domain (5). The variables entered into each analysis are described in Appendix C. A probability (p) value <0.1 was the criterion for retaining variables in the multivariate analyses; 70% confidence limits were used in all the presentations.

*CL denotes 70% confidence limits (intervals).

Table 5. Some Differences Between 36 Patients With Transposition of the Great Arteries and Ventricular Septal Defect and 187 With Simple Transposition of the Great Arteries*

Variable	TGA + VSD (n = 36)	Simple TGA (N = 187)	p Value for Difference
Birth weight (kg)	3.37 ± 0.649	3.32 ± 0.602	0.6
Age at entry (days)	2.7 ± 3.70	1.6 ± 2.48	0.09
No. without repair during study	16 of 36 (44%)	55 of 187 (29%)	0.08 (χ^2)
Age at repair (mo)	2.7 ± 3.28	2.2 ± 3.0	0.5

*The continuous variables are expressed as the mean value ± SD. TGA = transposition of the great arteries; VSD = ventricular septal defect.

Results

Morphologic subgroup differences. Major associated cardiac anomalies occurred more commonly ($p < 0.0001$) in patients with combined transposition of the great arteries and ventricular septal defect (10 [28%] among 36 patients) than among patients with simple transposition (8 [4.3%] among 187 patients). Patients with the combined defect tended to be older at the time of admission to the study than did patients with simple transposition (Table 5).

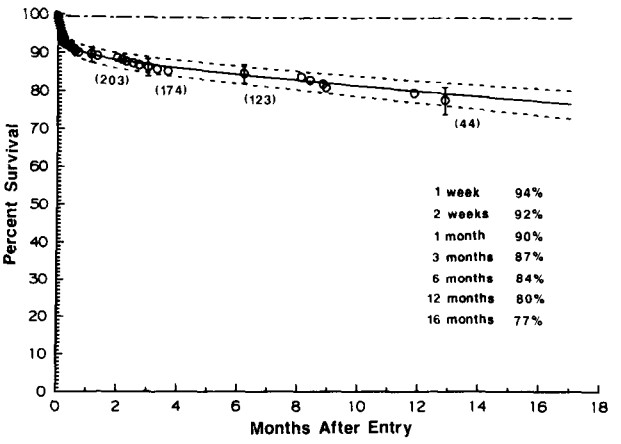
Morphologic changes after entry into the study. Among the 187 patients with the diagnosis of simple transposition of the great arteries on admission, 3 are known to have been without pulmonary stenosis initially and to have developed severe pulmonary stenosis during the study period and before repair. In all three, the stenosis was believed to be dynamic left ventricular outflow tract obstruction. In two of three, atrial switch repair was performed at age 3 and 7 months, respectively, and in the 7 month old infant, a muscular ridge was resected; both patients are surviving. The third patient of this group was taken to the operating room at age 7 months for a planned atrial switch repair, but because of the appearance of the ventricles an arterial switch was performed. The patient died, and autopsy demonstrated a small, thin-walled left ventricle.

Three of the 36 patients entering the study with combined transposition of the great arteries and ventricular septal defect, and either no gradient or one <20 mm Hg between the left ventricle and the pulmonary artery, later had evidence of important pulmonary stenosis. One of these initially had a gradient of 15 mm Hg across a bicuspid pulmonary valve, and by the age of 4 months the gradient had increased to 30 to 50 mm Hg. An atrial switch (Senning) repair, closure of the ventricular septal defect and pulmonary valvotomy were performed, and the patient remains well. A second patient had no gradient at entry, but at 5 months of age had a 60 to 80 mm Hg gradient between the left ventricle and the pulmonary artery. The left ventricular outflow tract obstruction was considered to be dynamic, and only an arterial switch repair and closure of the ventricular septal defect were performed; the patient remains well. The third patient had at entry into the study transposition of the great arteries and a large ventricular septal defect, with no pulmonary stenosis and a normal-appearing left ventricle. At 2 months of age, the ventricular septal defect was small and a 50 mm Hg pressure gradient was present across the pulmonary valve and subvalvar area. Repair has not yet been performed.

Survival. Survival among all morphologic subsets of the 245 patients entered into the treatment study is depicted in Figure 2. The hazard function (instantaneous risk of death at each moment after entry into the study) had a rapidly declining early phase of hazard and a constant phase of hazard extending out as long as the patients were followed up (Fig. 3).

Patients with a lower birth weight and those entering into the study at an earlier date were at greater risk of dying

Figure 2. Actuarial and percent survival after entry of 245 patients with transposition of the great arteries of all types entered into the study. There were 42 deaths. Each **circle** represents a death, and is positioned at the appropriate interval after entry on the **horizontal axis** and actuarially on the **vertical axis;** the **vertical bars** define the 70% confidence limits (intervals) of the actuarial estimates. The **solid line** depicts the parametrically estimated percent survival, and the **dashed lines** enclose the 70% confidence limits. The **dashed-dot line** represents the percent survival of an age-sex-race–matched general population and is taken from the 1976 U.S. Life Tables. (Parameter estimates for this and Fig. 3 are in Appendix C1.)



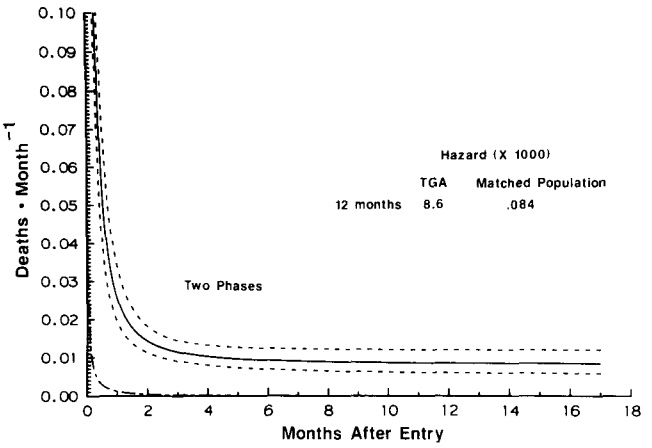


Figure 3. Hazard function for death (n = 42) after entry into the study in 245 patients with all types of transposition of the great arteries (TGA). The parametric and matched population depiction is as in Figure 2.

than were others (Table 6). No morphologic feature was identified with reasonable certainty as being a risk factor for death during the period of this study, either in multivariate or simple analysis (Table 7). Major associated congenital cardiac or noncardiac anomalies were risk factors. Institutions with a smaller case load were not risk factors. The "high risk for arterial switch repair group of institutions" was a risk factor for death.

The surgical repairs. Of the 154 repair procedures performed on the 245 patients during the study period to date, the arterial switch repair was the most common (Table 8), and by simple analysis (but not by multivariate analysis) percent survival was lower after this procedure than after the atrial switch repair (Fig. 4). By simple analysis, percent survival was highest after the atrial switch (Mustard) repair.

Overall, 84% of the patients survived ≥12 months after the repair (Fig. 5), and the time of highest instantaneous risk of death was immediately after the repair (Fig. 6). The diagnosis of transposition of the great arteries with ventricular septal defect did not increase the risk of death after the repair in detailed analyses (Table 9), nor did the arterial switch repair or atrial switch (Senning or Mustard) repair. Major associated cardiac anomalies were clearly an incremental risk for death after the repair. The other incremental risk factors differed depending on which repair was used (Table 9). Neither the duration of cardiopulmonary bypass (Table 10), the total circulatory arrest time (Table 11) nor the aortic crossclamp (global myocardial ischemia) times (Table 12) was a risk factor for death in the detailed multivariate analysis.

Table 6. Incremental Risk Factors for Death at Any Time in 42 of the 245 Patients With Transposition of the Great Arteries of All Types, Considering Only Those Factors Operative at Entry of the Patient into the Study

Incremental Risk Factors for Death After Entry	Hazard Phase	
	Early	Constant
Lower birth weight (kg)	•	•
Earlier date of entry (mo since 1/1/85)	•	
Major associated cardiac or noncardiac anomaly		•
High risk institutions for arterial switch repair	•	

See Appendix C2 for variables entered into the multivariate analysis and for the coefficients and p values.

Death before repair. Fourteen patients among the 245 died before undergoing repair. Two of these had severe congenital extracardiac anomalies and died 4 days and 3.4 months, respectively, after entry, before any procedure had been performed. All but 3 of the remaining 12 died within the first month of life. All died either in cardiac failure or with severe hypoxia. Risk factors for death before repair were low birth weight, earlier date of entry into the study and major associated cardiac anomalies (see Appendix C5).

Transposition of the great arteries with ventricular septal defect. An analysis of the 187 patients with simple transposition of the great arteries is published separately (6). For the 36 patients with combined transposition of the great arteries and ventricular septal defect survival after entry into the study is depicted in Figure 7. Two of the 36 died before repair. One, who died on a ventilator at 18 days of age, had a major associated noncardiac anomaly (absent left anterior rib cage) and the only procedure performed was a balloon atrial septostomy. The other, with a birth weight of 2.2 kg, died with cardiac failure and infection at age 14 days, before any procedure was performed.

Twenty of these patients underwent repair during the period of the study, most commonly an arterial switch repair (Table 13). The 12 month survival after repair was 69% (Fig. 8).

Transposition of the great arteries, ventricular septal defect and pulmonary stenosis. Eight of the 15 patients with transposition of the great arteries, ventricular septal defect and pulmonary stenosis had typical morphology, including subvalvular left ventricular outflow obstruction with or without pulmonary valve stenosis and similar peak pressures in the right and the left ventricle. Two other patients had similar findings but stenosis only at the valve. Three patients had transposition of the great arteries, ventricular septal defect and atresia of the subvalvular or valvular pulmonary (left ventricular) outflow. Two final patients had less severe stenosis than the others, but in both the gradient was >20 mm Hg.

Among the 15 patients with transposition of the great arteries, ventricular septal defect and pulmonary stenosis entered into the study, actuarial percent survival was 79% at 3 months, and within the follow-up period no deaths occurred after that time. Among the three patients who died,

Table 7. Morphologic Categories of 245 Patients With Transposition of the Great Arteries of All Types, and the 42 Deaths at Any Time According to the Category

		All Deaths		
Morphologic Category	n	No.	%	CL (%)
Simple TGA	187	29	16	13 to 19
TGA and important PS	2	0	0	0 to 61
TGA and VSD	36	9	25	17 to 35
TGA, VSD, PS	15	3	20	9 to 36
Unknown	5	1	20	3 to 53
Total	245	42	17	15 to 20
$p(\chi^2)$*			0.65	

*For difference between deaths in those with simple transposition of the great arteries (TGA) and those with ventricular septal defect (VSD) = 0.17; in hazard function domain, p for difference = 0.4. CL = 70% confidence levels; PS = pulmonary stenosis.

one with two major associated cardiac anomalies underwent an aortopulmonary shunting procedure at 3 days of age after which he died with continuing severe hypoxia. Another, with trisomy 13, underwent no procedure and died at 4 days of age. A third patient, with a major associated cardiac anomaly, died with hypoxia at 3 months of age, having undergone two aortopulmonary shunting procedures and one shunt revision.

Only one patient with transposition of the great arteries, ventricular septal defect and pulmonary stenosis has undergone repair, and he is surviving after receiving a central aortopulmonary shunt at 2 weeks of age, revision of the shunt a few days later and a Rastelli repair at 11 months of age. Seven patients have received a single aortopulmonary shunting procedure (usually a Gore-Tex interposition shunt). Another patient received a Blalock-Taussig shunt that required revision 25 days later and still another has received two aortopulmonary shunts. These nine patients are doing well and await repair. Two patients, aged 8 and 13 months respectively, have as yet received no procedure (other than a balloon atrial septostomy in one because of only mild hypoxia and they also await repair.

Transposition of the great arteries and pulmonary stenosis. Two patients, on entry into the study, had transposition of the great arteries and intact ventricular septum, but with severe pulmonary stenosis and essentially equal pressures in the two ventricles. In one, the stenosis seemed to be only in the pulmonary valve, and an aortopulmonary shunt was performed within a few days of admission. In the other patient, in whom no procedure has been performed,

Table 8. Repair Procedures (n = 154) Used in 245 Patients With Transposition of the Great Arteries of All Types

		All Deaths		
Type of Repair	n	No.	%	CL (%)
Arterial switch	86	16	19	14 to 24
Arterial switch as operating room crossover from planned atrial switch	1	1	100	15 to 100
Atrial switch	60	6	10	6 to 16
Mustard type	21	0	0	0 to 9
Senning type	39	6	15	9 to 24
Atrial switch as operating room crossover from planned arterial switch	5	3	60	29 to 86
Intraventricular repair	1	1	100	15 to 100
Rastelli operation	1	0	0	0 to 85
Total	154	27	18	14 to 21
CPB technique	47	11	23	17 to 31
TCA technique	107	16	15	11 to 19

CL = 70% confidence levels; CPB = cardiopulmonary bypass; TCA = total circulatory arrest.

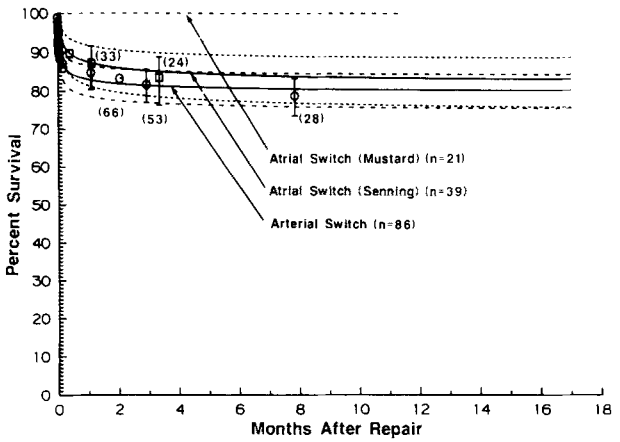


Figure 4. Actuarial and parametrically determined percent survival after arterial and atrial switch repairs in 148 of the 245 patients with all types of transposition of the great arteries (deaths = 23). The one Rastelli repair and the one intraventricular repair are not included, nor are the six switch procedures that were performed as operating room crossovers (see Table 8). Format as in Figure 2.

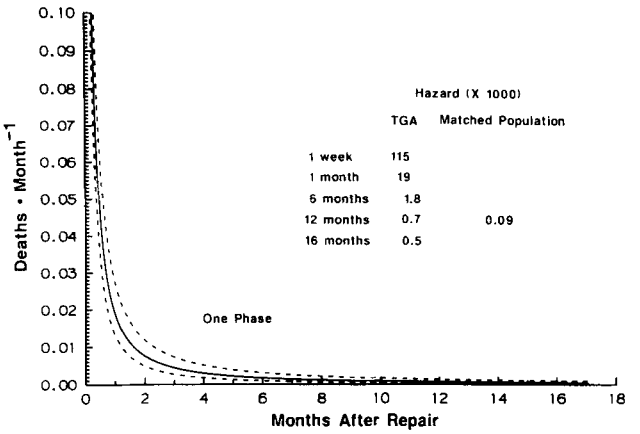


Figure 6. Hazard function for death after all types of planned repair in 148 patients with all morphologic subsets of transposition of the great arteries (TGA) (deaths = 23). Format as in Figure 3.

the stenosis was in the left ventricular outflow tract and the left ventricle was moderately hypoplastic. Both patients are alive and await repair.

Discussion

Risk factors for death. The study to date has identified no differences in survival that can with reasonable certainty be related to either the morphologic subset of transposition of the great arteries on the patient's entry into the study or the type of repair performed. This statement is based on the multivariate analyses and may seem to be at variance with some of the simple subset analyses, which are based on smaller numbers of patients and do not take into account varying prevalences of other risk factors. When more patients and a longer follow-up are available for analysis, some of the differences suggested by simple analyses (such as higher survival with the Mustard than with the Senning atrial switch repair) may be confirmed with reasonable certainty by more detailed analyses. Associated major cardiac anomalies did increase the risk of death, as has been demonstrated in patients with other kinds of congenital cardiac anomalies (7–9). This emphasizes the importance of identifying these associated anomalies as early as possible, and taking them into account in planning the therapeutic program.

Improvement in results. Even over a short period of 16 months, survival of patients in this study has improved.

Figure 5. Actuarial and parametrically determined percent survival after all types of planned repairs for 148 patients with all morphologic subsets of transposition of the great arteries (deaths = 23). Not included are the six patients in whom a switch repair was performed as a crossover in the operating room (see Table 8). The depiction is as in Figure 2. (Parameter estimates for this and Fig. 6 are in Appendix C3.)

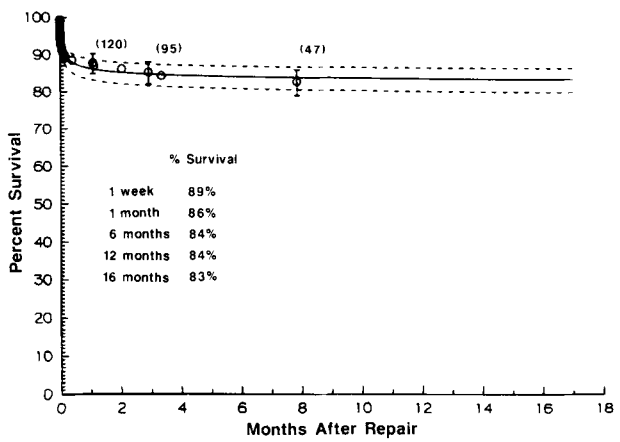


Table 9. Incremental Risk Factors for 23 Deaths After 148 Planned Repair Procedures (n = 148; deaths = 23)

Incremental Risk Factors for Death	Single Early Hazard Phase
Major associated cardiac anomaly	—
If arterial switch repair	
High risk for arterial switch repair group of institutions	—
Earlier date of operation	—
If atrial switch repair	
Lower birth weight	—

Note: The nonsignificant variables included atrial switch (Mustard) repair vs. (Senning) ($p = 0.11$), transposition of the great arteries + ventricular septal defect ($p = 0.5$) and interval between entry and repair ($p = 0.4$). (The variables entered into the analyses, the equations, coefficients and p values are detailed in Appendix C4.)

Table 10. Duration of Cardiopulmonary Bypass as Related to Death, in the 46 Patients Whose Repair Was Performed Under Cardiopulmonary Bypass*

Duration of CPB (min)	n	All Deaths		
		No.	%	CL (%)
<30	—	—		
≤30 to <60	6	2	33	12 to 62
≤60 to <120	15	3	20	9 to 36
≤120 to <150	9	1	11	1 to 33
≤150 to <180	5	0	0	0 to 32
≤180	4	1	25	3 to 63
Total	40	7	18	11 to 26
p (logistic)			0.46	
Unknown	6	3	50	24 to 76

*n = 46 of the 148 patients undergoing a planned repair. CL = 70% confidence limits; CPB = cardiopulmonary bypass.

Table 11. Duration of Total Circulatory Arrest as Related to Death, in the 102 Patients Who Underwent Repair During Profoundly Hypothermic Total Circulatory Arrest*

Circulatory Arrest Time (min)	n	All Deaths		
		No.	%	CL (%)
≤15 to <30	1	0	0	0 to 85
≤30 to <45	12	2	17	6 to 35
≤45 to <60	25	2	8	3 to 18
≤60 to <100	43†	7	16	10 to 24
≤100	5‡	2	40	14 to 71
Total	86§	13	15	11 to 20
p (logistic)			0.09	
Unknown	16	0	0	0 to 11

*n = 102 of the 148 patients undergoing planned repairs. †In eight patients more than one period of total circulatory arrest was used, and the time given is the sum of all the times. ‡Among the 43, 39 had only one period of arrest (mean 69 ± 8.4 minutes). §Among the five, all had multiple periods, the longest known single period among these being 65 and 93 minutes. CL = 70% confidence limits.

Table 12. Aortic Cross-clamp Time as Related to Death, in the 148 Patients With All Types of Transposition of the Great Arteries in Whom Planned Repair Was Performed

Aortic Crossclamp Time (min)	n	All Deaths		
		No.	%	CL (%)
<30	6	1	17	2 to 46
≤30 to <60	44	8	18	12 to 26
≤60 to <90	62	8	13	8 to 19
≤90 to <120	12	4	33	18 to 52
≤120	2	1	50	7 to 93
Total	126	22	17	14 to 22
p (logistic)			0.3	
Unknown	22	1	5	0.6 to 15

CL = 70% confidence limits.

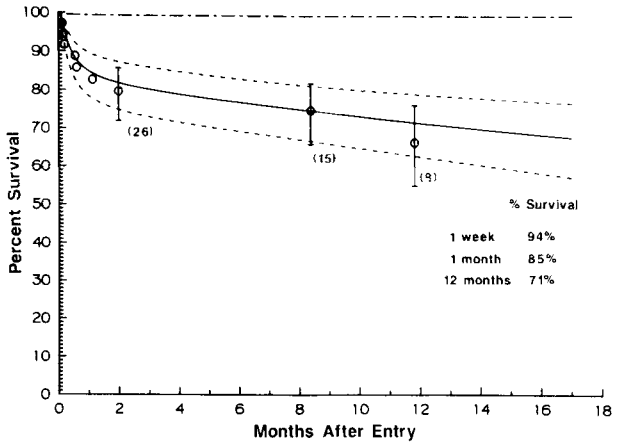


Figure 7. Actuarial and parametrically estimated percent survival after entry into the study of 36 patients with transposition of the great arteries and ventricular septal defect (deaths = 9). Format as in Figure 2. (Parameter estimates are detailed in Appendix C6.)

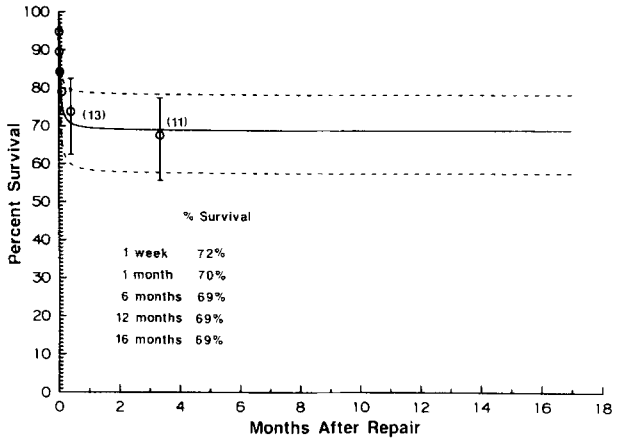


Figure 8. Actuarial and parametrically determined percent survival after planned repair in 36 patients with transposition of the great arteries and ventricular septal defect (planned repairs = 19; deaths = 6). The patient undergoing an atrial switch repair as an operating room crossover was excluded. Format as in Figure 2. (Parameter estimates for this are in Appendix C7.)

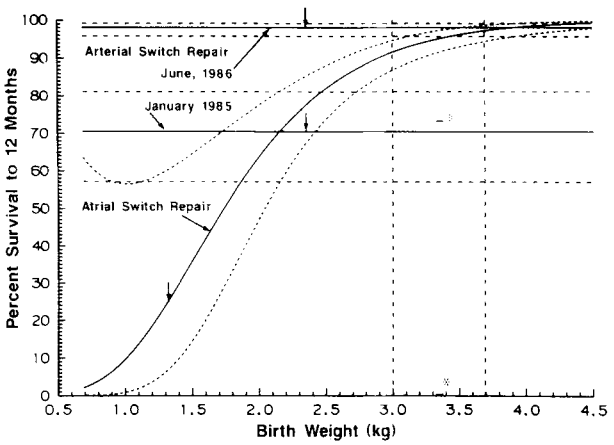


Figure 9. Nomogram of a solution of the multivariate risk factor for death after planned repair of transposition of the great arteries of all types (see Table 9). A major associated cardiac anomaly was entered as no. The high risk group of institutions for arterial switch repair was entered as no. The birth weights smaller than those in the patients are identified by being to the **left** of the small **downpointing vertical arrows.** The **horizontal dashed lines** enclose the 70% confidence limits around the continuous point estimates. The **vertical dashed lines** enclose the birth weights of 50% of the patients. The **asterisks** call attention to two additional solutions of the multivariate equation (indicated by the **short lines**), both with birth weight entered as 3.4 kg and the high risk group institutions as yes, the lower one with a January 1985 date of operation and the upper one with a June 1986 date.

This is probably related in part to improvement in the results of arterial switch repair (Fig. 9). This same improvement is not evident for atrial switch procedures, but the improved results in patients undergoing this procedure are due to a reduction in the number of deaths that occurred before repair. These improvements are such that currently, June 1986, the predicted 12 month survival after arterial or atrial switch repair of patients with simple transposition of the great arteries or transposition of the great arteries and ventricular septal defect and a birth weight of 3.4 kg is 95 to 98% (Fig. 9).

Table 13. The Types of Repair and Deaths After Repair in the 36 Patients With Transposition of the Great Arteries and Ventricular Septal Defect

Type of Repair	n	All Deaths		
		No.	%	CL (%)
Arterial switch	14	3	21	10 to 38
Atrial switch (Mustard)	—	—		
Atrial switch (Senning)	4	2	50	18 to 82
Atrial switch (Senning) as operating room crossover from arterial switch	1	1	100	15 to 100
Intraventricular repair	1	1	100	15 to 100
Total	20	7	35	23 to 49
$p(\chi^2)$			0.15	

*Two patients died before repair. CL = 70% confidence limits.

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"High risk for the arterial switch repair group of institutions". The reasons for the high mortality in the group of four institutions in which an arterial switch repair was accompanied by a mortality of ≥50% are not apparent currently. However, in these 4 institutions, as in the other 16, the results of arterial switch repair have improved during the study period (Fig. 9). There has been no improvement over time in the results of atrial switch repair, and no high risk group of institutions has been identified. This may be related to a greater general understanding of the factors relating to success with this older and more standardized technique.

Robert N. Brown contributed in many important ways to the compilation of the data and the data analysis. Debbie Nuby and Nancy Ferguson skillfully prepared the graphic materials and facilitated the development of the tables and text for this paper.

Appendix A

Participating Institutions

The 20 institutions participating in the study are Children's Hospital of Michigan (Detroit), British Columbia Children's Hospital (Vancouver), University of Michigan Medical Center and Mott Children's Hospital (Ann Arbor), Columbia-Presbyterian Medical Center (New York), The Children's Hospital (Boston), All Children's Hospital (St. Petersburg, FL), Mayo Clinic (Rochester, MN), The Montreal Children's Hospital, University of Utah Medical Center (Salt Lake City), University of California Medical Center (San Francisco), Children's Memorial Hospital (Chicago), University of Miami (and Jackson Memorial Hospital), University of California at Los Angeles, Children's Hospital of Los Angeles, Children's Hospital of Philadelphia, University of Alabama at Birmingham Medical Center, University of Chicago (and Michael Reese Hospital and Medical Center), Oregon Health Sciences University (Portland), State University of New York (Buffalo) and Hospital for Sick Children (Toronto).

Appendix B

Members of the Congenital Heart Surgeons Society. Eduardo Arciniegas, MD, Philip G. Ashmore, MD, Douglas M. Behrendt, MD, Frederick O. Bowman, MD, Aldo R. Castaneda, MD, Adnan Cobanoglu, MD, George R. Daicoff, MD, Gordon Danielson, MD, Anthony R. Dobell, MD, Donald B. Doty, MD, Paul A. Ebert, MD, L. Henry Edmunds, MD, Farouk S. Idriss, MD, George A. Kaiser, MD, James K. Kirklin, MD, John W. Kirklin, MD, Hillel Laks, MD, George G. Lindesmith, MD, James R. Malm, MD, Dwight C. McGoon, MD, William I. Norwood, MD, Albert D. Pacifico, MD, Robert L. Replogle, MD, Albert Starr, MD, Sambamurthy Subramanian, MD, George A. Trusler, MD, William G. Williams, MD.

Ms. Mary Lynn Mandy (Birmingham) was the study coordinator, and without her constant attention to the myriad of details this study could not have been performed with high quality. At each of the cooperating institutions a contact person at least weekly provided information to the data and analysis center in Birmingham. These people include Diana Ayton (Montreal), Claire Beckmann (Philadelphia), Karen Boot (Los Angeles), Robyne Campbell (Toronto), Carol Cohen (Los Angeles), Ann-Lynn Denker (Miami), Sue DeRubeis (Ann Arbor), Marsha Elixson (Boston), Robin Fawcett (Chicago), Jan Freitas-Nichols (Portland), Melanie Gevitz (Chicago), June Janson (Vancouver), Marsha Kwicinski (Detroit), Sharon Long (Rochester), Judy Martino (St. Petersburg), Vicki Miller (Birmingham), Linda O'Neill (New York), Carolyn Peterson (Salt Lake City), Darlene Schmeigal (Buffalo), Elizabeth Tong (San Francisco) and Mike Wallig (Chicago).

In each institution the pediatric cardiologists contributed in many ways to the study. The directors of pediatric cardiology involved were Rene Arcilla, MD (Chicago), Lionel Bargeron, Jr., MD (Birmingham), D. Woodrow Benson, Jr., MD (Chicago), Pipit Chiemmongkoltip, MD (Chicago), David Driscoll, MD (Rochester), Henry Gelband, MD (Miami), James G. Henry, MD (St. Petersburg), Arno R. Hohn, MD (Los Angeles), Allan Hordof, MD (New York), Bernardo Nadal-Ginard, MD (Boston), Garth S. Orsmond, MD (Salt Lake City), Marc Paquet, MD (Montreal), Daniel R. Pieroni, MD (Buffalo), William Pinsky, MD (Detroit), Amnon Rosenthal, MD (Ann Arbor), Richard D. Rowe, MD (Toronto), Abraham Rudolph, MD (San Francisco), George Sandor, MB, ChB (Vancouver), Cecille O. Sunderland, MD (Portland), Henry Wagner, MD (Philadelphia) and Roberta Williams, MD (Los Angeles).

Appendix C

Statistical Methods

1. Parameter estimates for survivorship and hazard function for death after entry into the study, 245 patients (see Fig. 2 and 3). The parametric method used in the analysis of time-related death is conceptualized in the cumulative hazard domain (5). Two hazard phases, early and constant, were found. The parameter estimates were: early phase, $\mu_1 = 0.1304$, $\delta = 0$, $\rho = 0.1295$, $\nu = 1.585$, m = 0; constant phase, $\mu_2 = 0.008259$.

2. Multivariate analysis for incremental risk factors for death after entry into the study in 245 patients (see Table 6). *A. Variables entered into the analysis.* These included *demographic* variables (date of entry (months since January 1, 1985), gender, age (days) at entry, birth weight in k); *morphologic* variables (simple transposition of the great arteries, transposition of the great arteries and ventricular septal defect, or transposition of the great arteries, ventricular septal defect, and pulmonary stenosis; presence of ventricular septal defect, pulmonary stenosis, or patent ductus arteriosus, presence of major associated cardiac anomaly, presence of major associated noncardiac anomaly); and *institutional* variables (institution of admission, number of cases entered from that institution, high risk for arterial switch repair group of institutions). Numerous interactions between variables were sought.

To make use of the multivariate regression coefficients, dichot-

omous (yes/no) variables were entered as a value of 1 when present (yes) and 0 when absent (no). For continuous variables the units of the variables were multiplied by the coefficient in the equation.

B. Equations and incremental risk factor coefficients and probability (p) values. Early phase: $\delta = 0$, $\rho = 0.1441$, $\nu = 1.660$, $m = 0$, intercept 1.496, birth weight (kg) -1.113 ± 0.35 ($p = 0.002$), date of entry (months since 1/1/85) -0.06944 ± 0.044 ($p = 0.1$), high risk for arterial switch repair group of institutions (0,1) 1.710 ± 0.45 ($p = 0.0002$); constant phase: intercept -2.982, birth weight (kg) -0.8265 ± 0.49 ($p = 0.09$), major associated cardiac or noncardiac anomaly (0,1) 2.539 ± 0.77 ($p = 0.0009$).

3. Parameter estimates for survivorship and hazard function for death after repair of transposition of the great arteries in 148 patients (see Fig. 5 and 6). Only one hazard phase, an early one, was found. Early phase: $\mu_1 = 0.2017$, $\delta = 0$, $\rho = 0.05758$, $\nu = 2.464$, $m = 0$.

4. Multivariate analysis for incremental risk factors for death after repair in 148 patients (Table 9 and Fig. 9). *A. Variables entered into the analysis.* These included those described in Appendix C3 and, in addition, *surgical* ones (atrial switch repair, type of atrial switch repair (Mustard or Senning), arterial switch repair, date of operation (months since January 1, 1985), interval (months) between date of entry and date of operation, aortic crossclamp time (minutes), repair performed during cardiopulmonary bypass versus during profoundly hypothermic total circulation arrest, duration (minutes) of total circulatory arrest) and age (months) at operation. Numerous interactions between variables were sought.

B. Equations and incremental risk factors, coefficients and p values. Early phase: $\delta = 0$, $\rho = 0.09105$, $\nu = 2.527$, $m = 0$, intercept for arterial switch repair -0.9116, intercept for atrial switch repair 2.632, major associated cardiac anomaly (0,1) 1.944 ± 0.56 ($p = 0.0006$); if arterial switch repair (interaction terms): high risk for arterial switch repair group of institutions (0,1) 2.779 ± 0.57 ($p = 0.0001$), date of operation (months since 1/1/85) -0.1704 ± 0.061 ($p = 0.005$); if atrial switch repair (interaction term): birth weight (kg) -1.641 ± 0.53 ($p = 0.002$).

5. Multivariate analysis for incremental risk factors for death before repair in 245 patients (see text). *A. Only one hazard phase, an early one, was found.* Early phase: $\mu_1 = 0.1378$, $\delta = 0$, $\rho = 1.124$, $\nu = 3.295$, $m = 0$.

B. Variables entered into the analysis included those described in Appendix C1.

C. Equations and incremental risk factor coefficients and p values. Early Phase: $\delta = 0$, $\rho = 1.026$, $\nu = 3.297$, $m = 0$, intercept 3.074, birth weight (kg) -1.488 ± 0.39 ($p = 0.0001$), date of entry (months since 1/1/85) -0.1240 ± 0.069 ($p = 0.08$), major associated cardiac anomaly (0,1) 1.555 ± 0.72 ($p = 0.03$).

6. Parameter estimates for survivorship and hazard function for death after entry into the study in patients with transposition of the great arteries and ventricular septal defect (Fig. 7). Two hazard phases, early and constant, were found. Early phase: $\mu_1 = 0.2076$, $\delta = 0$, $\rho = 0.3053$, $\nu = 1$, $m = 0$; constant phase: $\mu_2 = 0.01110$.

7. Parameter estimates for survivorship and hazard function for death after repair in patients with transposition of the great arteries and ventricular septal defect (Fig. 8). Only one hazard phase, an early one, was found. Early phase: $\mu_1 = 0.3732$, $\delta = 0$, $\rho = 0.03009$, $\nu = 1$, $m = 0$.

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