Late Outcome After Arterial Switch Operation for Transposition of the Great Arteries

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**Background**—Early and midterm results of the arterial switch operation (ASO) in transposition of the great arteries (TGA) are good, but late outcome data in large populations are still few.

**Methods and Results**—Twelve hundred patients had an ASO for TGA between 1982 and 1999, with prospective follow-up of 1095 survivors. Outcome measures included late death, reoperation, aortic insufficiency (AI), pulmonary stenosis (PS), and coronary anomaly. Median follow-up was 4.9 years (range 0.5 to 17 years). Late death occurred in 32 patients; survival was 88% at both 10 and 15 years. The hazard function for death declined rapidly, with no deaths after 5 years. Late mortality was correlated with reintervention and major events in the intensive care unit. Reoperation was performed in 103 patients, more often in complex TGA; the cause was mainly PS. Freedom from reintervention was 82% at 10 and 15 years, with a hazard function that declined rapidly but slowly increased after 3 years. At the last follow-up, PS was present in 3.9% of patients, and grade II or more AI was present in 3.2%, with a cumulative incidence of 9% at 15 years. Among the 278 patients who had a coronary arteriography, 8% had coronary lesions. Normal left ventricle and sinus rhythm were seen in 96.4% and 98.1%, respectively.

**Conclusions**—Fifteen years after ASO, late mortality was low, with no deaths after 5 years; reoperation, mainly owing to PS, occurred throughout the follow-up. AI and coronary obstruction are rare but warrant further follow-up. Good left ventricular function and sinus rhythm are maintained. *(Circulation. 2001;104[Suppl I]:I-121-I-126.)*

**Key Words:** transposition of great vessels ■ pediatrics ■ prognosis ■ surgery ■ survival

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Early and intermediate results of the arterial switch operation (ASO) make it the treatment of choice for transposition of the great arteries (TGA). Nevertheless, the rare postoperative complications observed in prior studies, such as pulmonary stenosis (PS), aortic insufficiency (AI), and coronary obstruction, warrant further follow-up. Furthermore, it is important to know whether the physiological advantages given by the ASO, ie, persistent sinus rhythm, normal systemic ventricular function, and systemic AV valve competence, are maintained in the long term and to compare arterial and atrial switch outcome as the length of follow-up begins to be similar.

Long-term studies are still few and do not include large numbers of patients. In the present study, long-term results obtained in 1200 newborns and infants operated on at the same center and prospectively followed up are presented.

**Methods**

From 1982 to December 1999, 1200 newborns and infants with TGA had an ASO at Marie Lannelongue hospital; 1181 had a 1-stage operation, and 19, all with simple TGA, underwent a 2-stage operation. Patient characteristics are shown in Table 1. Simple TGA is TGA with intact ventricular septum and an echocardiographic peak left ventricle–pulmonary artery gradient <50 mm Hg; complex TGA are TGA with ventricular septal defect (VSD) or Taussig-Bing anomaly.

Since 1982, it was prospectively determined that all survivors have an annual examination by the referring cardiologist that included clinical assessment, ECG, and echocardiogram with Doppler study. An exercise test, myocardial scintigraphy, and catheterization with aortography or coronary arteriography were done only if deemed necessary by the referring cardiologist. All data were regularly transmitted to our center, and missing data were completed by recall of the referring cardiologist. The hospital records of all patients were reviewed for details of preoperative assessment, operative management and incidents, and hospital course. Major intraoperative events were difficulties in coronary repositioning, left ventricular dysfunction, cardiac arrest, and need for temporary circulatory assistance at the end of the intervention; major events in the intensive care unit (ICU) were left ventricular dysfunction, complete AV block, cardiac arrest, and need for circulatory assistance. The surgical technique for the ASO at Marie Lannelongue hospital was standard and has been described previously.

**Statistical Analysis**

StatView 5.0 software (SAS Institute, Inc) was used for data analysis. Univariate analyses of continuous variables were performed with the Student *t* test. Univariate comparisons for categorical variables were performed with the 2-tailed *χ*² test or, when necessary, the Fisher exact test. Every univariate parameter that reached significance (*P*<0.05) was then tested in a multivariate logistic regression model. Time-related events were examined by the actuarial method; analyses were done with censoring of incompletely traced patients after the time of the last follow-up, and differences...
between groups were calculated by the log-rank test. The hazard function regression method was used to estimate time-related freedom from and hazard function of unfavorable outcome events. 9

Results

Population

Early death occurred in 102 patients (8.6%; 95% confidence intervals [CI] 7.1% to 10.3%); risk factors are shown in Table 2. Multivariate analysis confirmed a significant influence of bypass time \( P<0.001 \), occurrence of major intraoperative events \( P<0.001 \), years of surgery before 1990 \( P<0.006 \), and type II abnormal coronary pattern \( P<0.0023 \) on early mortality. Three of the survivors were lost to follow-up. The 1095 patients were followed up for a mean of 58.3 months (SD 40.9 months) and included 773 patients with simple TGA and 325 with complex TGA.

Late Deaths

Late death was observed in 32 patients a median of 2.68 months (range 0.97 to 55.50 months) after ASO. Survival rate including early mortality (Figure 1) was 89% at 1 year and 88% at 10 and 15 years in the group as a whole. It was higher in subjects with simple TGA (92% at the same intervals) than in complex TGA, which had a survival rate of 81% at 1 year and 80% at both 10 and 15 years \( P<0.001 \). The hazard function for death had a rapid declining phase that approached 0 by 5 years (Figure 1). Late death occurred 10 times within 30 days after reoperation. Indications for surgery in these patients were AI in 3, cava thrombosis in 3, residual shunt in 2, and mitral regurgitation or PS in 1 each. The primary cause of death was coronary related in 9 patients (0.8%; 95% CI 0.4% to 1.6%), due to myocardial infarction in 6 patients and sudden death in 3; death occurred within 6 months in 8 patients. Pulmonary hypertension, however rare, was the cause of 5 late deaths; 2 occurred in patients with simple TGA who underwent surgery on or before 1 month of age, and 3 occurred in patients with TGA with a VSD, 1 of whom underwent surgery at 9 months of age. Other causes are given in Table 3. Risk factors are given in Table 4. In univariate analysis, late deaths were more frequent (5.9%) in patients with complex TGA than in those with simple TGA (1.7%; \( P<0.001 \)), when associated cardiac lesions were present (11% versus 1.4%; \( P<0.001 \)), when a major cardiac event was observed in the ICU (22% versus 2%; \( P<0.001 \)), and when the patient had a reoperation (11.7% versus 2.1%;
multivariate analysis confirmed a significant influence of the occurrence of major ICU events ($P<0.002$) and reoperation after ASO ($P<0.001$).

Reoperations

Reoperations ($n=121$) were performed in 103 patients. The actuarial rate of reintervention is shown in Figure 2. Freedom from reintervention was observed in 90%, 83%, and 82% of the survivors at 5, 10, and 15 years, respectively; reoperations occurred at points throughout the follow-up period. After a rapid declining phase, the hazard function for all reoperations reached a nadir by 3 years but slowly increased thereafter. The reasons for reintervention are given in Table 5; the most frequent cause was PS. Reoperation for PS was observed up to 9 years after the ASO. Although reintervention for AI is rare (1.03% among survivors in the present study), it occurred throughout the follow-up period, with a freedom from aortic valve intervention of 99.8% at 3 months and 99.1%, 97.6%, and 96.2% at 5, 10, and 15 years, respectively. Surgical cure of AI was aortic valvuloplasty in 4 patients, 2 of whom had secondary valve replacement, and initial valve replacement in 7. Surgery for coronary obstruction was performed late in the follow-up period, after 5 years in 5 of the 6 patients with this complication. Patients with complex TGA had a greater

**TABLE 3. Causes of Late Deaths**

<table>
<thead>
<tr>
<th>Cause</th>
<th>n</th>
</tr>
</thead>
<tbody>
<tr>
<td>Coronary-related death</td>
<td>6</td>
</tr>
<tr>
<td>Myocardial infarction</td>
<td>3</td>
</tr>
<tr>
<td>Sudden death</td>
<td>5</td>
</tr>
<tr>
<td>Pulmonary artery hypertension</td>
<td>3</td>
</tr>
<tr>
<td>Cava thrombosis</td>
<td>3</td>
</tr>
<tr>
<td>Aortic regurgitation</td>
<td>3</td>
</tr>
<tr>
<td>Ventricular dysfunction</td>
<td>3</td>
</tr>
<tr>
<td>Sepsis</td>
<td>2</td>
</tr>
<tr>
<td>LVOT obstruction</td>
<td>2</td>
</tr>
<tr>
<td>Neurological</td>
<td>2</td>
</tr>
<tr>
<td>Pulmonary valve stenosis</td>
<td>1</td>
</tr>
<tr>
<td>AV block</td>
<td>1</td>
</tr>
<tr>
<td>Residual shunt</td>
<td>1</td>
</tr>
</tbody>
</table>

LVOT indicates left ventricular outflow tract.

**TABLE 4. Risk Factors for Late Death**

<table>
<thead>
<tr>
<th></th>
<th>Late Deaths</th>
<th>Late Survivors</th>
<th>$P$</th>
</tr>
</thead>
<tbody>
<tr>
<td>Univariate analysis, %</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>TGA with IVS vs complex TGA</td>
<td>5.9</td>
<td>1.7</td>
<td>$&lt;0.001$</td>
</tr>
<tr>
<td>Associated lesions vs 0</td>
<td>11</td>
<td>1.4</td>
<td>$&lt;0.001$</td>
</tr>
<tr>
<td>Major ICU events vs 0</td>
<td>22</td>
<td>2</td>
<td>$&lt;0.001$</td>
</tr>
<tr>
<td>Post-ASO surgery vs 0</td>
<td>9.1</td>
<td>2.2</td>
<td>$&lt;0.001$</td>
</tr>
<tr>
<td>Multivariate analysis, OR</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Major ICU events vs 0</td>
<td>5.6</td>
<td></td>
<td>0.002</td>
</tr>
<tr>
<td>Post-ASO surgery vs 0</td>
<td>7.0</td>
<td></td>
<td>0.001</td>
</tr>
</tbody>
</table>

IVS indicates intact ventricular septum.
TABLE 5. Causes of Reoperations*

<table>
<thead>
<tr>
<th>Cause</th>
<th>n</th>
</tr>
</thead>
<tbody>
<tr>
<td>PS</td>
<td>43</td>
</tr>
<tr>
<td>PM implantation</td>
<td>16</td>
</tr>
<tr>
<td>Residual shunt</td>
<td>16</td>
</tr>
<tr>
<td>CoA</td>
<td>15</td>
</tr>
<tr>
<td>AI</td>
<td>13</td>
</tr>
<tr>
<td>Cava thrombosis</td>
<td>11</td>
</tr>
<tr>
<td>LVOT stenosis</td>
<td>9</td>
</tr>
<tr>
<td>Mitral insufficiency</td>
<td>7</td>
</tr>
<tr>
<td>Coronary stenosis</td>
<td>6</td>
</tr>
</tbody>
</table>

PM indicates pacemaker; CoA, coarctation of the aorta; and LVOT, left ventricular outflow tract.

*110 Patients had 128 reoperations; 1 patient could have 2 simultaneous repairs.

frequency of reinterventions (19.2%) than did those with simple TGA (5.3%; P<0.001). Some causes of reintervention were more frequent in complex TGA (PS 6.6% versus 2.3%, P<0.01, and aortic regurgitation 2.5% versus 0.4%, P<0.01), and some were only observed in patients with complex TGA, such as left ventricular outflow tract obstruction (1.9% versus 0%), pacemaker implantation (4.6% versus 0%), and residual shunt closure (3.1% versus 0%; all P<0.001). Reinterventions on aortic arch, cava thrombosis, or mitral valve or for coronary obstruction had the same incidence in both groups.

Last Follow-Up

At the last follow-up, cardiac complications related to the ASO were few. A peak systolic gradient ≥50 mm Hg between the right ventricle and the pulmonary artery was observed in 41 patients (3.9%; 95% CI 2.9% to 5.2%). AI of all grades was seen in 165 patients (15.5%; 95% CI 13.5% to 17.8%), but only 39 (3.8%; 95% CI 2.8% to 5.1%) had regurgitation of grade II or more. Actuarial evolution of AI is shown in Figure 3; as for aortic valve intervention, aortic regurgitation appearance was observed throughout the follow-up period. The rate of freedom from grade II AI was 95.6%, 93.6%, and 91% at 5, 10, and 15 years, respectively. Coronary obstruction or stenosis was seen in 23 of the 278 patients who had coronary arteriography or aortography either systematically or, in most cases, when indicated by symptoms, ECG, or exercise test anomalies. Five of these patients had an aortocoronary bypass with the left internal mammary artery.

After ASO, almost all patients had normal systemic ventricular function; 1.7% (95% CI 1.1% to 2.7%) had some kinetic anomalies with good global contractility, and 1.9% (95% CI 1.2% to 2.9%) had a shortening fraction <30%. Sinus rhythm was present at last follow-up in 98.1% (95% CI 97.1% to 98.8%) of the patients, with 6 patients having episodes of supraventricular tachycardia; 15 had AV block, of whom 13 required pacemaker implantation.

Discussion

Mortality

The late outcome of this large population who underwent surgery in 1 center confirms the early and midterm follow-up data of prior ASO studies,1–5 with very good late survival at 15 years, including early mortality, and with a decline in the hazard function for death to 0 after a few years. These data finally establish the ASO as the procedure of choice for all types of TGA. The same low late mortality rate was reported in other recent smaller studies after ASO.6,7 Late mortality of recent Senning operations is low but still higher than after ASO.8–14 Because postoperative mortality often is not included. Moreover, late death is observed throughout the follow-up period after Senning operation, with a late hazard function above 0 that even increases in the second decade.10,14 Univariate analysis showed that complex TGA, associated cardiac lesions, major ICU events, and reoperation were factors that significantly increased late mortality. The presence of a complex TGA was a factor related to higher late mortality in 1 study6 but did not reach statistical significance in others,3,5,7 and multivariable analysis retained only 2 risk factors for late mortality in this population (major ICU events and reoperation). The first can be related to less than perfect coronary switch, pulmonary artery hypertension, or residual associated cardiovascular malformation. Reoperation is expected more often in TGA with VSD or Taussig-Bing complex or if associated malformations are present. Factors such as earlier year of surgery, bypass time, major perioperative event, and abnormal coronary pattern did not correlate with late death because patients with these factors more often died early after ASO. Coronary death, certain or presumed, was rare and was observed only early in the follow-up period, as reported previously.15 One third of these patients had a coronary reimplantation problem during the ASO. As described previously,3,6,7 pulmonary artery hypertension is one of the most frequent causes of late death; among the 3 patients with VSD, earlier ASO could have prevented pulmonary vascular disease in the patient who underwent surgery at 9 months of age.

Reoperations

Ten percent of survivors had a reoperation, an incidence similar to that observed in large series3,6 with longer follow-up. The hazard function for reoperation reached 0 in our population at 3 years but thereafter showed an ascending phase, with a slightly ascending phase at the end of the follow-up; late reinterventions for PS and AI accounted for the late increasing phase; among the 3 patients with VSD, earlier ASO could have prevented pulmonary vascular disease in the patient who underwent surgery at 9 months of age.

Figure 3. Actuarial survival free from grade II or more AI (Ao insufficiency) for 1095 survivors. Numbers in parentheses indicate number of patients observed at beginning of interval.
The most frequent cause for reoperation after ASO was PS in the present population, as in other studies. Reoperation for PS was more frequent early after ASO; its incidence decreased afterward but persisted at least 9 years after ASO in our population. In other large studies, the hazard function for PS reoperation also has a late constant phase slightly above 0. Factors related to reoperation for PS are technical or anatomic. In opposition to Williams et al, we found that reoperation for PS was more frequent in complex TGA. The present technique to reconstruct the pulmonary artery and avoid late PS includes previously described principles with some minor modifications. Basically, fresh autologous pericardium is used to fill the gap in the pulmonary root due to button harvesting of coronary arteries. This pericardium is fine sutured around the edges of the pulmonary root and is tailored so as to restore preoperative anatomy. Moreover, the division of the pulmonary artery before the Lecompte maneuver is performed as low as possible, namely, a very few millimeters above the pulmonary valve commissures, so that the suture of the neopulmonary trunk is away from the pulmonary bifurcation. Other common causes of reintervention were observed shortly after ASO, such as pacemaker implantation, residual shunt closure, and cava thrombosis, and except for the latter, these causes were seen only in patients with complex TGA. Aortic valve repair or replacement was rare (1.1%), as in other studies. Its incidence was low for the whole population but increased with the length of follow-up, as shown previously, and was higher with complex TGA. Longer follow-up is needed to determine its true incidence, and close observation is warranted. As reported previously, left ventricular outflow tract obstructions for which surgery is needed are few, most often subvalvar, and occur more frequently in complex TGA. Coronary revascularization was observed in only 5 patients (0.46%) rather late in the follow-up. The same low prevalence has been seen in other long-term studies, but as in our population, prospective aortography and coronary arteriography or stress test were not done systematically but rather only if ECG or echocardiographic signs were present; the true incidence of coronary obstruction and the need for aortocoronary bypass could be underestimated. In a prospective study of coronary arteries after ASO, 30 of 165 patients had coronary obstruction, often related to a specific surgical technique, and 9 had complete occlusion of the left coronary. Only 4 had surgery, but late death occurred in 2 patients with left coronary stenosis who did not have any evidence of ischemia before catheterization.

Morbidity
At the last follow-up, in all survivors, including those who had surgical repair or balloon dilatation, PS with an echo peak systolic gradient ≥50 mm Hg was observed in 3.9% of the population. The same prevalence has been reported before. AI of all grades was observed in 15.5% of the population; AI of grade II or more was seen more rarely (3.8%) but increased in frequency with time. In a study with a comparable length of follow-up, similar prevalences and increasing incidences were found. In older studies with smaller populations, a higher prevalence of all grades of AI was observed, with moderate or severe regurgitation being exceptional.

The ASO technique keeps its promise. The present study showed good left ventricular function in the overwhelming majority of patients, as did all other population studies previously reported. In addition, sinus rhythm was present in almost all patients; the most frequent arrhythmia was complete AV block, and supraventricular tachycardia was observed in only a very few patients, as shown previously.

The multicenter follow-up of the patients is the main limitation of the present study. Quantification of AI or right ventricle–pulmonary artery gradient can change with the observers and the centers. In addition, appreciation of left ventricular function was certainly less rigorous than if it had been done by the same observer. Nevertheless, the main end points of death, reoperation, and presence of PS or AI were independent of the observer. End points and protocol of the follow-up were determined prospectively.

Conclusions
Up to 15 years of follow-up, the good late outcome of TGA after ASO is confirmed and is better than that of the atrial switch operation. ASO is the procedure of choice for all TGA types. The late mortality was low, with a hazard function for late death that reached 0 after 2 years in TGA with intact ventricular septum and after 5 years in complex TGA. Mortality was related to cardiac reoperations and to major events that occurred immediately after the ASO. Reoperations were less frequent than after atrial switch but were observed throughout the follow-up period, with a hazard function above 0 up to 15 years. Patients with complex TGA were more prone to reintervention. PS was the main cause of reoperation. Late morbidity related to the ASO technique mainly consisted of PS or AI, which had a low prevalence but whose incidence increased with the length of follow-up. Coronary stenosis manifestations were rare, observed early and late after ASO; better pre-screening with systemic aortography at 4 to 5 years of age should be done. As observed previously, good left ventricular function and sinus rhythm were maintained in almost all patients after ASO.

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References


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