Results over a Ten-Year Period of Palliation followed by Corrective Surgery for Complete Transposition of the Great Arteries

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SUMMARY
One hundred and twenty patients with transposition of the great arteries (TGA) were encountered over a decade. Survivors have been followed until after definitive repair, and 39% were alive when reviewed.

The majority (69%) had no significant communication between the pulmonary and systemic circulations. Of 48 patients in this poor-mixing group who had an atrial septectomy, 23 (48%) survived to have an atrial baffle repair at an average age of 37 months, and 37% were alive at the time of review. In contrast, 18 of 22 (82%) patients with poor mixing who had a balloon septostomy had a definitive operation at an average age of 13 months, and 17 (77%) survived.

Twenty patients (17%) had good mixing between the two circulations due to the presence of a large ventricular septal defect (VSD) or patent ductus arteriosus, and presented with mild cyanosis and heart failure. Of this group, 35% were alive when reviewed. Four of the five patients who had a successful atrial baffle repair and correction of associated lesions were less than 4 months of age when this was performed. Where TGA was associated with VSD and pulmonary stenosis, 36% survived.

Definitive operation at an early age has been made possible by the introduction of a surgical technic using profound surface-induced hypothermia and limited cardiopulmonary bypass.

Additional Indexing Words:
Atrial baffle repair  Atrial septectomy  Balloon atrial septostomy
Mustard operation  Profound hypothermia  Rastelli operation

The high mortality associated with complete transposition of the great arteries (TGA) has been substantially reduced by palliative and subsequent corrective procedures. Although previous reports have provided data on patient survival after either palliative1-3 or corrective measures,4,5 the combined effect of these procedures on improving the overall survival of such patients is currently not clear. This study reviews the outcome in a group of patients with TGA from the time of their presentation in infancy until after the time of definitive operation.

Material and Methods

Clinical Material
Between 1961 and October 1970, 120 patients were admitted to Green Lane Hospital with a diagnosis of TGA confirmed at cardiac catheterization or autopsy of whom 83 (69%) were considered to have “poor mixing.” They presented with severe cyanosis and did not have any adequate communication providing a site for significant mixing between the pulmonary and systemic circulations. While most patients in this

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Received October 11, 1971; revision accepted for publication January 7, 1972.
category had only a small interatrial communica-
tion, some also had a small ventricular septal
defect or patent ductus arteriosus but hemody-
namically appeared similar to those without such
additional communications. Only one patient in
this group had pulmonary stenosis.

Twenty patients (17%) were classified clinical-
ly as having “good mixing.” These infants
presented with mild cyanosis and heart failure
associated with good mixing between the two
circulations and a large pulmonary blood flow due
to the presence of a large communication at
ventricular or great vessel level, or both. At
cardiac catheterization these patients had a
systemic arterial saturation of at least 70%.

In 11 patients (9%) TGA was associated with
a large ventricular septal defect and pulmonary
stenosis.

The remaining six patients (5%) had TGA with
aortic interruption or coarctation, patent ductus
arteriosus, and large ventricular septal defect.
Patients with TGA associated with uncorrectable
lesions (single ventricle, tricuspid atresia) have
not been included in this study.

Procedures

We first undertook atrial septectomy as
palliative treatment in 1961, excising the septum
during a short period of caval occlusion with
the infant cooled by surface means to 32°C. This
type of initial palliation, combined where appro-
priate with other palliative measures, was utilized
until 1967. All long-term survivors (apart from
two patients with ventricular septal defect and
pulmonary stenosis and two who developed
severe pulmonary vascular obstructive disease)
subsequently had an atrial baffle repair and
correction of associated lesions when present or a
Rastelli operation, usually between 2 and 4 years
of age.

Since 1967, all infants, with the exception of
one with ventricular septal defect and pulmonary
stenosis, have been palliated at the time of
diagnostic catheterization by balloon atrial sep-
tostomy. From September 1969, with the
development of surgical technics utilizing pro-
found surface-induced hypothermia, circulatory
arrest, and limited cardiopulmonary bypass, the
subsequent definitive operation has been per-
formed at an increasingly younger age until, in
recent months, definitive operation has been
performed electively during the first year of life or
at any time the clinical status of the patient
demanded this, regardless of age or size.

Results

Patients have been grouped into those with
poor mixing between the two circulations,
those with good mixing, and those with other
associated anomalies, and have been further
subdivided according to their initial manage-
ment (table 1).

Poor Mixing

Early in the series, eight patients received
no palliation (table 1) because they were
moribund when referred and died before
diagnostic or palliative surgical measures were
instituted.

Between 1961 and 1967, 48 patients had an
atrial septectomy as the initial palliative
procedure, and this was associated with 14
hospital deaths (table 1). Eleven of the 34
surviving patients died after hospital dis-
charge while awaiting atrial baffle repair.
Death in all was related to the underlying
heart disease and occurred in six of the 11
patients before 1 year of age, highlighting the
need for early definitive treatment. The 23
surviving patients had an atrial baffle repair
(including ligation of a small patent ductus in
two and relief of subpulmonary stenosis in
one) performed between 2 and 4 years of age
(average 37 months). Five failed to survive
the early postoperative period, but the re-
mainder are clinically satisfactory up to 5
years after operation.

Between 1967 and October 1970, balloon
atrial septostomy was performed as initial
palliation in 27 patients. In five patients, a
Fogarty embolectomy catheter was used to
perform the septostomy (table 1), but this
was found to be unsatisfactory as three of the
five had an inadequate atrial communication
created (confirmed at the time of septectomy
at 1 week to 2 months of age). Only one of
these patients is alive.

A no. 5 Edwards dilatation or Rashkind
catheter was used for the septostomy in 22
patients (table 1). One patient died as a result
of excessive blood loss during the procedure.
Early in the series, three patients appeared
clinically unsatisfactory and had a septectomy
1 day, 3 weeks, and 3 months, respectively,
after the septostomy, with one death. At the
time of septectomy the atrial defect was large
in one patient but was inadequate in two who
had an anatomically small fossa ovalis.
**Table 1**

Summary of Clinical Data

<table>
<thead>
<tr>
<th>Initial treatment</th>
<th>No. cases</th>
<th>Hospital deaths</th>
<th>Late deaths*</th>
<th>Atrial baffle repair</th>
<th>Rastelli operation</th>
<th>Final outcome</th>
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<td></td>
<td></td>
<td></td>
<td></td>
<td>No. cases</td>
<td>Hospital deaths</td>
<td>No. cases</td>
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<tr>
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<td>8</td>
<td>—</td>
<td>—</td>
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<tr>
<td>Septectomy</td>
<td>48</td>
<td>14</td>
<td>11</td>
<td>23</td>
<td>5</td>
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<td>Septostomy (Fogarty)</td>
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<td>1</td>
<td>2</td>
<td>1</td>
<td>1 (20)</td>
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<tr>
<td>Septostomy (Rashkind or Edwards)</td>
<td>22</td>
<td>2</td>
<td>2</td>
<td>18</td>
<td>1</td>
<td>17 (77)</td>
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<tr>
<td>Total</td>
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<td>26</td>
<td>14</td>
<td>43</td>
<td>7</td>
<td>36 (43)</td>
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<tr>
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<td>3</td>
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<td>4</td>
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<td>Total</td>
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<td>2</td>
<td>5</td>
<td>6</td>
<td>4</td>
<td>3 (21)</td>
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<td>0</td>
<td>0</td>
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<td>2</td>
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<td>2 (67)</td>
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<td>Total</td>
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<td>2</td>
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<td>3</td>
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<td>4 (67)</td>
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<td>1</td>
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<td>1</td>
</tr>
<tr>
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<td>2</td>
<td>0</td>
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<td>1</td>
<td>0</td>
<td>—</td>
<td>1 (1)</td>
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<tr>
<td>Total</td>
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<td>3</td>
<td>3</td>
<td>1</td>
<td>2</td>
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</tr>
<tr>
<td><strong>Aortic obstruction, VSD, and PDA</strong></td>
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<td></td>
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<td>2</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>0</td>
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<td>Relief of aortic obstruction = MPA banding</td>
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<td>3</td>
<td>0</td>
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<td>1</td>
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<tr>
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<td>1</td>
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</tbody>
</table>

*Excludes those who subsequently died following definite repair.
†Alive following palliation only with severe pulmonary vascular obstructive disease.
‡Includes two patients who previously had an interatrial communication created.
§Two patients who have not had a definitive operation.

Abbreviations: MPA = main pulmonary artery; PDA = patent ductus arteriosus; VSD = ventricular septal defect.
There were two late deaths among the surviving 20 patients who left the hospital following septostomy using an Edwards or Rashkind catheter. One occurred at 2 months of age from complications related to a Pierre Robin syndrome, and the other at 6 months from meningitis. Two other patients survived three episodes of cerebral thrombosis between 4 and 10 months of age.

The 18 surviving patients in this group had an atrial baffle repair at 4 to 25 months of age (average 13 months). Sixteen operations were performed using profound hypothermia and limited cardiopulmonary bypass and two using conventional cardiopulmonary bypass. The 17 operative survivors are clinically well up to 22 months postoperatively.

In summary (table 1), of the total of 83 patients in this poor-mixing group, there were 26 hospital deaths (eight without palliation and 18 following palliation) and 14 late deaths while awaiting definitive repair. All 43 survivors have undergone atrial baffle repair and 36 (43%) are currently alive.

Figure 1 compares the outcome in the two major treatment groups. Where atrial septectomy was followed by atrial baffle repair at an average age of 37 months, 37% were alive at the time of this review. Where atrial septectomy using a Rashkind or Edwards catheter was followed by atrial baffle repair at an average age of 13 months, 77% were alive. These results are contrasted (fig. 1) with the natural history of transposition of the great arteries in patients with an essentially intact ventricular septum and either a patent foramen ovale or a naturally occurring atrial septal defect, using the data provided by Liebman et al.10

Information concerning the size of the interatrial communication was obtained at operation or autopsy in 20 of the 22 patients who had a septostomy using a Rashkind or Edwards catheter. In nine patients the defect was large (10 mm or more in diameter). In five patients there was a moderate-sized defect (7–9 mm), and in six a small defect (6 mm or less in diameter). In four of the patients with a small defect there was an unusually large coronary sinus opening (usually associated with a left superior vena cava) or an abnormally prominent limbus. In only one patient with a small defect was limitation of the size of the interatrial communication due to persistence of septum primum tissue.

Good Mixing

Twenty patients had good mixing due to a large communication at ventricular or ductus level (table 1). In 14 the major communication was a large ventricular septal defect, and in six a large patent ductus arteriosus.

Ventricular Septal Defect

Two of the 14 patients with a large ventricular defect seen initially in 1961 received no palliation and died in early childhood. One patient had a septectomy only, but died soon afterward.

The course in seven patients who underwent septectomy and banding of the main pulmonary artery was complicated by the use of pericardium for the band in three patients. Only one of these patients survives, and at 3 years of age he was found to have a severely elevated pulmonary vascular resistance. Three of the four patients banded with Dacron survived palliation, but two died while awaiting correction, and the third following definitive repair.
Commmencing in 1967, four patients with a large ventricular defect had a balloon atrial septostomy. One patient underwent definitive operation without further palliation at 16 months of age but did not survive. The other three who remained in heart failure had the ventricular defect closed and an atrial baffle inserted, using profound hypothermia at 1–3 months of age, with one operative death which occurred in a patient in whom closure of a patent ductus arteriosus was also undertaken.

In summary (table 1), there were three survivors from a total of 14 patients with a large ventricular septal defect. Two have been corrected, and one with severe pulmonary vascular disease has not.

**Patent Ductus Arteriosus**

Two of the six patients with a large patent ductus arteriosus were not palliated (table 1). One died at 11 days of age, with pulmonary collapse, and the other progressed satisfactorily and had a successful atrial baffle repair and closure of the ductus at 3 years of age.

One patient had a septostomy at 4 months of age, but the ductus was not divided. At 3 years of age he was found to have severe pulmonary vascular obstructive disease so that definitive repair could not be undertaken.

Three patients had a septostomy but persisted in heart failure, and one died without surgical treatment at 15 days of age. Atrial baffle repair, including closure of the ductus, was successfully accomplished in the other two patients at 11 and 55 days of age, using profound hypothermia. Thus, four of the six patients with a large patent ductus arteriosus were alive (table 1), three following complete correction and one without correction because of pulmonary vascular disease.

In summary, seven (35%) of the 20 patients with a good-mixing situation (TGA with large ventricular septal defect or patent ductus arteriosus) were alive at the time of review. Two were inoperable because of a high pulmonary vascular resistance, and four of the five patients with a successful complete repair were less than 4 months of age at the time of operation which was performed using the profound-hypothermia technic.

**Ventricular Septal Defect and Pulmonary Stenosis**

Eleven patients with TGA had a large ventricular septal defect and important pulmonary stenosis. A systolic pressure difference of more than 40 mm Hg between the left ventricle and main pulmonary artery was recorded in seven patients. One patient had acquired pulmonary valve atresia. In the remaining three, there was necropsy or angiographic evidence of important left ventricular outflow obstruction.

Initial management varied (table 1). Four patients appeared clinically satisfactory and received no palliation. However, one of those died at 6 months of age following a cerebral thrombosis and another at 7 years of age with a cerebral abscess. Septectomy alone was performed in two patients. In five patients, including two who previously had an interatrial communication created, a Blalock anastomosis was performed because of diminishing pulmonary blood flow. There was one death associated with this procedure and another from hypoxia at 34 months of age despite a functioning anastomosis.

Five of the seven long-term survivors have had a definitive operation (table 1). Three patients, aged 3 to 7 years, had an atrial baffle repair along with closure of the ventricular septal defect and relief of the pulmonary stenosis (valvular in one and subvalvular in two patients), and this was successful in two. One patient with valvular pulmonary stenosis and another with pulmonary valve atresia had a Rastelli procedure at 3 and 6 years of age, respectively, but both died postoperatively. The first of these operations was performed in 1966, 3 years before this procedure was described by Rastelli et al. Two patients await definitive correction.

In summary (table 1), four (36%) of the 11 patients in this group are alive, but two of these four remain uncorrected.
Aortic Obstruction, VSD, and PDA

Six patients with TGA had either coarctation or interruption of the aorta with ventricular septal defect (VSD) and patent ductus arteriosus (PDA). All were in severe heart failure, and none has survived. Two patients died without palliation. In four patients, the aortic obstruction was relieved and the ductus divided, but symptoms were unrelieved in the two operative survivors, and subsequently one of these died following banding of the main pulmonary artery. The other underwent atrial baffle repair and closure of the ventricular defect at 13 days of age using profound hypothermia, and although a satisfactory repair was achieved he died postoperatively from pulmonary complications.

Results of Atrial Baffle Repair

A total of 56 patients had an atrial baffle repair with 13 hospital deaths (23%). The hospital mortality in 45 “simple” cases where the only associated lesion requiring correction was a patent ductus arteriosus (five patients) was 15.5%. In 11 “complex” cases where there were more complex lesions requiring attention at the time of repair, the hospital mortality was 54.5%. All patients dismissed from the hospital were clinically well at the time of review which extended to 5 years postoperatively.

The mortality according to the year in which operation was performed is shown in figure 2, and in figure 3 patients are subdivided according to their age at operation. In simple cases hospital mortality was 20.8% in the 24 children over 2 years of age and 9.5% in the 21 patients less than 2 years of age (fig. 3). This reduced mortality in younger patients was related in part to increasing experience, as the profound-hypothermia technic used in those under 2 years of age was introduced in 1969, and since this date the mortality in simple cases has been reduced to 8.6% (three deaths in 35 patients).

Discussion

Use of the terms “poor mixing” and “good mixing” to define the two major groups of transposition patients provides a terminology which categorizes both the hemodynamic state and the clinical presentation of the patient and relates directly to management. Using this terminology, the hemodynamically insignificant ventricular septal defect (or patent ductus) that is too small to affect mixing needs no special mention. The confusion that results from definitions which rely on whether or not the ventricular septum is intact is obviated. The occasional patient who presents with a large atrial defect, particularly if this is associated with a small ventricular defect and a small patent ductus, may have reasonably good mixing with moderate cyanosis only and be difficult to classify. To avoid
confusion the two such patients in this series have been included in the poor-mixing group.

The outcome in this series of 120 patients with potentially correctable TGA indicates that there is still room for considerable improvement in management, for only 47 (39%) were alive at the time of review. The results were best in the poor-mixing group (43% survival), less satisfactory in those with good mixing (35%) and in those with ventricular septal defect combined with pulmonary stenosis (36%), and disastrous where there was also aortic obstruction (0%).

The results reflect improvement in management in the decade under review, particularly in the poor-mixing group, which is the largest. The safety of palliative balloon atrial septostomy compared with atrial septectomy is clearly shown, as is the importance of early atrial baffle repair. Thus, between 1961 and 1967, when atrial septectomy was the method of palliation, eight of 56 (14%) patients with poor mixing died before palliation was possible, a further 14 (25%) died in the hospital during or after palliation, and 11 (20%) died while awaiting atrial baffle repair. In this group, therefore, only 23 (41%) of the original 56 patients came forward for repair using conventional cardiopulmonary bypass at an average age of 37 months, and 18 (32%) remain alive and well. In contrast, with the advent of balloon atrial septostomy, all poor-mixing patients were palliated. Furthermore, when a Rashkind or Edwards catheter was used for this maneuver and was followed by atrial baffle repair at an average age of 13 months, 18 of 22 patients (82%) came forward for atrial baffle repair, and 17 (77%) remain alive and well. Safe early repair has been made possible by the use of the profound-hypothermia technic, two of these infants being under 6 months of age and five others under 1 year.

Currently, now that the profound-hypothermia technic has been firmly established and the backlog of patients has been dealt with, we carry out atrial baffle repair in the poor-mixing group electively between 3 and 6 months of age, or earlier than this when mixing is inadequate. With this management there is no place for repeat balloon septostomy or septectomy. In addition, both the late mortality during the waiting period and the not insignificant morbidity associated with cerebrovascular accidents are reduced to a minimum. In relation to the former, it should be noted that late mortality may prove to be higher following balloon atrial septostomy than following septectomy, for in 20% of our patients with poor mixing the defect created by the balloon was small due to an anatomically small fossa ovalis. The data presented by Tynan support this view. In only one case was the communication limited by persistent septum primum tissue, so that it is unlikely that results would be improved by using larger balloon catheters.

In TGA with good mixing due to the persistence of a large patent ductus arteriosus without a ventricular septal defect, conventional management consists of septostomy followed by closure of the ductus where necessary to control heart failure and to prevent the development of pulmonary vascular disease, and postponement of atrial baffle repair to an older age. With the advent of safe atrial baffle repair at any age these infants now come forward soon after septostomy for one-stage correction which includes ligation of the ductus from the anterior sternal splitting approach. While our experience with this form of management is still small, the results have been encouraging and there seems every reason to expect them to be as good as those achieved in the poor-mixing group.

When a large ventricular septal defect is present our results following palliation by septostomy and pulmonary artery banding have been disappointing, for three of six patients have died while awaiting definitive correction, and one has developed severe pulmonary vascular disease because of inadequate banding with pericardium. While others have achieved a higher survival rate following similar forms of palliation, it is clear that pulmonary artery banding does not provide absolute protection against the development of obstructive pulmonary vascular disease.
particularly if, as recently suggested, \textsuperscript{13} it is delayed until relatively late in infancy. Against this background a strong case can be made for balloon septostomy followed by early one-stage intracardiac repair. With this management, atrial baffle repair plus ventricular septal defect closure has been successful in two of three small infants. With increasing experience the survival rate should improve.

Up to the present time we have not attempted definitive treatment of patients with TGA pulmonary stenosis and large ventricular septal defect in infancy but have relied on palliative procedures when indicated. However, the fact that four of the 11 children in this group have died prior to definitive repair is disturbing. The success attending correction under profound hypothermia in infancy of pulmonary atresia with large ventricular septal defect and truncus arteriosus, using an aortic homograft (diameter 16-18 mm) to reconstruct the right ventricular outflow tract (unpublished data), indicates that a Rastelli type of operation would be feasible at a young age. This may prove the more appropriate management.

The correct treatment of patients with TGA aortic obstruction, patent ductus arteriosus, and large ventricular septal defect remains in doubt as there have been no long-term survivors, regardless of the form of management.

References


8. RASHKIND WJ, MILLER WW: Creation of an atrial septal defect without thoracotomy: Palliative approach to complete transposition of the great arteries. JAMA 196: 991, 1966


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Circulation. 1972;45:1251-1258
doi: 10.1161/01.CIR.45.6.1251

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