Radionuclide Angiographic Evaluation of Right and Left Ventricular Function During Exercise After Repair of Transposition of the Great Arteries

Comparison with Normal Subjects and Patients with Congenitally Corrected Transposition

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SUMMARY We assessed the incidence, clinical significance and etiology of ventricular dysfunction after intraatrial repair of d-transposition of the great arteries in 11 patients, mean age 9 ± 3 years, who had had Mustard operations. We compared the results to 15 patients who were considered to have normal ventricular function, two patients who had Rastelli operations and five patients with congenitally corrected transposition. Gated equilibrium radionuclide angiography with supine exercise stress testing was used to assess these children. We found no significant difference between our patient groups in exercise capacity, heart rate, or blood pressure response to exercise. However, we found a high incidence of right ventricular dysfunction in the patient groups, manifested by an abnormal right ventricular ejection fraction response to exercise in six of 11 patients with a Mustard repair, both patients with a Rastelli repair and all five with congenitally corrected transposition. In addition, the left ventricular response to exercise was abnormal in 10 of 11 patients who had undergone a Mustard repair, both patients with a Rastelli repair, and two of five patients with congenitally corrected transposition. We conclude that biventricular dysfunction is frequently present after intraatrial repair of d-transposition of the great arteries. Despite this dysfunction, no significant decrease in exercise tolerance is found in childhood.

RIGHT VENTRICULAR dysfunction has been reported in many patients after repair of d-transposition of the great arteries.1-6 Although left ventricular dysfunction has also been reported in these patients,7 it is not a uniform finding.8 The incidence, clinical significance and etiology of these functional disturbances is unknown.

We assessed the incidence and severity of right and left ventricular dysfunction after operation in our patients with d-transposition of the great arteries, using radionuclide angiography and exercise stress testing. These results were contrasted to findings in a small group of patients with congenitally corrected transposition of the great arteries and a third group of patients without significant cardiac defects. We also assessed various surgical factors and hemodynamic residua as contributors to functional disturbances.

Patients and Methods

We performed radionuclide ventriculograms on 13 children with d-transposition of the great arteries, all of whom had undergone intracardiac repair. All patients older than age 6 years who had undergone repair of transposition of the great arteries or who had congenitally corrected transposition and who were evaluated in our Cardiology Clinic between June 1980 and January 1982 were referred for radionuclide ventriculography. Studies were performed 3 months to 14 years after repair. Eleven patients, mean age 9.1 ± 3 years, received a Mustard-type repair9 and two patients, mean age 9.9 ± 4.9 years, required a Rastelli repair.10 The two patients who had a Rastelli repair were significantly older than the group of patients with a Mustard repair at the time of complete repair (9.6 ± 4.9 vs 1.5 ± 1.2 years). Eight of the 11 patients with a Mustard repair had significant hemodynamic residua postoperatively: Five had mildly obstructed systemic venous...
return, one patient mildly obstructed pulmonary venous return, two patients ventricular septal defect with a greater than 30% left to right shunt, two patients junctional rhythm and one patient complete atrioventricular block. Both patients who had a Rastelli repair had severe pulmonary stenosis and a large ventricular septal defect before repair. One patient with a Mustard repair and one patient with a Rastelli repair were taking digoxin at the time of study. Both complained of mild exercise intolerance. All other postoperative patients were asymptomatic and were taking no medications at the time of study.

We compared our findings in patients with d-transposition of the great arteries with those in a group of patients with congenitally corrected transposition and a group without significant cardiac defects. The five patients with congenitally corrected transposition were older at the time of study (mean 14 ± 3.9 years) than the group of patients with a Mustard repair. The patients with congenitally corrected transposition had associated problems: Two patients had pulmonary stenosis and a ventricular septal defect, one patient had complete atrioventricular block, and one had undergone intracardiac surgery. Although two of these patients were mildly cyanotic and had mild exercise intolerance, none was taking inotropic or diuretic drugs at the time of study.

We studied 15 patients who had no significant cardiac disease (mean age 11.3 ± 3.4 years). Nine of these patients underwent operations, including five who received intracardiac repair of atrial septal defects, one a coarctation repair, one repair of partial anomalous pulmonary venous drainage and two repair of pectus excavatum. Two patients had mild pulmonary stenosis that did not require operation (pressure gradient less than 30 mm Hg), two had transient arrhythmias, one patient had type II hyperlipidemia, and one had occasional chest pain, but was believed to have a normal heart. For patients who underwent operations, the time from surgery to radionuclide study was 1.5–15.5 years (mean 5.4 ± 5.1 years). Although this group of patients had diverse diagnoses, all were considered clinically to have no significant cardiac disease or residua at the time of radionuclide study. These patients were thus designated as a normal comparison group.

Multiple-gated equilibrium radionuclide studies were performed on all patients in the supine position. Red blood cells were labeled in vivo with technetium-99m using an adult dose of 20 mCi, adjusted downward for children based on their body surface area (approximately 14 mCi/m²). The cardiac blood pool was imaged with a Picker Dyna-Mo single-crystal mobile gamma camera interfaced to a dedicated GAMMA-11 computer system (Digital Equipment Corporation). We used an all-purpose, medium-resolution collimator. The camera head was oriented to the patient so as to maximize ventricular separation. This was usually accomplished with a 30–80° left anterior oblique orientation with 10–15° of caudal tilt.

The cardiac blood pool was imaged for 5 minutes at rest, obtaining 2 to 3 million total counts. We used 40-msec frame durations for heart rates less than 100 beats/min and 30-msec frame durations for rates greater than 100 beats/min.

After the resting collection, patients undertook supine exercise on a bicycle ergometer, using a continuous staged protocol similar to that described by Godfrey. Exercise was performed in 4-minute stages, with incremental increases in work load between each stage up to the point of maximal voluntary patient effort. Work loads were adjusted to the patient’s size as described by James et al. Pedal speed was maintained at 60–80 rpm for the duration of the exercise procedure. All patients completed at least two of the four stages of exercise. The reason for discontinuing exercise was leg fatigue. Cardiac imaging was performed during the final 3 minutes of each exercise stage.

Serum lactic acid levels were determined on our most recently studied patients, including eight patients from the normal group, three from the group with congenitally corrected transposition and six from the group who had received Mustard repairs. Neither of the patients who received a Rastelli repair had a lactic acid determination. Free-flowing venous blood samples were obtained 15 minutes before starting exercise and 3 minutes after cessation of exercise.

All studies were analyzed to obtain right and left ventricular ejection fraction. The radionuclide ejection fraction was determined by the formula

\[
\frac{(EDC - BK) - (ESC - BK)}{EDC - BK}
\]

where EDC = end-diastolic counts, ESC = end-systolic counts, and BK = background counts. Hand-drawn regions of interest were used for left and right ventricle using guidelines similar to those described by Maddahi et al. and validated in children by us. A region for background correction adjacent to the left ventricle was chosen and used for both right and left ventricular calculations.

To calculate absolute cardiac output at rest, geometric estimates of end-diastolic ventricular volume were performed using validated methods. Calibration of the image size was performed with phantom grids before determining ventricular volumes. The following area-length formula was used for the left ventricle:

\[
\frac{8}{3} \left[ \frac{\text{area}^2}{\pi \times \text{longest axis}} \right]
\]

For the right ventricle, Simpson’s rule is used to estimate ventricular volume. The cardiac output for the systemic ventricle at rest was then calculated using the formula

\[
\text{End-diastolic volume} \times \text{ejection fraction} \times \text{heart rate}
\]

In this calculation, ejection fraction is determined from end-diastolic and end-systolic images using formula 1.

In addition to calculating the absolute cardiac output at rest, we also calculated the percent increase in cardi-
ac output at peak exercise. Geometric assessment of ventricular volumes during exercise is technically difficult because of blurring of the chamber borders. Thus, we assessed increases in cardiac output with exercise using a count-based formula:

$$\frac{(EX \text{ stroke CTS}) \cdot (EX \text{ HR}) - (rest \text{ stroke CTS}) \cdot (rest \text{ HR})}{(rest \text{ stroke CTS}) \cdot (rest \text{ HR})} \times 100$$

where EX = exercise, CTS = counts, and HR = heart rate. This assessment of the change in cardiac output is independent of geometric assumptions.

Statistical comparisons between group means were made using one way analysis of variance followed by Student-Newman-Keuls test. Resting and exercise studies within a single patient group were compared using a $t$ test for paired data. Discrete data in each patient group were compared using Fisher’s exact test. The level of statistical significance for all analyses was $p < 0.05$.

**Results**

**Exercise Capacity**

We found no significant difference between our patient groups in exercise capacity (work load), heart rate, blood pressure or serum lactic acid response to exercise.

**Cardiac Function**

The mean right ventricular ejection fractions at rest and at peak exercise are shown in figure 1. We found no significant difference in this variable between the groups. The right ventricle is the systemic ventricle for the patients with a Mustard repair and patients with congenitally corrected transposition, but is the pulmonic ventricle for the patients with a Rastelli repair and the normal patients.

The groups responded differently to exercise. At peak exercise, the mean ejection fractions for the patients who had a Mustard repair and the patients with congenitally corrected transposition were not significantly different from the resting values for these groups (paired $t$ test). However, in the normal group, right ventricular ejection fraction increased significantly from rest to peak exercise. The two patients with a Rastelli repair (not shown) had a mean decrease of 10% in their right ventricular ejection fractions with exercise.

The mean left ventricular ejection fractions at rest and peak exercise are shown in figure 2. Again, at rest there was no significant difference between groups. In response to exercise, both the normal subjects and the patients with congenitally corrected transposition showed a significant increase in left ventricular ejection fraction. In contrast, the patients with the Mustard repair demonstrated no significant change in left ventricular ejection fraction from rest to peak exercise. The two patients with a Rastelli repair decreased their left ventricular ejection fraction by a mean of 3%.

Table 1 displays the ejection fraction response to exercise for individual patients. Significantly fewer patients in the transposition groups (postoperative Mustard repair, postoperative Rastelli repair and congenitally corrected transposition) showed an increase in right ventricular ejection fraction than did the normal group. In contrast, only the group of patients with a Mustard repair had significantly fewer patients showing an increase in left ventricular ejection fraction.

We found no statistically significant difference in
Table 1. Ejection Fraction Response to Exercise

<table>
<thead>
<tr>
<th></th>
<th>Control</th>
<th>After Mustard</th>
<th>After Rastelli</th>
<th>CCTGA</th>
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<tr>
<td>Right ventricle</td>
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<tr>
<td>Increase EF ≥ 5%</td>
<td>13/15</td>
<td>5/11*</td>
<td>0/2*</td>
<td>0/5*</td>
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<tr>
<td>∆EF &lt; 5%</td>
<td>2/15</td>
<td>4/11</td>
<td>0/2</td>
<td>4/5*</td>
</tr>
<tr>
<td>Decrease EF ≥ 5%</td>
<td>0/15</td>
<td>2/11</td>
<td>2/2*</td>
<td>1/5</td>
</tr>
<tr>
<td>Left ventricle</td>
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<tr>
<td>Increase EF ≥ 5%</td>
<td>11/15</td>
<td>1/11*</td>
<td>0/2</td>
<td>3/5</td>
</tr>
<tr>
<td>∆EF &lt; 5%</td>
<td>4/15</td>
<td>3/11</td>
<td>1/2</td>
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</tr>
<tr>
<td>Decrease EF ≥ 5%</td>
<td>0/15</td>
<td>7/11*</td>
<td>1/2</td>
<td>0/5</td>
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</tbody>
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*Significantly different from control group (p < 0.05).

Abbreviations: CCTGA = congenitally corrected transposition; EF = ejection fraction.

cardiac index between our patient groups. At rest, the mean cardiac index (see formula 3) was 3.68 ± 0.64 l/min/m² for the normal group, 2.95 ± 0.81 l/min/m² for the group of patients with a Mustard repair, 4.65 ± 2.19 l/min/m² for the patients with a Rastelli repair and 3.97 ± 0.60 l/min/m² for the congenitally corrected transposition patients. Figure 3 displays the cardiac output response to exercise in our normal group, the group of patients with a Mustard repair and the group of patients with congenitally corrected transposition. The patients with a Mustard repair showed significantly less change in cardiac output than did the normal group. The group of patients with congenitally corrected transposition was not significantly different from the normal group.

Cardiac Function and Residual Defects

We attempted to relate residual cardiac defects to the ejection fraction response to exercise in our patients with a Mustard repair. An abnormal ventricular response was defined as a failure to increase the ejection fraction by 5% or more. Although we found a smaller percentage of the abnormal right ventricular responses in patients without residual defects (33% vs 62% in those with residual defects), this difference was not statistically significant (Fisher’s exact test). We also found no statistically significant difference in the occurrence of abnormal ventricular responses in the patients repaired before 1 year of age (abnormal left ventricle in 83% and abnormal right ventricle in 66%) compared with those repaired after 1 year of age (abnormal left ventricle in 80% and abnormal right ventricle in 40%). We examined the effect of the duration of cardiac arrest on ventricular function and found no statistically significant difference between patients who required less than 75 minutes of arrest time (abnormal left ventricle in 100% and abnormal right ventricle in 75%) vs those who required more than 75 minutes (abnormal left ventricle in 80% and abnormal right ventricle in 50%). Two patients from the normal comparison group required 60 minutes of cardiac arrest for repair of sinus venosus-type atrial septal defects. Both of these patients had normal right and left ventricular responses to exercise.

Discussion

Superb surgical results are being reported with several intraatrial techniques for repair of d-transposition of the great arteries. However, despite these excellent immediate results, pediatric cardiologists and surgeons remain concerned about potential complications, including systemic or pulmonary venous obstruction, tricuspid incompetence, sinus node dysfunction, atrioventricular block and ventricular dysfunction. Recently, a significant incidence of left ventricular dysfunction in these postoperative patients has also been suggested, although this remains controversial. The frequency of right ventricular dysfunction has led Hagler et al. to suggest increased surgical efforts to use the left ventricle as the systemic ventricle.

Before advocating a deemphasis of the intraatrial repair of d-transposition, we elected to determine the incidence and severity of both right and left ventricular dysfunction in patients who have had intraatrial repair. We used radionuclide angiography to study these patients. Although this technique has been widely used and validated in adult patients, it has had limited appli-
cation to the pediatric population. The diverse ventricular shapes and sizes in children may cause technical difficulty with this method. In addition, children with large right ventricles (as in the patients with a Mustard-type repair) require an almost complete left lateral orientation of the camera to obtain images perpendicular to the ventricular septum. In contrast, patients with congenitally corrected transposition require almost a straight anterior-posterior camera orientation. Despite these considerations, we have found excellent correlations between radionuclide assessment of ventricular ejection fraction and cineangiographic assessment of ejection fraction in children with diverse cardiac diseases, including transposition of the great arteries.

Combining exercise with radionuclide angiography, we found statistically significant abnormalities of right ventricular function in patients with a Mustard repair, patients with a Rastelli repair and patients with congenitally corrected transposition (fig. 1, table 1). However, as a group, only the patients with a Mustard repair had abnormal left (pulmonary) ventricular function (fig. 2, table 1). Despite these functional abnormalities, we could not detect significant differences in exercise tolerance between the normal patients and patients with a Mustard repair. This suggests that for most of these patients, the abnormalities of ventricular function are not important clinically in childhood. Masden and Franch, in a review of isolated congenitally corrected transposition, found no reports of clinical congestive heart failure before age 35 years. However, seven of 12 patients older than age 35 years showed evidence of congestive heart failure. These data suggest that a systemic right ventricle functions well for several decades, but may decompensate over a full life span. Longitudinal studies will be needed to determine if the right ventricular dysfunction found in children with intraatrial repair of complete transposition progressively worsens or causes a deterioration in exercise capacity later in life.

The left ventricular dysfunction in our postoperative Mustard patients indicates that the functional disturbances are probably multifactorial. Although the intrinsic geometry of the right ventricle might partially account for the abnormal exercise response, the normal left ventricular response in patients with congenitally corrected transposition suggests that other factors are involved. We could find no correlation between cardiac dysfunction and either residual hemodynamic problems, age at complete repair, or length of cardiac arrest at the time of repair. We have speculated that intermittent episodes of myocardial hypoxia (occurring at times of stress), during which myocardial oxygen demands exceed supply, lead to myocardial functional abnormalities in patients with complete transposition before repair. The abnormalities of left and right ventricular function found in this investigation are consistent with that hypothesis. Intraoperative hypoxia or ischemia may also contribute to the myocardial functional abnormalities.

We conclude that both right and left ventricular dysfunction are common in children after intraatrial repair of d-transposition of the great arteries. Both right and left ventricular dysfunction are also present after the Rastelli repair of d-transposition. Patients with congenitally corrected transposition of the great arteries frequently demonstrate right ventricular dysfunction, but left ventricular dysfunction is less common. Despite the frequency of ventricular dysfunction in patients with complete transposition, no significant decrease in measured exercise capacity is found in childhood. Although we could not implicate specific factors in the etiology of this ventricular dysfunction, we speculate that the cause is multifactorial, including myocardial hypoxia (preoperative and intraoperative) and a ventricle that is geometrically suboptimal for function at systemic pressures.

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Ventricular and Pulmonary Artery Volumes in Patients with Absent Pulmonary Valve
Factors Affecting the Natural Course

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SUMMARY Right and left ventricular (RV and LV) volumes were determined in 19 patients with absent pulmonary valve syndrome using Simpson’s rule and area-length methods. The volume of the proximal right pulmonary artery (RPV) was calculated at maximal and minimal size using the area-length method. Patient groups included four newborns who responded to medical management (group 1A), seven critically ill newborns who died (group 1B), four infants ages 1-10 months (group 2) and four children ages 2-8 years (group 3). The RV end-diastolic volume in groups 1B and 2 was significantly greater than that in groups 1A and 3. The RV ejection fraction in groups 1B and 2 was significantly less than that in normal patients and groups 1A and 3. Maximal RPV correlated well with RV stroke volume and end-diastolic volume. The maximal RPV in group 1B was significantly greater than that in groups 1A and 3. Pulmonary arterial compliance was greater than normal in all groups, and the compliance in group 1B was more than two times that in the other groups.

We conclude that the increased right pulmonary artery compliance and pulmonary regurgitation in patients with absent pulmonary valve contribute to bronchial obstruction and right-heart failure and are the causes of the high morbidity and mortality in these patients. The management should be directed to the alleviation of bronchial obstruction and right-heart failure.

THE ABSENT pulmonary valve syndrome (APVS) usually consists of an absent pulmonary valve, a ventricular septal defect, mild-to-severe right ventricular (RV) outflow obstruction, and aneurysmal dilatation of the pulmonary arteries. The obstruction is almost always located at the pulmonary valve ring, and sometimes at the infundibulum as well.1-3 This combination of the lesions is better known as tetralogy of Fallot with absent pulmonary valve.

Calder et al.4 reviewed 233 cases with APVS and reported that many infants die early from severe respiratory distress and intractable cardiac failure.1-3 Bronchial compression by distended pulmonary arteries is a particular problem in patients with APVS in early infancy.2-5,6 However, the relationship between RV function and the aneurysmal dilatation of the pulmonary arteries is not known. Furthermore, it is not clear how often RV and left ventricular (LV) function influence the morbidity and mortality of these patients. In this study we describe the characteristics of RV and LV performance in newborns, infants and children

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