Assessment of left ventricular contractile state after anatomic correction of transposition of the great arteries

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ABSTRACT When compared with intra-atrial baffle repairs for d-transposition of the great arteries (TGA), anatomic correction offers the theoretic advantage that it results in the use of the left ventricle (LV) as the systemic ventricle. Although the long-term success of this procedure depends on the function of the LV, little is known regarding LV postoperative contractile state. The LV end-systolic pressure–dimension and wall stress–shortening (%ΔD) relationships, sensitive indexes of contractility, were studied during methoxamine-induced increases in afterload in eight patients with TGA and intact ventricular septa and in four patients with TGA and associated lesions. The patients with TGA and intact ventricular septa underwent pulmonary artery banding when they were between the ages 0.1 and 1.1 years (mean 0.4) to prepare the LV for anatomic correction. Age at repair ranged from 0.3 to 1.8 years (mean 1.0) and that at study from 1.7 to 6.7 years (mean 3.3). The interval from correction to study was 0.4 to 4.8 years (mean 2.3). End-systolic pressure was estimated from a calibrated suprasternal notch tracing. End-systolic dimension, wall thickness, and %ΔD were determined by M mode and two-dimensional echocardiography, and end-systolic wall stress was then calculated. Results were compared with previously reported normal values. The pressure–dimension and wall stress%ΔD relationships were normal in 10 of 12 TGA patients. The two patients with abnormal study results had TGA with intact ventricular septa and they underwent correction after 1.5 years of age. There was no relationship between contractile state and either interval from repair to study or age at study. Thus, LV contractility is normal in most patients with TGA who undergo anatomic correction.


When compared with the Mustard or Senning repairs for d-transposition of the great arteries (TGA), anatomic correction at the arterial level offers the advantage of normalizing the reversed role of the two ventricles. The importance of this advantage depends on the assumption that the left ventricle (LV) in transposition is normal before surgery and is not affected by the operative procedures. To date, the validity of these assumptions has not been adequately tested. We believe, therefore, that it is essential to critically evaluate LV contractility after anatomic correction. Recently the noninvasively determined slope value of the end-systolic pressure (Pes)–dimension (Des) relationship and the position of the end-systolic wall stress (ses)–shortening (%ΔD) relationship, as determined by methoxamine challenge, have been proposed to be sensitive indexes of LV contractile state in man. This method has been used to detect preclinical abnormalities in children at risk for LV dysfunction. The purpose of this article is to report on the use of this noninvasive method to evaluate LV contractile state after anatomic correction of TGA.

Patients and methods

Our patient population consisted of 12 children (10 boys and 2 girls) who had undergone anatomic correction for TGA (table 1). Only patients in close geographic proximity to the study site in Harefield, England were evaluated. Before surgery eight children had TGA with intact interventricular septa (IVSs) and four had additional defects (large ventricular septal defects in three, and aortopulmonary window in one). All of the children with TGA/IVSs underwent two-stage repair with initial pulmonary artery banding performed when they were from 0.1 to 1.1 years of age (mean 0.4). The patients’ ages at repair ranged from 0.3 to 1.8 years (mean 1.0), and their ages at postoperative study ranged from 1.7 to 6.7 years (mean 3.3); the interval between definitive repair and study ranged from 0.4 to 4.8 years (mean 2.3). The technique used for anatomic correc-
tion has been described previously\(^1,2\) and consists of switch-over anastomoses of the aorta and pulmonary arteries with transfer of the coronary ostia to the future systemic great artery. There was no evidence of LV or right ventricular outflow tract obstruction on physical examination, two-dimensional echocardiographic study, or postoperative cardiac catheterization in any of the patients. The nine control subjects ranged in age from 6 to 15 years (mean 9). They had normal cardiac examination results, electrocardiograms (ECGs), and intracardiac anatomy, as determined by M mode and two-dimensional echocardiography. Informed consent was obtained from the parents of each child studied.

**Experimental protocol.** The experimental protocol was similar to that reported previously.\(^3,4\) A Cambridge medical instrument and Smith-Kline model E-20A ultrasound module with a 3.5 MHz transducer were used for M mode echocardiographic recordings. Two-dimensional echocardiographic imaging was performed with an Advanced Technical Laboratories model No. 851B real-time digital scanner. An external microphone was placed at the right upper sternal border area for phonocardiographic recording. Peak systolic and diastolic blood pressure measurements were made with the Dinamap 845 vital signs monitor (Critikon, Inc., Tampa, FL). This instrument can accurately estimate central aortic pressures over a wide range of systolic and diastolic values in both children and adults.\(^5\)

Subjects under 6 years of age were given light sedation with oral trimetrazine (2.5 mg/kg) followed in 1 hr by an intramuscular injection of papaveretum (0.33 mg/kg) and scopolamine (0.0067 mg/kg). All patients were premedicated with intravenous atropine (0.01 mg/kg) to abolish reflex cardiac slowing. Each subject underwent simultaneous recordings of systolic and diastolic blood pressures, an M mode echocardiogram of the left ventricle, a phonocardiogram, an indirect carotid or suprasternal notch pulse tracing, and an ECG under baseline conditions. Blood pressure was then elevated by the intravenous infusion of methoxamine beginning at 25 \(\mu\)g/kg/min and titrating upward to achieve the desired systolic blood pressure effect. The LV response to the methoxamine was assessed by repeating the recordings every 1 to 2 min during the infusion. When peak systolic pressure had increased by 30 to 60 mm Hg above baseline, the methoxamine infusion was discontinued. Peak pressure effect lasted 2 to 3 min. Parasternal long-axis and short-axis as well as subxiphoid views of the LV were obtained before initiation and immediately after cessation of the methoxamine infusion. Data points were excluded when heart rate varied by more than 10 beats/min from baseline. The LV end-diastolic dimension (Ded) was measured from the M mode echocardiogram at the onset of the Q wave of the ECG while the Des and wall thickness (h\(_w\)) were measured at the first high-frequency component of the second heart sound. The measurements for Ded, Des, and h\(_w\) were determined as the mean values for five cardiac cycles. LV %AD was calculated as:

\[
\%\Delta D = \frac{\text{Ded} - \text{Des}}{\text{Ded}}
\]

The external pulse tracings were calibrated with the automated blood pressure-monitoring device with systolic pressure assigned to the peak and diastolic pressure assigned to the nadir of the tracing. PEs was estimated by linear interpolation to the height of the dicrotic notch. This method of estimating PEs in children ranging in age from 1 day to 15 years has been shown to have a mean error of 2% when compared with values measured from simultaneously recorded central aortic pressures. Ninety-seven percent of the noninvasively determined PEs values were within 5 mm Hg of the central aortic values.\(^6\) LV ßes was calculated with the following angiographically validated formula\(^7\):

\[
\beta_{es} = \frac{(\text{Pes} - \text{Des}) (1.35)}{(\text{h}_w) \left[ 1 + \left(\frac{\text{h}_w}{\text{Des}}\right) \right] (4)}
\]

**Statistical analysis.** Data are presented as individual data points as well as the mean ± SD. The hemodynamic response to the afterload challenge was assessed with the \(t\) test for paired data. A \(p\) value < .05 was taken as statistically significant. Simple linear regression (least squares method) was used to fit each subject's data to a pressure-dimension equation \([\text{Pes} = (m) \text{Des} + b]\) where \(m\) is the slope value and \(b\) the y intercept. Since Des for normal subjects between infancy and young adulthood varies in a linear manner with the cube root of the body surface area \((\text{Des/BSA})^{0.33}\), this function was chosen as a method of standardizing Des for patients of different ages.\(^8\) Abnormality was defined as a "corrected" slope value (m*) greater than 2 SD below the mean value for the control group (i.e., m* < 96 mm Hg/cm). The patients' end-systolic stress-shortening points were compared with previously reported 95% confidence limits for this relationship.\(^4\) Points outside these limits were considered statistically different from those for the normal population.

**Results**

Table 2 summarizes the hemodynamic response of the patients with TGA to the afterload challenge. LV dimensions and pressures as well as ßes varied directly, whereas %\(\Delta D\) varied inversely with augmented afterload. Heart rate remained unchanged.

The individual patients' responses to the increased afterload are shown in Table 3. Representative M mode echocardiographic, suprasternal notch pulse, and phonocardiographic recordings from a 1.8-year-old child who underwent anatomic correction at 0.3 years of age are shown in Figure 1. In all cases Pes and Des were linearly related, with correlation coefficients

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**Table 1** Data profile of study patients

<table>
<thead>
<tr>
<th>Patient</th>
<th>Age at banding (yr)</th>
<th>Duration of banding (yr)</th>
<th>Age at anatomic correction (yr)</th>
<th>Interval, correction to study (yr)</th>
<th>Age at study (yr)</th>
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<tr>
<td>3(^a)</td>
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<td>—</td>
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<td>9(^a)</td>
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<td>—</td>
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\(^a\)Associated lesion present.
ranging from 0.92 to 0.98. For the nine control subjects, the corrected slope values for the Pes-Des relationship ranged from 106 to 151 mm Hg/cm (mean ± SD = 123 ± 14). Two of the 12 patients with TGA (Nos. 4 and 11) had slope values <2 SDs below the mean value for the control group (i.e., m* < 96 mm Hg/cm). Resting %ΔD was normal in patient No. 11 and abnormal in patient No. 4. These two patients had TGA/IVS, underwent banding relatively late, and underwent anatomic correction after they were 1.5 years old. When the mean m* value for the patients with simple TGA that was surgically corrected at or before 1.0 years of age was compared with that for the control subjects, no statistical difference was present (121 ± 14 vs 123 ± 14; p = ns). All four patients with TGA and associated lesions had normal responses to the afterload challenge regardless of age at repair. There was no relationship between the slope value and age at study (figure 2) or time interval between anatomic correction and study (figure 3). Patient No. 4, who had a depressed m* value, was studied 4 months after anatomic correction, while all other patients were studied at least 1 year after repair. On two-dimensional echocardiographic imaging of the LV, 10 patients had normal and two patients (Nos. 1 and 4) had mildly flattened septal motion. No patient had paradoxical motion of the IVS. There was no evidence of significant LV regional wall motion abnormalities either at baseline or under peak afterload conditions.

When the σes-%ΔD relationship for the individual TGA patients was plotted against previously reported normal values (figure 4), two major findings were evident. First, the position of the linear regression line, when analyzed over a wide range of afterload conditions, was highly predictive of a normal or abnormal value for the corrected slope of the Pes-Des relationship. Second, the position of the resting σes-%ΔD point was as good a predictor of the results of the Pes-Des analysis as was the entire σes-%ΔD regression line. This reflects the relatively parallel nature of the mean regression line for the normal σes-%ΔD values and the regression lines for the individual patients with TGA.

### Discussion

Systemic ventricular dysfunction after the Mustard or Senning procedures for TGA has been well documented.12-14 No apparent correlation has been found between systemic ventricular dysfunction and age at intra-atrial repair, events at time of operation, or findings at postoperative cardiac catheterization.15 In addition to overt right ventricular failure,13 there is growing evidence that many children have subclinical right
### Table 3

<table>
<thead>
<tr>
<th>Patient</th>
<th>HR</th>
<th>Des</th>
<th>Ded</th>
<th>%ΔD</th>
<th>$b_0$</th>
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<th>Pd</th>
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<th>$\sigma$es</th>
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$m = \text{slope value of the Pes-Des relationship}; m^* = \text{corrected m}; \text{other abbreviations are as in table 2.}$
ventricular dysfunction with exercise or pharmacologic afterload challenge. This dysfunction might be due to inherent differences in chamber shape and fiber orientation between the right and left ventricles. The large right ventricle, when functioning in a systemic capacity, must generate higher than usual peak, mean, and end-systolic wall stresses. This increase in systolic wall stress results in enhanced myocardial oxygen consumption. Since in TGA the right ventricle has only a single coronary artery available to perfuse its myocardium, an imbalance between oxygen supply and demand can theoretically occur under circumstances of augmented heart rate, afterload, sympathetic tone or contractile state. The importance of this anatomic difference between left and right ventricles is unclear since many patients with TGA have a rather extensive and enlarged right coronary artery supplying the right ventricle.

The problems inherent to intra-atrial repair have prompted the exploration of a totally different approach to the correction of TGA. The potential advantages and disadvantages of this operation have been discussed previously. One of the most important questions relates to the ability of the LV to function normally after anatomic correction, particularly in view of the fact that the LV in TGA may be congenitally abnormal or could undergo structural changes early in life, after banding, or during anatomic repair. We have previously reported good postoperative ventricular function, as determined by catheterization and digitized echocardiographic assessment, in patients with TGA undergoing anatomic correction. In this study, none of the patients in our postoperative population had prolonged overt systemic ventricular failure. In our group of patients with TGA/IVS there was a striking inverse correlation between the age at anatomic correction and the slope value for the Pes-Des relationship (figure 5). In a previously reported study, we demonstrated a similar age-related trend towards better systemic ventricular function in cyanotic children with tetralogy of Fallot who underwent anatomic repair at an early age.

Pathologic specimens from small children with TGA/IVS have shown a relative regression of LV wall thickness and an increase in LV chamber size with
time. Such changes would result in very high systolic wall stress values if the LV were suddenly converted from the pulmonary to the systemic pumping chamber. Since there is an inverse relationship between systolic wall stress (or afterload) and the extent of LV fiber shortening, an abrupt increase in afterload would markedly compromise LV performance. It is therefore not surprising that small children who undergo anatomic correction without prior pulmonary artery banding to prepare the LV for high workloads frequently demonstrate a diminished LV %ΔD and die as a result of problems associated with low cardiac output. All of the TGA/IVS patients in our study underwent a two-step surgical procedure involving initial pulmonary artery banding and subsequent anatomic correction. Recently, anatomic correction within the first few weeks of life in selected patients with TGA has been performed successfully, thus eliminating the need for pulmonary artery banding.

Potential limitations of our noninvasive method for assessing LV contractility have been noted previously. In this study, we assumed that the LV minor-axis dimension measured from the M mode echocardiogram was representative of overall LV function and that there was no significant coronary artery narrowing after anatomic correction. These assumptions seem reasonable since no patients showed evidence of significant regional wall motion abnormality on two-dimensional echocardiographic study even under peak afterload conditions. While our study patients and control subjects were not age matched, the slope values for the Pes-Des relationships were normalized for body surface area. There was no difference among corrected slope values for the patients with TGA/IVS who underwent repair when they were under 1.5 years old, for control subjects in this study, and our previously reported normal values for older children, adolescents, and adults. This suggests that LV contractility reaches its adult potential relatively early in life. Since the σes-%ΔD relationship under resting conditions accurately predicted which subjects would have depressed Pes-Des slope values, methoxamine infusion may not be needed in the future to evaluate contractile state in patients with TGA who undergo anatomic correction.

Our LV dimension data showed good reproducibility. We believe that several factors were important in the acquisition of the echocardiographic data. First, the study was performed over a short period of time (less than 25 min) in mildly sedated patients lying in a stationary position. Care was taken to keep the transducer in the same intercostal space with the same amount and position of chordae tendineae. Finally, LV dimensions and shortening fractions were determined as they related to ventricular afterload. This eliminated much of the variation in dimensions that would otherwise occur if LV loading conditions were not addressed. In addition, LV dimension values were averaged over at least five cardiac cycles, thus blunting respiration variations in LV measurements.

LV contractile state, as analyzed by the Pes-Des and σes-%ΔD relationships, was normal in 10 of 12 patients with TGA studied after anatomic correction. Preservation of normal LV contractility is accomplished in most patients who undergo pulmonary artery banding and subsequent anatomic correction before they are 1.5 years of age. Further studies addressing the relationship between contractile state and age at time of anatomic correction are needed.

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