associated with interpretation of the S2 vibratory complex in the conventional phonocardiogram. It provides clinically relevant information about the splitting interval at times when the phonocardiogram fails to do so, and is therefore offered as a supplement to phonocardiography.

References
1. Leatham A: The second heart sound, key to auscultation of the heart. Acta Cardiol (Brux) 19: 395, 1964

Influence of Age on Wall Thickness, Cavity Dimensions and Myocardial Contractility of the Left Ventricle in Simple Transposition of the Great Arteries

ENRIQUE MAROTO, M.D., JEAN-CLAUDE FOURON, M.D., MARIE-YVONNE DOUSTE-BLAZY, M.D., ANA-MARIA CARCELLER, M.D., NICOLAAS VAN DOESBURG, M.D., CHRISTA KRATZ, M.D., AND ANDRE DAVIGNON, M.D.

SUMMARY This study was carried out to establish a reference table of echocardiographic values for the left ventricle of simple d-transposition of the great arteries (d-TGA) and to determine at what age left ventricular dimensions in these patients become different from those of a normal population. Fifty-three patients with d-TGA and normal pulmonary pressure and 395 normal children ages 1 day to 10 years were studied by M-mode echocardiography. Results show that in d-TGA, left ventricular systolic and diastolic internal diameters are normal at birth. After 1 month, however, both diameters were below normal and despite a progressive increase with age, the mean values were always below normal. The mean posterior wall thickness of patients with d-TGA was also normal at birth but did not increase with age (2.3 mm in diastole and 4.3 mm in systole) and became significantly thinner than normal at 10 months of age in diastole and 7 months in systole. Septal thickness of patients with d-TGA did not differ from that of the control group. The shortening fraction and mean velocity of circumferential fiber shortening were significantly greater in d-TGA at all ages. Left ventricular measurements related to age are presented and should be of help in interpreting M-mode echocardiograms of patients with d-TGA.

MEASUREMENTS of anatomic specimens1-4 and by echocardiography5 have shown that patients with d-transposition of the great arteries (d-TGA) have a thinner left ventricular (LV) wall than subjects with normally related great arteries. This is expected because in transposition, the left ventricle is connected to the low-pressure pulmonary circulation. However, the influence of age on LV characteristics has only been studied in anatomic specimens1-2 and never, to our knowledge, in living patients with d-TGA. This information is important for at least three reasons. First, a reference table based on echocardiographic measurements related to age from patients with uncomplicated d-TGA is needed to interpret echocardiograms of patients with d-TGA, because comparison with normal subjects is obviously erroneous. Second, studies of fixed anatomic specimens cannot provide information about the dynamic characteristics of the LV wall. Third, with the increasing popularity of anatomic correction of d-TGA, it has become important to establish the age at

From the Cardiology Section, Departments of Pediatrics and Pediatric Research, Sainte-Justine Hospital and University of Montreal, Quebec, Canada.
Supported by the Quebec Heart Foundation.
Presented in part at the Annual meeting of the Canadian Cardiovascular Society, Calgary, October 1982.
Address for correspondence: Jean-Claude Fouron, M.D., Sainte-Justine Hospital, 3175 Sainte-Catherine Road, Montreal, Quebec, Canada H3T 1C5.
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which the anatomic and functional characteristics of the left ventricle start to differ significantly from that of the normal population. We therefore performed an echocardiographic study to determine the influence of age on LV wall thickness, cavity dimensions and indexes of myocardial contractility in patients with simple d-TGA.

**Materials and Methods**

**Subjects**

The study group consisted of 53 patients with simple d-TGA, ages 1 day to 10 years. To avoid undue influence of individual cases on the data of the group, each patient was represented by only one echocardiographic study. Only patients with normal pressure in the pulmonary circulatory system were selected. Patients older than 1 month who had an LV systolic pressure higher than 40 mm Hg were excluded. In patients younger than 1 month, pulmonary pressure was considered normal if it was 50% of systemic or less and if noninvasive criteria of normal pulmonary pressure were noted on subsequent echocardiograms. Patients with a gradient of 20 mm Hg or less in the LV outflow tract were included in the study. Twenty-three patients had undergone surgical correction by the Mustard procedure. The rest of the patients had had an interatrial balloon septostomy or a surgically created atrial septal defect or both.

A control group was taken from an ongoing study of normal echocardiographic data. This group consisted of 395 subjects matched for age. As in the d-TGA group, each subject is represented by one echocardiographic study.

**Echocardiographic Technique**

All echocardiograms were taken with an Ekoline 20A ultrasonoscope coupled with a Cambridge fiberoptic recorder. An electrocardiographic lead showing a well-identified Q wave was recorded simultaneously. Each value represents the average of at least five measurements. In the few instances in which this was not possible, the value for this variable was rejected. Posterior wall and septal thickness as well as dimensions of the LV cavity were measured at end-systole and end-diastole according to the recommendations of the American Echocardiographic Society. Ejection time was measured from the pulmonary valve as previously described. From these data, the shortening fraction (SF) (end-diastolic dimension – end-systolic dimension)/end-diastolic dimension) and the mean velocity of circumferential fiber shortening (Vcf) ([end-diastolic dimension – end-systolic dimension]/end-diastolic dimension × ejection time) of the left ventricle were calculated. Septal motion was classified as normal, flat or paradoxical. The SF and the mean Vcf were not calculated if the septal motion was paradoxical.

**Statistical Analysis**

To make proper inference, normality of the data was verified using Lilliefors’ test, at the 0.10 level, each time theory required it. In a preliminary study, linear and nonlinear multiple regression analyses of the control group showed that an excellent prediction of the wall thickness and cavity dimensions was obtained by using the square root of age as regressor (R² > 70%). The same analyses were also applied to the d-TGA group. Covariance analysis was performed to evaluate the effect of the Mustard procedure on the ventricular dimensions. For this analysis, an age range including both operated and nonoperated patients was chosen. The range of 30–54 months gave the greatest number of subjects.

As for shortening fraction and mean Vcf, significant but nonlinear variations were noted with age in the control group. For this reason, the results were subdivided into three subgroups, so that the within-group variations were not significant: 0–6 months, 6 months to 5 years and 5 years and older. Values for the d-TGA group were similarly divided. Comparisons were carried out between these three subgroups by analysis of

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**Figure 1. Left ventricular internal dimensions in diastole (LVIDd) in normal subjects and in patients with d-transposition of the great arteries. In this and all other figures, patients 0–6 months old are presented separately (A) to better illustrate the changes during the postnatal period (B). Patients less than 1 month of age are excluded. Each patient with transposition is represented by a circle (before Mustard) or a dot (after Mustard). The dashed lines are the mean and 95% tolerance limits. Regression equation for the control group: y = 1.831 + 0.193(age), (R² = 92%); for the d-TGA group: y = 1.364 + 0.147(age) (R² = 60%).**
variance, and with the normal group using the Bonferroni \( r \) statistic.\(^\text{14} \) The absence of correlation with age precluded the use of covariance analysis to evaluate the influence of Mustard correction on SF and mean Vcf. Therefore, this influence was tested by \( t \) test applied to data obtained in patients 6 months to 5 years old, since only this subgroup contained enough operated and nonoperated patients.

All 95% tolerance limits about mean values were estimated using the method outlined by Guttman.\(^\text{15} \) Ninety-five percent tolerance limits about regression line were also calculated.\(^\text{16} \) For clinical application, it was more useful to present the latter tolerance limits in table form.

**Results**

**Left Ventricular Internal Dimensions**

In diastole, the LVID of the transposition group was normal during the first days of life (fig. 1A). However, a rapid fall below the 95% tolerance limits of normal was observed in the following weeks. From 1–6 months, no change in LV dimensions was observed. Thereafter, LV dimensions increased progressively with age (fig. 1B). This increase followed the pattern of the normal population. Although patients with d-TGA occasionally fell within the 95% tolerance limits of normal, the regression curve for the group was always below these limits after 1 month of age.

The systolic LVID was normal at birth (fig. 2A), but dropped below the 95% tolerance limits a few weeks after birth. The cavity remained significantly smaller than normal throughout the first 10 years of life, although a progressive increase in size was noted during this period (fig. 2B). No significant difference was found between uncorrected patients and those corrected with the Mustard procedure. The mean values according to age for LVID in d-TGA and their upper tolerance limits are listed in table 1. The regression equations for weight and body surface are given in the Appendix.

**Left Ventricular Posterior Wall Thickness**

Most values for LVPW were normal, in both diastole and systole, for subjects 1 day to 6 months old (figs. 3A and 4A). However, for subjects 1 month to 10 years old, wall thickness in the d-TGA group remained constant, while a significant increase with age was observed in the normal population (figs. 3B and 4B). The mean value for LVPW in d-TGA was 2.3 mm in diastole and 4.3 mm in systole. The upper tolerance limits are shown in table 1. Because of the difference in growth between d-TGA and normal subjects, mean
values for LVPW were below the lower tolerance limit of the control group at about 10 months of age in diastole and 7 months in systole.

Interventricular Septum

During the first 6 months of life, values for diastolic septal thickness in d-TGA were all normal (fig. 5A). From 1 month to 10 years, a progressive thickening was observed (fig. 5B), following the trend in the normal population. However, the regression line of the d-TGA group remained at the lower limit of normal. The mean values and their upper tolerance limits are shown in table 1. The septal motion was flat in 13 patients and paradoxical in two. All 15 children with abnormal septal motion were older than 3 years of age (fig. 5B).

Shortening Fraction and Mean Vcf

The values in the normal subjects and the d-TGA patients for SF and mean Vcf are shown in table 2. For both variables, the values in the d-TGA patients were constantly higher than those in the control group ($p < 0.005$). Patients who had undergone the Mustard operation had lower values for both SF and mean Vcf, but this difference was not significant (table 3).

Discussion

M-mode echocardiography is a well-established noninvasive technique for measuring LV size, wall thickness and wall motion velocities.17 Our study shows that although LV transverse diameter is normal at birth in patients with simple d-TGA, both systolic and diastolic measurements decrease in the very first weeks of life below the 95% tolerance limits of normal. Using angiographic measurements, Graham and co-workers18 showed that patients with uncomplicated transposition had a normal end-diastolic volume before 6 months of age, whereas those older than 6 months had elevated volumes and outputs. Keanes et al.,19 using the same technique, found the same trend, although the difference was present at age 2 months. The increase in end-diastolic volume in the older in-

### Table 1. Means and Upper Tolerance Limits of Left Ventricular Parameters for Different Age Groups in Patients With Simple d-TGA

<table>
<thead>
<tr>
<th>Age (months)</th>
<th>LVIDs (cm)</th>
<th>Age (months)</th>
<th>LVIDd (cm)</th>
<th>Age (months)</th>
<th>IVSd (mm)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1-3</td>
<td>0.7 (1.4)</td>
<td>1-3</td>
<td>1.6 (2.3)</td>
<td>1-2</td>
<td>2.7 (4.6)</td>
</tr>
<tr>
<td>3-5</td>
<td>0.8 (1.5)</td>
<td>3-6</td>
<td>1.7 (2.4)</td>
<td>2-4</td>
<td>2.8 (4.7)</td>
</tr>
<tr>
<td>5-8</td>
<td>0.9 (1.6)</td>
<td>6-9</td>
<td>1.8 (2.5)</td>
<td>4-6</td>
<td>2.9 (4.8)</td>
</tr>
<tr>
<td>8-12</td>
<td>1.0 (1.7)</td>
<td>9-14</td>
<td>1.9 (2.6)</td>
<td>6-8</td>
<td>3.0 (4.9)</td>
</tr>
<tr>
<td>12-16</td>
<td>1.1 (1.8)</td>
<td>14-19</td>
<td>2.0 (2.7)</td>
<td>8-11</td>
<td>3.1 (5.0)</td>
</tr>
<tr>
<td>16-22</td>
<td>1.2 (1.9)</td>
<td>19-26</td>
<td>2.1 (2.8)</td>
<td>11-14</td>
<td>3.2 (5.1)</td>
</tr>
<tr>
<td>22-28</td>
<td>1.3 (2.0)</td>
<td>26-33</td>
<td>2.2 (2.9)</td>
<td>14-18</td>
<td>3.3 (5.2)</td>
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<td>28-35</td>
<td>1.4 (2.1)</td>
<td>33-41</td>
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<td>49-55</td>
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<td>110-120</td>
<td>3.0 (3.7)</td>
<td>55-63</td>
<td>4.1 (6.0)</td>
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<td></td>
<td>63-70</td>
<td>4.2 (6.1)</td>
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<td></td>
<td></td>
<td></td>
<td></td>
<td>95-104</td>
<td>4.6 (6.5)</td>
</tr>
<tr>
<td></td>
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<td></td>
<td>104-114</td>
<td>4.7 (6.6)</td>
</tr>
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<td></td>
<td></td>
<td></td>
<td>114-120</td>
<td>4.8 (6.7)</td>
</tr>
</tbody>
</table>

Values in parentheses represent the upper limit of normal. Because of the nonlinearity of the regressions for LVID and IVS, variable age intervals were obtained to minimize the error that occurs when a whole region bounded by two curve segments is condensed into a single interval. This was done in such a way that the difference between the minimum and maximum value on the upper tolerance limit within an age interval did not exceed 0.1 unit (cm or mm), ensuring that the reported bounds are not farther away from any point on the curves delimiting the tolerance limits for the age group by more than 0.05 unit.

Abbreviations: LVIDd and LVIDs = left ventricular internal dimensions in diastole and systole; IVSd = interventricular septal thickness in diastole; LVPWd and LVPWs = left ventricular posterior wall thickness in diastole and systole.
fants was ascribed to the progressive increase in pulmonary blood flow. Our data on LV cavity dimensions do not seem to correlate with these findings. The angiographic LV volumes were calculated by the area-length method of Dodge et al.\textsuperscript{20} based on the assumption that the cavity is ellipsoid. However, in d-TGA, posterior bulging of the septum into the LV cavity changes the ventricular geometry.\textsuperscript{21} For this reason, until variations in LV geometry of patients with d-TGA are taken into account in volume determinations, any inference to volumes estimated from linear measurements should be interpreted with caution.

The most striking difference between the normal and the d-TGA groups is the absence in the latter of any significant increase in wall thickness from birth to 10 years of age (figs. 4A and 4B). Previous studies of anatomic specimens have shown the same observation.\textsuperscript{1,3} This point should always be considered in the interpretation of echocardiograms of patients with transposition. For instance, in a 5-year-old child with transposition and suspected pulmonary vascular obstruction, a diastolic LVPW of 5 mm could be interpreted as normal, corresponding exactly to the average value found at this age in the normal population (fig. 4B). However, looking at table 1, a diastolic LVPW thickness of 5 mm in d-TGA means LV hypertrophy.

Similarly, assessment of LV contractility in patients with TGA should not be based on values of SF and mean Vcf for the normal population. Indeed, in the present study, the values of these two widely used echocardiographic indexes of myocardial contractility have been significantly higher in transposition patients at all ages. The reasons for this difference cannot be inferred from the present data, but are probably related to the peculiar hemodynamics of d-TGA and the changes in LV geometry.

Anatomic reports showed that LVPW thickness starts to differ significantly from that of the normal population at 5 months\textsuperscript{3} or 8 months\textsuperscript{1} of age. These figures are closer to those found during systole in our study, confirming that measurements of fixed specimens correspond to systolic LV thickness measured by echocardiography.\textsuperscript{22}

The time at which the left ventricle of patients with d-TGA becomes thinner than normal could have some effect on the choice of the safest age for anatomic correction of TGA in patients with an intact ventricular septum and normal pulmonary pressure. Despite a
consensus that an underdeveloped left ventricle cannot withstand the sudden increase in afterload created by the arterial switch operation,\(^1\) \(^3\) \(^23\) the exact time at which the left ventricle can no longer function as a systemic ventricle has not been determined. Other factors, such as changes in septal position and structure,\(^24\) marked hypertrophy and dilatation of the right ventricle and myocardial hypoxia, must also be considered. The left ventricle in patients with d-TGA is probably inadequate for systemic work some time before the regression line of the measurements of wall thickness crosses the 95% tolerance limits of normal.

The increase in septal thickness in the d-TGA group was similar to that of normal subjects. This increase is probably due to the progressive hypertrophy of the right side of the septum. Asymmetric hypertrophy of the septum in relation to the posterior wall is thus created. Similar observations have been reported.\(^5\) \(^25\)

In d-TGA, LV dimensions could be used to assess pressures in the pulmonary circulatory system indirectly. For instance, an absence of a decrease in systolic and diastolic LVID after the first weeks of life strongly suggests persistence of a high LV pressure. The same conclusion should be drawn from any increase in LVPW.

Acknowledgment

The authors gratefully acknowledge the skillful technical assistance of Marguerite Poitier-Mégélas and Jean Boileau and the excellent work of Micheline Raymond in typing this manuscript.

References


Appendix

Table A1. Regression Equations for Weight and Body Surface Area

<table>
<thead>
<tr>
<th></th>
<th>R²</th>
<th>SER</th>
</tr>
</thead>
<tbody>
<tr>
<td>LVIDd</td>
<td>1.30 + 1.68 (BSA)</td>
<td>0.64</td>
</tr>
<tr>
<td></td>
<td>1.54 + 0.05 (weight)</td>
<td>0.61</td>
</tr>
<tr>
<td>LVIDs</td>
<td>0.58 + 1.02 (BSA)</td>
<td>0.40</td>
</tr>
<tr>
<td></td>
<td>0.70 + 0.03 (weight)</td>
<td>0.41</td>
</tr>
<tr>
<td>Septum</td>
<td>2.41 + 2.40 (BSA)</td>
<td>0.35</td>
</tr>
<tr>
<td></td>
<td>2.71 + 0.08 (weight)</td>
<td>0.34</td>
</tr>
</tbody>
</table>

Abbreviations: LVIDd = left ventricular internal diameter in diastole; LVIDs = left ventricular internal diameter in systole; BSA = body surface area.
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