PATHOPHYSIOLOGY AND NATURAL HISTORY
CONGENITAL HEART DISEASE

Left ventricular geometry and function in adults with Ebstein’s anomaly of the tricuspid valve

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ABSTRACT We postulated that the abnormal shape, size, and function of the right heart and adjoining ventricular septum in adults with Ebstein’s anomaly of the tricuspid valve might in turn alter the shape and function of the left ventricle. Seven adult patients with uncomplicated Ebstein’s anomaly were studied. Left ventricular geometry was determined by two-dimensional echocardiography. Left ventricular function was assessed by treadmill exercise and radionuclide angiography at rest and with exercise. Paradoxical ventricular septal motion was consistently present. Left ventricular eccentricity (ratio of two minor axes in the short-axis view) was uniformly abnormal, averaging 1.35 ± 0.23 (normal = 1.02 ± 0.05). The ratio of right to left ventricular cavity size averaged 1.70 ± 0.44 (normal 0.65 ± 0.30), and tricuspid valve displacement into the right ventricular cavity averaged 52% (normal 8%). Functional right atrial size averaged 27.6 ± 5.2 cm² (normal right atrial area = 13.1 ± 2.2 cm²). Resting left ventricular ejection fractions were below 50% in all but two patients. In response to Bruce protocol exercise stress, there were consistently appropriate increments in heart rate, blood pressure, and peak double product and, with one exception, radionuclide left ventricular ejection fraction. There were significant correlations between tricuspid valve displacement and functional right atrial size versus resting left ventricular ejection fraction and left ventricular eccentricity. These data support the hypothesis that derangements in right heart morphology and function in Ebstein’s anomaly contribute to significant alterations in left ventricular geometry, but the geometric alterations are associated with tangible but less significant changes in left ventricular systolic function.


EBSTEIN’S ANOMALY of the tricuspid valve is an uncommon but not rare congenital cardiac malformation whose basic anatomic fault is downward displacement of tricuspid valve leaflets into the cavity of the morphologic right ventricle.¹ Patients often survive into the third decade with little or no disability,² but attrition increases after age 30 years, and fewer than 5% of patients reach or exceed age 50 years.³ Despite detailed information on the morphology and function of the deranged tricuspid valve and right heart,⁴ little or no information is available on the geometry and function of the left ventricle. This study was undertaken to assess the effects of abnormal shape, size, and function of the right heart on the shape and function of the left ventricle in Ebstein’s anomaly.

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Methods

Seven sequential patients were selected from the Adult Congenital Heart Disease Program of the UCLA Hospital and Clinics. The criterion for selection was uncomplicated Ebstein’s anomaly of the right (tricuspid) atrioventricular valve (situs solitus, atrioventricular, and ventriculoarterial concordance, intact ventricular septum, and absent right ventricular outflow obstruction). Studies were performed during one outpatient visit after informed consent was obtained. The protocol was approved by the UCLA Human Subject Protection Committee.

There were four male and three female patients, 15 to 59 years old (mean 35.7). Four patients were asymptomatic. Three had supraventricular arrhythmias, and two were on antiarrhythmic medications. Two were cyanotic due to right-to-left interatrial shunts (table 1). Patient 5 was studied before and 1 year after tricuspid valve replacement, and patient 7 had a ventricular demand pacemaker (VVI mode).

Each patient had a complete physical, chest roentgenographic, and 12-lead scalar electrocardiographic examination. Treadmill exercise testing (Bruce protocol) was by published methods.³ Multiple electrocardiographically gated left ventricular equilibrium blood pool radionuclide angiograms were obtained in patients at rest and in response to supine leg exercise by previously reported protocol.⁵ Cardiac radionuclide imaging was accomplished with 20 mCi of ⁹⁹ᵐTc on autologous red blood cells labeled in vitro. Images were acquired with a standard gamma scintillation camera (Series 420 Mobile Gamma Camera, Technicare) equipped with a high-resolution, low-en-
energy, parallel-hole colimator. The detector was tilted 10 to 15 degrees caudally in the left anterior oblique projection, and was adjusted until the left and right ventricles were optimally separated on the persistence oscilloscope. Data were recorded for 4 min at rest and for 3 min during exercise. Left ventricular ejection fraction was calculated from the left ventricular time-activity curve constructed from 16 sequential equilibrium cardiac blood pool images corrected for background activity. Ejection fraction by this technique agrees well with data derived from contrast ventriculography, and in our laboratory the correlation coefficient between these measurements was 0.9 in 21 patients. 8 Count-based changes in volumes at peak exercise relative to rest were determined at end-systole and end-diastole. A study was defined as abnormal if the ejection fraction fell or failed to increase by more than 5% from rest to peak exercise.

Two-dimensional echocardiograms were recorded with the subject at rest in the left lateral decubitus position with the use of a commercially available electronically phased-array echocardiographic machine. Images were recorded in real-time on ½ inch videotape for later review and analysis. Left ventricular geometry was assessed in light of measurement of the area of the functional right atrium, of the extent of tricuspid valve displacement and/or the relationship of the size of the right and left ventricular cavities, and of the degree of left ventricular eccentricity. The size of the right ventricular cavity relative to that of the left ventricular cavity was estimated from averaged values of the minor axes bisecting the interventricular septum in the short- and long-axis parasternal views at end-diastole (figure 1). In the apical four-chamber view, the area (cm²) of the functional right atrium (morphologic right atrium plus atrialized right ventricle) was estimated in the plane of the displaced tricuspid valve (figure 2). The extent of tricuspid valve displacement was estimated relative to the mitral valve septal insertion as one minus the ratio of the tricuspid septal leaflet-to-apex length divided by the mitral valve leaflet-to-apex length, after the method of Ports et al. 7 (figure 2). Left ventricular eccentricity was determined by the method of Schrieber et al. 8 in the short-axis view at the level of mitral chordal transition at end-diastole as the ratio (B/A) of the two minor axes, B and A, of the left ventricle (figure 3). In our laboratory, healthy control subjects (n = 12, mean age 36 years, range 18 to 57) were found to have an end-diatolic right-to-left ventricular mean ratio of 0.65 ± 0.30(SD), right atrial mean area in end-systole of 13.1 ± 2.2(SD) cm², mean extent of tricuspid valve displacement of 8 ± 6(SD)%, and an end-diastolic left ventricular mean eccentricity index of 1.02 ± 0.05(SD).

**Statistical analysis.** Multiple correlation and linear regression analyses were performed on a dedicated microcomputer (Jerrod 6600) with ABSTAT (Anderson-Bell, Canon City Co.) with statistical software. Significant correlations were considered present at the p ≤ .05 level.

**Results**

Clinical data are summarized in table 1.

**Treadmill exercise.** Six patients (Nos. 1 to 6) completed the Bruce treadmill protocol. Heart rate averaged 84 ± 13 beats/min at rest and rose to 183 ± 17 beats/min at peak stress (217% increase). Blood pressure was 114 ± 12 mm Hg at rest and increased to 160 ± 12 mm Hg at peak exercise (140% increment). Exercise duration averaged 8.5 ± 2.0 min. Peak exercise double product (peak systolic blood pressure × peak heart rate) was 250 ± 90 × 10² heart rate-mm Hg. Three patients experienced dyspnea (Nos. 1, 3, and 4) during exercise, and two (Nos. 1 and 5) developed ST segment and T wave abnormalities immediately after exercise.

**Equilibrium blood pool radionuclide angiograms.** Left ventricular ejection fraction averaged 45 ± 6% at rest and was greater than 55% in only two patients. Five of the six patients who completed this study had appropriate exercise-induced increases in left ventricular ejection fraction, averaging 53 ± 5%; in patient 3, left ventricular ejection fraction fell significantly (figure 4, A). Heart rate at rest was 78 ± 12 beats/min, rising to 119 ± 7 beats/min at peak exercise (152% increase). Similarly, blood pressure rose from 120 ± 13 to 165 ± 23 mm Hg at peak exercise (137% increase). Changes in left ventricular "volumes" based on counts

<table>
<thead>
<tr>
<th>Patient No.</th>
<th>Age (yr)/sex</th>
<th>Symptoms</th>
<th>CTR (%)</th>
<th>Data from resting ECG</th>
<th>Medications</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>50/M</td>
<td>Palpitations</td>
<td>68</td>
<td>AF, RAD, RBBB</td>
<td>Procainamide, digoxin</td>
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<td>2</td>
<td>15/M</td>
<td>None</td>
<td>56</td>
<td>SR, WPW (type B)</td>
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</tr>
<tr>
<td>3</td>
<td>35/F</td>
<td>None</td>
<td>62</td>
<td>SR, 1° AVB, RBBB</td>
<td>None</td>
</tr>
<tr>
<td>4</td>
<td>35/M</td>
<td>None</td>
<td>62</td>
<td>SR, RBBB</td>
<td>None</td>
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<tr>
<td>5</td>
<td>27/M</td>
<td>Dyspnea, cyanosis, polycythemia, palpitations</td>
<td>62</td>
<td>SR, 1° AVB, RBBB, WPW (type B)</td>
<td>None</td>
</tr>
<tr>
<td>6</td>
<td>29/M</td>
<td>Palpitations</td>
<td>56</td>
<td>SR, LAD, RBBB</td>
<td>None</td>
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<tr>
<td>7</td>
<td>59/F</td>
<td>Dyspnea, cyanosis</td>
<td>72</td>
<td>WPW (type B)</td>
<td>Procainamide</td>
</tr>
</tbody>
</table>

AF = atrial flutter; 1° AVB = first-degree atrioventricular block; CTR = cardiothoracic ratio; ECG = electrocardiogram; LAD = left-axis deviation; RAD = right-axis deviation; RBBB = right bundle branch block; SR = sinus rhythm, VVI = ventricular paced, ventricular sensed, and inhibited; WPW = Wolff-Parkinson-White syndrome.
(figure 4, B) demonstrated that the increment in ejection fraction was due to a reduced end-systolic volume (.05 < p < .1) with an unchanged end-diastolic volume.

Two-dimensional echocardiography. Paradoxical motion of the “atrialized” portion of the interventricular septum and superior systolic displacement toward the left atrium of the mitral leaflets were present in all patients with Ebstein’s anomaly and left ventricular eccentricity index averaged $1.35 \pm 0.23$. The ratio of right ventricular to left ventricular cavity size averaged $1.7 \pm 0.44$ in these patients; the tricuspid valve was displaced into the right ventricular cavity an average of 52% of the mitral-to-apex distance. Functional right atrial size averaged $27.6 \pm 5.2$ cm$^2$. Each of these measurements was significantly different from that in healthy control subjects (table 2). Improvement in these variables occurred postoperatively in patient 6 (table 2).

Correlations. Linear regression analysis defined a significant relationship ($r = .85$) between left ventricular eccentricity and the area of the functional right atrium. Not surprisingly, tricuspid valve displacement and increased functional right atrial area also were related ($r = .76$). A significant relationship ($r = .95$) was also found among tricuspid valve displacement, functional right atrial area, and the resting left ventricular ejection fraction.

Discussion

Despite detailed scrutiny of the right heart in individuals with Ebstein’s anomaly of the tricuspid valve, there has been comparatively little attention paid to the effects of the right heart abnormalities on the geometry and function of the left ventricle. Consequent functional and/or anatomic abnormalities of the left ventricle, if present, might influence net cardiac function and thereby affect prognosis. In a previous retrospective review of cineangiograms from 13 patients with Ebstein’s anomaly, 12 showed abnormal left ventricular contour and/or contraction patterns. Furthermore, a reduction in exercise capacity and ventilating reserve has been recently documented. We sought to prospectively establish the presence and extent of geomet-
ric and functional abnormalities of the left ventricle in adults with Ebstein’s anomaly, and to determine whether and to what degree the abnormalities were due to altered geometry of the right heart.

In typical, uncomplicated Ebstein’s anomaly, the effective tricuspid valve orifice is displayed into the cavity of the right ventricle at the junction of the inlet trabecular septum. The pattern of septal and posterior leaflet displacement is surprisingly constant, with circumferential enlargement of the right atrioventricular junction. The displaced tricuspid valve functionally divides the right ventricle into two parts. The inlet portion performs as part of the right atrium — the “atrialized” ventricle. The distal portion — the trabe-

TABLE 2

<table>
<thead>
<tr>
<th>Patient No.</th>
<th>Eccentricity of LV</th>
<th>Ratio RV/LV</th>
<th>Atrial area (cm²)</th>
<th>TV displacement (%)</th>
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<tbody>
<tr>
<td>1</td>
<td>1.1</td>
<td>1.6</td>
<td>9.9</td>
<td>38</td>
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<td>2</td>
<td>1.2</td>
<td>0.8</td>
<td>17.8</td>
<td>42</td>
</tr>
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<td>3</td>
<td>1.4</td>
<td>1.9</td>
<td>30.4</td>
<td>59</td>
</tr>
<tr>
<td>4</td>
<td>1.5</td>
<td>1.4</td>
<td>20.9</td>
<td>62</td>
</tr>
<tr>
<td>5</td>
<td>Preop 1.8</td>
<td>2.1</td>
<td>52.9</td>
<td>71</td>
</tr>
<tr>
<td></td>
<td>Postop 1.0</td>
<td>1.4</td>
<td>17.4</td>
<td>24</td>
</tr>
<tr>
<td>6</td>
<td>1.4</td>
<td>2.1</td>
<td>30.4</td>
<td>59</td>
</tr>
<tr>
<td>7</td>
<td>1.1</td>
<td>1.4</td>
<td>17.8</td>
<td>63</td>
</tr>
<tr>
<td>Mean ± SD</td>
<td>1.35 ± 0.23</td>
<td>1.7 ± 0.44</td>
<td>27.6 ± 5.2</td>
<td>52 ± 16</td>
</tr>
<tr>
<td>Control subjects</td>
<td>1.02 ± 0.05</td>
<td>0.65 ± 0.30</td>
<td>13.1 ± 2.2</td>
<td>8 ± 6</td>
</tr>
<tr>
<td>p value</td>
<td>&lt;.001</td>
<td>&lt;.001</td>
<td>&lt;.001</td>
<td>&lt;.001</td>
</tr>
</tbody>
</table>

LV = left ventricle; RV = right ventricle; TV = tricuspid valve.
overload of the right heart.\textsuperscript{15} In a clinical study of normal individuals, acute volume overload of the right heart was accompanied by leftward displacement of the ventricular septum and reduction in left ventricular volume,\textsuperscript{16} observations supported by experimental studies in animals.\textsuperscript{17,18} Patients with left-to-right interatrial shunts and enlarged right atria and right ventricles tend to have decreased left ventricular end-diastolic volumes and cardiac outputs; this reduction in left ventricular size has been attributed to encroachment on the left ventricular cavity by the dilated right heart.\textsuperscript{19–21} Weyman et al.\textsuperscript{22} have suggested that the paradoxical ventricular septal motion accompanying an atrial septal defect acts as a dyskinetic segment and affects left ventricular systolic function; postoperative studies disclosed reversal of these abnormalities.\textsuperscript{5} Radionuclide assessment of left ventricular function in adults with left-to-right interatrial shunts indicate decreased functional reserve during preoperative exercise testing.\textsuperscript{19} Postoperative normalization of left ventricular dimensions and ejection fraction implies reversible mechanical factors related to preoperative right-sided volume overload and right heart geometry. Accordingly, apart from preload, afterload, and intrinsic contractility, the shape and position of the ventricular septum in response to right ventricular volume overload per se may also affect the function of the left ventricle.\textsuperscript{16–22} In Ebstein's anomaly, the "atrialyzed" right ventricle is volume overloaded. All of our patients had paradoxical septal motion of the "atrialyzed" right ventricle, with significant correlations among the extent of tricuspid valve displacement, functional right atrial size, alterations in left ventricular eccentricity, and resting left ventricular ejection fraction. Nevertheless, six patients completed the Bruce treadmill protocols with appropriate increments in heart rate, blood pressure, and peak exercise double product, and five of the patients in whom rest and exercise equilibrium blood pool radionuclide angiograms were obtained had normal exercise-induced augmentation of left ventricular

\begin{figure}
\centering
\includegraphics[width=\textwidth]{figure3.png}
\caption{Two-dimensional echocardiographic parasternal short-axis view (SAX) of the left ventricle (LV) used to calculate left ventricular eccentricity, where eccentricity = ratio of minor axes B/A, illustrated in schematic and in still-frame format.}
\end{figure}

\begin{figure}
\centering
\includegraphics[width=\textwidth]{figure4.png}
\caption{Radionuclide multiple-gated equilibrium blood pool results in adults with Ebstein's anomaly. A, Left ventricular ejection fraction (EF, %) at rest (R) and peak exercise (EX). B, Count-based changes in end-systolic (ES) and end-diastolic (ED) "volumes" as a percent of resting values.}
\end{figure}

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ejection fractions (figure 4). In patient 3, ejection fraction fell significantly.

Based on our data, we propose the following relationships between right and left ventricular shape and function in patients with Ebstein’s anomaly. Leftward diastolic displacement of the ventricular septum results in a reduction in left ventricular diastolic volume and resting ejection fraction. Exercise provokes an increase in left ventricular ejection fraction due to a reduction in end-systolic volume with no change in end-diastolic volume. With respect to right ventricular function, the right ventricular free wall contributes feebly to forward flow, which is materially assisted by the paradoxical movement of the septum that functions as part of the right ventricle as in Uhl’s anomaly. Regarding left ventricular function, the adverse effects of diastolic septal position, reduced end-diastolic volume, and paradoxical septal motion tend to be countered by left ventricular free wall contraction, which supports an increase in exercise ejection fraction despite a low and unchanging end-diastolic volume. In brief, the inadequate right ventricular free wall is functionally countered by paradoxical septal motion that materially assists in forward flow; the adverse effect on the left ventricle of abnormal diastolic septal position and paradoxical septal motion is functionally countered by contraction of the normal free wall, so a low resting ejection fraction increases with exercise owing to a reduction in end-systolic volume. Thus, right and left ventricular functions are intimately coupled in Ebstein’s anomaly.

MitraI valve prolapse has been reported in patients with Ebstein’s anomaly. In our study, two-dimensional echocardiography consistently identified mild-to-moderate superior systolic displacement of either or both mitral leaflets. This finding appears to be analogous to “mitral valve prolapse” in individuals with ostium secundum atrial septal defects with decreased left ventricular cavity size. In Ebstein’s anomaly, superior systolic displacement of the mitral valve is the response of otherwise normal leaflets and chordae tendineae housed in a left ventricular cavity that is re-
duced in size and altered in shape — there is valvuloventricular disproportion without "pathologic" mitral valve prolapse due to intrinsic disease of the mitral valve apparatus.

References
13. Fabian CE, M undt WP, Abrams ML: Ebstein's anomaly, the direct demonstration of contractile synchrony between the two parts of the right ventricle. Invest Radiol 1: 63, 1966
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