Progressive Tricuspid Valve Disease in Patients With Congenitally Corrected Transposition of the Great Arteries

Lourdes R. Prieto, MD; Allan J. Hordof, MD; Michelle Secic, MS; Marlon S. Rosenbaum, MD; Welton M. Gersony, MD

Background—The outcome of patients with corrected transposition of the great arteries (CTGA) is variably affected by associated intracardiac defects, tricuspid valve competence, and systemic right ventricular (RV) function. The relative importance of these factors in long-term outcome has not been evaluated.

Methods and Results—Since 1958, 40 patients with CTGA were studied to determine risk factors for poor outcome, including age, open heart surgery, tricuspid insufficiency (TI), cardiac rhythm, pulmonary overcirculation, and RV dysfunction. Follow-up ranged from 7 to 36 years (mean 20 years). Intracardiac repair was performed in 21 patients; 19 were unoperated or had closed heart procedures. For the purposes of this study the designation TI refers to at least moderately severe TI as delineated by echocardiogram and/or angiography. TI was the only independently significant factor for death (P=0.01), and in turn, only the presence of a morphologically abnormal TV predicted TI, (P=0.03). Twenty-year survival without TI was 93%, but only 49% with TI. Poor long-term postoperative outcome was due to TI in all but 1 patient; 20-year survival rates for operated patients with and without TI were 34% and 90%, respectively (P=0.002). Similarly, 20-year survival rates for unoperated patients with and without TI were 60% and 100%, respectively, whether or not attempts to repair the TI were made (P=0.08).

Conclusions—TI represents the major risk factor for CTGA patients; RV dysfunction appears to be almost always secondary to long-standing TI. Decisions related to surgical interventions with or without associated lesions must be strongly influenced by the status of the tricuspid valve. (Circulation. 1998;98:997-1005.)

Key Words: transposition of great vessels ■ valves ■ survival ■ pediatrics

Morphologic abnormalities of the tricuspid valve (TV) are frequently found in patients with congenitally corrected transposition of the great arteries (CTGA).1-3 Autopsy studies of patients with this lesion have documented TV abnormalities in 91% of cases, most commonly an Ebstein-like anomaly with short, thickened chordae tendineae.1,4 Clinically significant tricuspid insufficiency (TI) has been reported in 20% to 50% of patients with CTGA.2,3,5-7 In addition to the severity of the anatomic abnormality of the valve, other potential predisposing factors for the development of important TI have been proposed but not well documented. Several investigators have noted the development or exacerbation of TI shortly after open heart surgery for closure of a ventricular septal defect (VSD) with or without pulmonic stenosis (PS),2,3,5,8 whereas others have not found such a relation.5,9

No series to date has carefully defined the progression of TV disease in operated as well as unoperated patients in order to establish the role of open heart surgery and other potential risk factors in the natural history of this disease. This study examines the long-term course and outcome of patients with CTGA with and without open heart surgery with particular attention to the status of the TV. It addresses the important and controversial question as to whether TI or intrinsic right ventricular (RV) dysfunction causes deterioration of the cardiovascular status of patients with CTGA.

Methods

Definitions

Open heart surgery (OHS) is defined as repair of any intracardiac lesion other than TV disease and is distinguished from repair or replacement of the TV, which is referred to as TV surgery. Patients were categorized as non–open heart surgical (NOHS) if they had not had open heart surgery for associated lesions before the development of significant TI. Patients in this group either had no significant intracardiac lesions, were well balanced with their existing lesions, or had been palliated with closed heart procedures. Patients undergoing repair of other intracardiac lesions at the time of TV surgery were included in the NOHS group because they had developed significant TV disease before undergoing open heart surgery for other defects.

TI refers to at least moderately severe tricuspid insufficiency, as defined below.

Evaluation of Tricuspid Valve Function

The status of the TV was determined from clinical information, echocardiogram, catheterization, and angiographic data at the time of surgery. Several investigators have noted that the development or exacerbation of TI shortly after open heart surgery for closure of a ventricular septal defect (VSD) with or without pulmonic stenosis (PS), whereas others have not found such a relation.5,9

No series to date has carefully defined the progression of TV disease in operated as well as unoperated patients in order to establish the role of open heart surgery and other potential risk factors in the natural history of this disease. This study examines the long-term course and outcome of patients with CTGA with and without open heart surgery with particular attention to the status of the TV. It addresses the important and controversial question as to whether TI or intrinsic right ventricular (RV) dysfunction causes deterioration of the cardiovascular status of patients with CTGA.
Presentation and during follow-up. All patients underwent cardiac catheterization before open heart surgery (OHS), 20 of 21 after OHS, and 12 of 13 before TV surgery. Catheterization was performed in 18 of 19 patients who did not undergo OHS, either for diagnostic purposes, before closed heart palliation, or because of TV disease. Thus 39 (98%) of 40 patients were catheterized, with 28 of 39 having had multiple studies. The severity of TI was graded angiographically as follows: mild (1+); contrast clears with each beat and never opacifies the entire left atrium; moderate (2+); contrast does not completely clear with 1 beat, may opacify the entire left atrium after several beats, but not as densely as the “left” ventricle (morphologic RV in these patients); moderately severe (3+); the left atrium is completely opacified as densely as the “left” ventricle; and severe (4+); the left atrium is completely opacified with 1 beat, the opacification becomes more dense with subsequent beats, and contrast can be seen refluxing into the pulmonary veins.

Of the 40 patients, 20 had echocardiograms performed from the mid 1980s to the present, during which time echocardiographic assessment of atrioventricular valve insufficiency severity was possible. The degree of TI was determined qualitatively by taking into account the TI jet area and distance the jet extended into the left atrium. If there was evidence of systolic flow reversal in the atrium, the TV was classified as morphologically abnormal. The degree of TI was determined qualitatively by taking into account the TI jet area and distance the jet extended into the left atrium. If there was evidence of systolic flow reversal in the pulmonary veins the TI was graded as severe. When there was disagreement between the angiographic and echocardiographic assessment (which was no more than 1 grade for any patient), the angiographic grade was used. If more than 1 year had elapsed between angiography and echocardiography, the degree of TI was determined from the more recent of the two. Thus TI severity at last follow-up was graded by echocardiography in 10 patients in whom angiography had been performed at least 1 year before the most recent echocardiogram.

Evaluation of RV Function

TV function was evaluated qualitatively from angiography and/or echocardiography as either normal or significantly decreased. All except 1 of the 40 patients were catheterized, and in 30 of those RV function was evaluated by angiography. Ten patients had echocardiograms performed at least 1 year after the most recent catheterization, in which case RV function was assessed qualitatively by echocardiography with 2 or more observers.

Patient Population

Since 1958, 40 consecutive patients with CTGA and 2 normal-sized ventricles have been followed at Columbia-Presbyterian Medical Center. There were 13 female and 27 male patients. Clinical records, including cardiac catheterization, angiographic, echocardiographic, operative, and autopsy reports were retrospectively reviewed. Of the 40 patients, 37 had associated intracardiac anomalies, of which 30 were hemodynamically significant (most commonly VSD and PS), whereas 3 had no intracardiac lesions (Table 1). Twenty-one of the 40 patients underwent OHS between 1965 and 1990, at a median age of 11 years (range 2 to 60 years). Of those 21 patients, 10 (47.6%) underwent intracardiac repair of VSD and PS, 4 (19.0%) VSD, 3 (14.3%) VSD and coarctation, 2 (9.5%) atrial septal defect and PS, 1 (4.8%) VSD and pulmonary atresia (PA), and 1 (4.8%) PS. Nineteen of the 40 patients were categorized as NOHS. 2 of 19 were palliated with Blalock-Taussig shunts, 4 were well balanced with VSD and PS, 1 had severe PS but refused surgery, 2 had TV surgery at the same time as repair of VSD, PS and VSD, PA, and 10 had no clinically significant lesions associated with CTGA.

Risk Factors for Death

The impact on survival of the following variables was examined: age at presentation and at last follow-up, OHS, TI, cardiac rhythm, pulmonary overcirculation, and RV dysfunction. For the purpose of survival analysis, patients were classified as having RV dysfunction if it occurred at any time during the follow-up, whether or not preceded by TI. Survival of the 21 OHS patients was compared with that of the 19 NOHS patients, and the impact of TI on survival for these 2 subgroups was examined.

Risk Factors for Tricuspid Insufficiency

A number of potential risk factors for the development of TI, were evaluated, including OHS, morphology of the TV, degree of preoperative TI in patients who underwent OHS, cardiac rhythm, RV volume overload caused by increased pulmonary blood flow (referred to below as pulmonary overcirculation), and RV function. Patients who had TI, at presentation with no prior documentation of RV function were not included in the analysis of RV function as a risk factor. The TV was classified as morphologically abnormal if there was evidence from angiography, echocardiography, direct intraoperative visualization or autopsy of a structural abnormality such as an Ebstein-like malformation, TV prolapse, or dysplastic features (eg, thickened or redundant leaflets).

To examine pulmonary overcirculation as a risk factor, the clinical course and catheterization data of each patient were reviewed to determine whether their physiology was one of increased, decreased, or normal pulmonary flow. Two sets of comparisons were made: (1) patients whose pulmonary flow was increased throughout the entire period of observation were compared with those whose pulmonary flow was either decreased, normal, or increased only for a limited time, (2) patients whose pulmonary flow was either always increased or increased for a limited time were compared with patients whose flow was always either normal or decreased.

Statistical Methods

Descriptive statistics were presented as means, medians, standard deviations, frequencies, percentages, and confidence intervals, as appropriate. Group comparisons were completed with the use of t tests, χ² tests, or Fisher’s exact tests, as appropriate. Univariate Cox proportional hazards regression analysis techniques were used to examine the potential risk factors for death. Linearity and proportionality assumptions were checked before modeling. The Kaplan-Meier procedure was used to estimate event rates throughout the study period and associated curves were graphed to support the findings. After checking for multicollinearity with Fisher’s exact tests on the univariately significant risk factors, these factors were considered for the multivariable Cox proportional hazards regression model.

Next, the total group was divided into 2 subgroups, OHS and NOHS patients. The Kaplan-Meier procedure and Cox proportional hazards regression analysis techniques were used to examine whether TI was a risk factor for death within each of these subgroups.

Finally, the associations between TI, and potential risk factors for its development were examined with Fisher’s exact tests.

Results

The mean ± SD age at presentation of the 40 patients was 5.3 ± 12.9 years (range birth to 62 years). The median age was 3 months. Mean ± SD and median age at last follow-up were 25 ± 14 and 23 years, respectively (range 7 to 69 years). Follow-up from the time of presentation to the time of last visit, heart transplantation, or death ranged from 7 to 36 years (mean = 20 years, median = 19 years). Seventeen subjects (42.5%) had TI, during their clinical course. Twelve subjects (30%) had RV dysfunction at last follow-up, 11 of whom also had TI. Pulmonary overcirculation occurred in 14 (35%) patients, either from associated lesions or after surgical palliation, and 13 (32.5%) patients had complete heart block.

Survival Analysis

Considering death and heart transplantation as the same outcome, the Kaplan-Meier estimate of survival for this group of 40 patients with CTGA was 74% at 20 years of follow-up. The results of univariate survival analysis of risk factors including age at presentation, TI, RV dysfunction, OHS,
<table>
<thead>
<tr>
<th>Patient No.</th>
<th>Associated Lesions</th>
<th>Age at Initial Visit, y</th>
<th>Follow-up, y</th>
<th>OHS</th>
<th>TI Severity</th>
<th>TVR</th>
<th>RV* Function</th>
<th>RV Function (Last Follow-up)</th>
<th>Status† (Last Follow-up)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>VSD, PS</td>
<td>8</td>
<td>34</td>
<td>Y</td>
<td>Severe</td>
<td>Y</td>
<td>Normal</td>
<td>Decreased</td>
<td>Dead</td>
</tr>
<tr>
<td>2</td>
<td>PS</td>
<td>&lt;0.1</td>
<td>22</td>
<td>N</td>
<td>None</td>
<td>N</td>
<td>Normal</td>
<td>Normal</td>
<td>II</td>
</tr>
<tr>
<td>3</td>
<td>VSD, PS</td>
<td>5</td>
<td>29</td>
<td>Y</td>
<td>Mild</td>
<td>N</td>
<td>Normal</td>
<td>Normal</td>
<td>II</td>
</tr>
<tr>
<td>4</td>
<td>VSD, PS</td>
<td>7</td>
<td>33</td>
<td>Y</td>
<td>None</td>
<td>N</td>
<td>Normal</td>
<td>Normal</td>
<td>I</td>
</tr>
<tr>
<td>5</td>
<td>VSD, PS</td>
<td>1</td>
<td>31</td>
<td>Y</td>
<td>Mild</td>
<td>N</td>
<td>Normal</td>
<td>Normal</td>
<td>I</td>
</tr>
<tr>
<td>6</td>
<td>VSD, PA</td>
<td>&lt;0.1</td>
<td>19</td>
<td>Y</td>
<td>Mild</td>
<td>N</td>
<td>Normal</td>
<td>Normal</td>
<td>I</td>
</tr>
<tr>
<td>7</td>
<td>VSD</td>
<td>&lt;0.2</td>
<td>23</td>
<td>Y</td>
<td>Severe</td>
<td>Y</td>
<td>Normal</td>
<td>Decreased</td>
<td>Dead</td>
</tr>
<tr>
<td>8</td>
<td>VSD, PS</td>
<td>&lt;0.1</td>
<td>14</td>
<td>N</td>
<td>Moderate</td>
<td>N</td>
<td>Normal</td>
<td>Normal</td>
<td>I</td>
</tr>
<tr>
<td>9</td>
<td>VSD, PS</td>
<td>&lt;0.1</td>
<td>26</td>
<td>Y</td>
<td>None</td>
<td>N</td>
<td>Normal</td>
<td>Normal</td>
<td>I</td>
</tr>
<tr>
<td>10</td>
<td>VSD, PA</td>
<td>&lt;0.1</td>
<td>28</td>
<td>N</td>
<td>None</td>
<td>N</td>
<td>Normal</td>
<td>Normal</td>
<td>I</td>
</tr>
<tr>
<td>11</td>
<td>VSD, PS</td>
<td>&lt;0.1</td>
<td>27</td>
<td>N</td>
<td>Mild</td>
<td>N</td>
<td>Normal</td>
<td>Normal</td>
<td>I</td>
</tr>
<tr>
<td>12</td>
<td>VSD</td>
<td>9</td>
<td>10</td>
<td>Y</td>
<td>Severe</td>
<td>Y</td>
<td>Normal</td>
<td>Decreased</td>
<td>II</td>
</tr>
<tr>
<td>13</td>
<td>PS</td>
<td>&lt;0.1</td>
<td>24</td>
<td>Y</td>
<td>Mild</td>
<td>N</td>
<td>Normal</td>
<td>Normal</td>
<td>I</td>
</tr>
<tr>
<td>14</td>
<td>VSD, PS</td>
<td>&lt;0.1</td>
<td>26</td>
<td>Y</td>
<td>None</td>
<td>N</td>
<td>Normal</td>
<td>Normal</td>
<td>I</td>
</tr>
<tr>
<td>15</td>
<td>VSD, PS</td>
<td>1</td>
<td>26</td>
<td>N</td>
<td>Severe</td>
<td>Y</td>
<td>Normal</td>
<td>Normal</td>
<td>II</td>
</tr>
<tr>
<td>16</td>
<td>VSD, PS</td>
<td>0.3</td>
<td>13</td>
<td>Y</td>
<td>Severe</td>
<td>Y</td>
<td>Normal</td>
<td>Decreased</td>
<td>Dead</td>
</tr>
<tr>
<td>17</td>
<td>VSD, PS</td>
<td>3</td>
<td>22</td>
<td>Y</td>
<td>Mild</td>
<td>N</td>
<td>Normal</td>
<td>Normal</td>
<td>I</td>
</tr>
<tr>
<td>18</td>
<td>ASD, PS</td>
<td>&lt;0.1</td>
<td>16</td>
<td>Y</td>
<td>None</td>
<td>N</td>
<td>Normal</td>
<td>Normal</td>
<td>I</td>
</tr>
<tr>
<td>19</td>
<td>ASD, PS</td>
<td>50</td>
<td>19</td>
<td>Y</td>
<td>Severe</td>
<td>Y</td>
<td>Normal</td>
<td>Normal</td>
<td>Dead</td>
</tr>
<tr>
<td>20</td>
<td>VSD</td>
<td>0.4</td>
<td>17</td>
<td>Y</td>
<td>None</td>
<td>N</td>
<td>Normal</td>
<td>Normal</td>
<td>I</td>
</tr>
<tr>
<td>21</td>
<td>VSD, PS</td>
<td>&lt;0.2</td>
<td>13</td>
<td>Y</td>
<td>Severe</td>
<td>Y</td>
<td>Normal</td>
<td>Decreased</td>
<td>Transplanted</td>
</tr>
<tr>
<td>22</td>
<td>VSD, PS</td>
<td>0.3</td>
<td>16</td>
<td>N</td>
<td>Mod-Sev</td>
<td>N</td>
<td>Normal</td>
<td>Normal</td>
<td>I</td>
</tr>
<tr>
<td>23</td>
<td>VSD, Coa</td>
<td>&lt;0.1</td>
<td>20</td>
<td>Y</td>
<td>Mild</td>
<td>N</td>
<td>Normal</td>
<td>Normal</td>
<td>I</td>
</tr>
<tr>
<td>24</td>
<td>VSD, PS</td>
<td>10</td>
<td>13</td>
<td>N</td>
<td>None</td>
<td>N</td>
<td>Normal</td>
<td>Normal</td>
<td>I</td>
</tr>
<tr>
<td>25</td>
<td>VSD, Coa</td>
<td>0.2</td>
<td>18</td>
<td>Y</td>
<td>Mild</td>
<td>N</td>
<td>Decreased</td>
<td>Decreased</td>
<td>Transplanted</td>
</tr>
<tr>
<td>26</td>
<td>VSD, PS</td>
<td>&lt;0.2</td>
<td>8</td>
<td>Y</td>
<td>Severe</td>
<td>N</td>
<td>Normal</td>
<td>Normal</td>
<td>Dead</td>
</tr>
<tr>
<td>27</td>
<td>VSD</td>
<td>&lt;0.1</td>
<td>13</td>
<td>Y</td>
<td>Mild</td>
<td>N</td>
<td>Normal</td>
<td>Normal</td>
<td>I</td>
</tr>
<tr>
<td>28</td>
<td>VSD, Coa</td>
<td>&lt;0.1</td>
<td>10</td>
<td>Y</td>
<td>None</td>
<td>N</td>
<td>Normal</td>
<td>Normal</td>
<td>I</td>
</tr>
<tr>
<td>29</td>
<td>VSD, PA</td>
<td>1.5</td>
<td>12</td>
<td>N</td>
<td>Mild</td>
<td>N</td>
<td>Normal</td>
<td>Normal</td>
<td>II</td>
</tr>
<tr>
<td>30</td>
<td>VSD, PA</td>
<td>&lt;0.2</td>
<td>7</td>
<td>N</td>
<td>Severe</td>
<td>N</td>
<td>Normal</td>
<td>Normal</td>
<td>II</td>
</tr>
<tr>
<td>31</td>
<td>Small VSD</td>
<td>&lt;0.1</td>
<td>28</td>
<td>N</td>
<td>Severe</td>
<td>Y</td>
<td>Unknown</td>
<td>Decreased</td>
<td>Dead</td>
</tr>
<tr>
<td>32</td>
<td>Mild PS</td>
<td>1</td>
<td>36</td>
<td>N</td>
<td>Severe</td>
<td>Y</td>
<td>Decreased</td>
<td>Decreased</td>
<td>Dead</td>
</tr>
<tr>
<td>33</td>
<td>Small VSD</td>
<td>&lt;0.2</td>
<td>15</td>
<td>N</td>
<td>Severe</td>
<td>Y</td>
<td>Unknown</td>
<td>Decreased</td>
<td>Dead</td>
</tr>
<tr>
<td>34</td>
<td>None</td>
<td>5</td>
<td>28</td>
<td>N</td>
<td>Mild</td>
<td>N</td>
<td>Normal</td>
<td>Normal</td>
<td>I</td>
</tr>
<tr>
<td>35</td>
<td>Mild AS</td>
<td>12</td>
<td>30</td>
<td>N</td>
<td>Severe</td>
<td>Y</td>
<td>Normal</td>
<td>Decreased</td>
<td>III</td>
</tr>
<tr>
<td>36</td>
<td>Mild PS</td>
<td>5</td>
<td>8</td>
<td>N</td>
<td>None</td>
<td>N</td>
<td>Normal</td>
<td>Normal</td>
<td>I</td>
</tr>
<tr>
<td>37</td>
<td>Mild AI</td>
<td>27</td>
<td>20</td>
<td>N</td>
<td>None</td>
<td>N</td>
<td>Normal</td>
<td>Normal</td>
<td>I</td>
</tr>
<tr>
<td>38</td>
<td>None</td>
<td>1.5</td>
<td>16</td>
<td>N</td>
<td>Severe</td>
<td>N</td>
<td>Unknown</td>
<td>Decreased</td>
<td>Transplanted</td>
</tr>
<tr>
<td>39</td>
<td>Small VSD</td>
<td>&lt;0.2</td>
<td>15</td>
<td>N</td>
<td>Severe</td>
<td>Y</td>
<td>Normal</td>
<td>Normal</td>
<td>Dead</td>
</tr>
<tr>
<td>40</td>
<td>None</td>
<td>62</td>
<td>7</td>
<td>N</td>
<td>Severe</td>
<td>N</td>
<td>Unknown</td>
<td>Decreased</td>
<td>II</td>
</tr>
</tbody>
</table>

AI indicates aortic insufficiency; AS, aortic stenosis; ASD, atrial septal defect; Coa, coarctation; Mod-Sev, moderately severe; N, no; PA, pulmonary atresia; PS, pulmonary stenosis; RV, right ventricle; TI, tricuspid insufficiency; TVR, tricuspid valve replacement; VSD, ventricular septal defect; Y, yes.

Patients 1 to 30 have hemodynamically significant intracardiac anomalies; patients 31 to 40 have hemodynamically insignificant or no intracardiac anomalies.

*RV function before onset of TI. Patients who already had TI at presentation are labeled as “Unknown” because RV function before onset of TI could not be assessed.

†Roman numerals refer to New York Heart Association functional class.
complete heart block, and pulmonary overcirculation are shown in Table 2. Both TI (relative risk \( RR = 14.8 \), 95% confidence interval [CI] = 1.9 to 117.1, \( P = 0.01 \)) and RV dysfunction (\( RR = 5.5 \), 95% CI = 1.4 to 21.4, \( P = 0.01 \)) were significantly related to increased mortality rates. Those with TI were 14.8 times more likely to die than those without TI, and those with RV dysfunction were 5.5 times more likely to die than those without RV dysfunction. TI and RV dysfunction were significantly associated with each other (\( P = 0.001 \)); 11 of the 17 (65%) patients with TI had RV dysfunction, and 22 of the 23 (96%) patients without TI had normal RV function. By multivariable analysis, TI was the only independent risk factor for death among the factors considered in this analysis. Kaplan-Meier estimates of survival for the 23 patients free of TI yielded a 93% survival rate at 20 years of follow-up, whereas the 17 patients with TI had a 20-year survival of 49% (Figure 1).

Age at last follow-up was not associated with death. Mean age at death or heart transplantation (24.9 ± 16.5 years) for the 12 patients who died or were given transplantation was similar to the age at last follow-up for the 28 patients in New York Heart Association class II (25.1 ± 12.8 years) (\( P = 0.96 \)).

No difference was found in the long-term survival of patients who underwent OHS and those who did not (Figure 2). Survival was 72% for OHS patients and 77% for NOHS patients at 20 years of follow-up. When OHS patients were divided into those who subsequently developed TI, and those who did not, there was a marked difference in survival: 90% 20-year survival for those who remained free of TI, in contrast to 34% for those who developed TI, some time after surgical repair (\( P = 0.002 \)) (Figure 3A). NOHS patients who remained free of TI during the entire period of observation had a 100% 20-year survival rate, whereas those who developed TI, at any time during the follow-up period had a 20-year survival of 60%. This relation was not statistically significant (\( P = 0.08 \)) (Figure 3B).

The clinical course of patients with TI was one of rapid deterioration whether or not TV surgery was undertaken. Survival 1 year after the diagnosis of TI was 70% and by 10 years 38% (Figure 4A) despite surgical intervention on the TV in 13 of the 17 patients. Outcome after TV surgery was poor; 14% survival 10 years after TV replacement (\( n = 12 \)) or repair (\( n = 1 \)) (Figure 4B). Nine of the 12 patients whose tricuspid valves were replaced later died (\( n = 8 \)) or were given transplantation (\( n = 1 \)). Of the 6 patients with TI, still alive and not given transplantation at last follow-up, 1 was in NYHA class III, 4 in class II, and only 1 in class I. In contrast, there were no deaths in the 23 patients without TI, 19 were in NYHA class III, 4 in class II, and 1 was given transplantation because of RV failure.

### Table 2: Risk Factors for Death

<table>
<thead>
<tr>
<th>Factor</th>
<th>Yes n (n1)*</th>
<th>No n (n1)*</th>
<th>PE</th>
<th>SE</th>
<th>RR</th>
<th>95% CI</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>TI</td>
<td>17 (11)</td>
<td>23 (1)</td>
<td></td>
<td></td>
<td>2.69</td>
<td>1.06</td>
<td>14.8 (1.9, 117.1)</td>
</tr>
<tr>
<td>RV dysfunction</td>
<td>12 (9)</td>
<td>28 (3)</td>
<td></td>
<td></td>
<td>1.70</td>
<td>0.69</td>
<td>5.5 (1.4, 21.4)</td>
</tr>
<tr>
<td>OHS</td>
<td>21 (7)</td>
<td>19 (5)</td>
<td></td>
<td></td>
<td>0.40</td>
<td>0.63</td>
<td>1.5</td>
</tr>
<tr>
<td>CHB</td>
<td>13 (8)</td>
<td>27 (4)</td>
<td></td>
<td></td>
<td>0.97</td>
<td>0.65</td>
<td>2.6</td>
</tr>
<tr>
<td>Increased PBF</td>
<td>14 (5)</td>
<td>26 (7)</td>
<td></td>
<td></td>
<td>0.81</td>
<td>0.62</td>
<td>2.3</td>
</tr>
<tr>
<td>Age at presentation</td>
<td>. . .</td>
<td>. . .</td>
<td></td>
<td></td>
<td>0.01</td>
<td>0.03</td>
<td>1.0</td>
</tr>
</tbody>
</table>

CHB indicates complete heart block; CI, confidence interval; n, number of patients; OHS, open heart surgery; PBF, pulmonary blood flow; PE, parameter estimate; RR, risk ratio; RV, right ventricle; SE, standard error; TI, at least moderately severe tricuspid insufficiency.

*\( n_1 \) refers to the number of patients dead or given transplantation at last follow-up.

**Figure 1.** Kaplan-Meier estimate of survival for all 40 patients with CTGA. The 40 patients are then broken down into 23 patients without TI, and 17 patients with TI. Note significantly different survival between the two groups (\( P = 0.01 \)). \( n \) indicates number of patients.
Risk Factors for Tricuspid Insufficiency

Only the presence of a morphologically abnormal TV was significantly associated with development of TI during follow-up. OHS, preoperative TI, complete heart block, RV dysfunction, and pulmonary overcirculation were not significant risk factors.

Open Heart Surgery

Of the 21 OHS patients 7 (33%) developed TIs at a median age of 14 years (range 8 to 69 years), and 6 of the 7 required TV replacement a median of 8 years after OHS. One patient died of congestive heart failure awaiting TV surgery. Preoperative TI was insignificant in 19 and moderate in 2, both of whom developed severe TI on long-term follow-up. Five of the 19 (26%) OHS patients without significant preoperative TI developed TI, ranging from immediately after surgery to 12 years later. Three of the 7 OHS patients with TI after surgery developed it within 2 months of OHS despite having no significant TI before surgery.

TI developed in 10 (53%) of 19 NOHS patients at a median age of 19 years (range 7 to 68 years). Six of the 10 patients required TV replacement and 1 tricuspid valvuloplasty, 1 had deterioration of RV function after severe TI and underwent heart transplantation, and 2 are moderately symptomatic with congestive heart failure. There was no difference in the incidence of TI in the operated and unoperated patients (P=0.34).

VSD closure alone (as opposed to any type of OHS) was also not significantly associated with development of TI, which occurred in 6 (33%) of 18 patients who underwent VSD closure and in 11 (50%) of 22 patients who did not undergo VSD closure (P=0.35).

Tricuspid Valve Morphology

The morphology of the TV was ascertained in 27 of the 40 patients. The remaining 13 patients were not entered in the analysis. The valve was abnormal in 19 (70%) of the 27, with an Ebstein-like anomaly in 13, dysplasia in 5, and slight hypoplasia in 1. Twelve (63%) of the 19 developed TI. The valve appeared normal in 8 of the 27 patients, and 1 (12.5%) of the 8 developed TI (P=0.03).

Cardiac Rhythm

Complete heart block (CHB) occurred in 13 patients; 2 were diagnosed at birth, 7 developed it spontaneously at a mean of 12 years and 4 after OHS. Eight of the 13 (62%) subsequently developed TI. Time from diagnosis of CHB to onset of TI ranged from 1 month to 28 years (mean 13 years). In 2 patients the 2 events were closely linked temporally, CHB preceding TI, by 1 month and 1.5 months, respectively. Nine of 27 (33%) patients in sinus rhythm developed TI. There was no significant difference in TI between patients with CHB and sinus rhythm (P=0.13).

Pulmonary Overcirculation

Of the 40 patients, 5 had increased pulmonary blood flow during the entire follow-up time, whereas in 35 pulmonary blood flow was either never or only temporarily increased. One of the 5 patients with chronic pulmonary overcirculation developed TI, as compared with 16 of the 35 (46%) whose pulmonary flow was either never or only temporarily increased (P=0.37). Pulmonary blood flow was increased during part or all of the follow-up time in 14 patients, 6 of whom (43%) developed TI. Twenty-six patients always had either normal or decreased pulmonary flow, and 11 of the 26 (42%) developed TI (P=1.0).

Right Ventricular Dysfunction

Thirty six of the 40 patients had documentation of RV function by echocardiogram and/or angiography before onset of TI, and 2 of the 36 had decreased function. One of these 2 patients had RV dysfunction, subaortic obstruction, and mild TI documented angiographically 3 years after VSD closure and coarctation repair. He had heart transplantation 8 years later, at which time he still had only mild TI and severe RV dysfunction. The second patient had deterioration of RV function with no obvious preceding event and later developed TI. Of the 34 patients with normal RV function, 12 developed TI, and 6 of those 12 went on to develop late RV dysfunction. The TV remained competent in 22 of the 34 patients, and all had normal RV function at last follow-up.

Discussion

The natural history and postoperative outcome of patients with CTGA and the commonly associated lesions of VSD and...
PS are known to be less satisfactory than those of patients with normal atrioventricular connections and similar intracardiac lesions. Several features render these patients more fragile than their counterparts with atrioventricular concordance. Among these features is the propensity for atrioventricular conduction abnormalities and for TV dysfunction as well as the much-debated capability of the RV to function adequately in the systemic circulation over the course of a normal life span, regardless of the state of the TV.

Several investigators have reported that TV function in patients with CTGA appears to be adversely affected by surgical repair of associated lesions. Anatomic distortion of a structurally abnormal TV by VSD closure has been implicated, as has annular dilation after cardiopulmonary bypass—induced RV dysfunction or large preoperative left-to-right shunts. In this series, however, multivariable analysis indicates that in general, the long-term incidence of TV failure was not affected by intracardiac repair of associated lesions, although 3 patients were identified in whom onset of TI was temporally related to OHS. It should also be noted that the diagnosis of TI was made at a younger median age in the operated patients (14 years) than in the unoperated patients (19 years). Therefore it is reasonable to speculate that OHS can hasten the development of TV failure in that fraction of patients with CTGA already predisposed to the development of TV disease. However, at this time, data are insufficient to validate this concept.

This study indicates that patients who have morphologic abnormalities of the TV identified early in life are at increased risk for developing TIs. In some cases, cardiologists’ ability to diagnose mild TV abnormalities is limited because autopsy series have demonstrated a much higher incidence (91%) than among previously reported clinical cases or in our series (70%). The autopsy/clinical findings may become more similar as diagnostic imaging techniques improve and the presence of milder forms of TV deformity are identified during life. No factors examined other than TV anatomy, including complete heart block, pulmonary overcirculation, or primary RV dysfunction were associated with TV dysfunction.

The interplay between TI and RV dysfunction observed in this group of patients with CTGA is of interest, and the

Figure 3. Kaplan-Meier estimate of survival for A, 21 patients who underwent open heart surgery, and B, 19 unoperated patients broken down into those without TIs and those with TIs. Note significantly decreased survival for open heart surgery patients with TIs (P=0.002) and trend toward decreased survival for unoperated patients with TIs (P=0.08). n indicates number of patients.
“which is the cart-or-horse” question as to whether TI most often leads to RV dysfunction or vice versa is often raised. Several studies have documented normal RV function at rest and normal increase in ejection fraction with exercise in patients with CTGA into adulthood, even in the presence of hemodynamically significant lesions not including TI. A number of patients with CTGA and no hemodynamically significant lesions have been described who are doing well past age 50 years, attesting to the ability of the systemic RV to sustain long life in the presence of normal hemodynamics. In our group, 2 elderly patients were seen, one with no intracardiac lesions who was seen at age 62 years in atrial fibrillation and is now in NYHA class II at age 69; and another who underwent corrective surgery for atrial septal defect and PS at age 60 years and died at age 69 with severe TI. A tendency toward deterioration of RV function with age and the lack of increase in ejection fraction with exercise have been reported in patients with CTGA and minimal hemodynamic abnormalities. Because of the very small number of such patients with no significant associated lesions, it has been difficult to determine whether the commonly observed deterioration of RV function in patients with CTGA is a primary process, the result of long-standing associated lesions, related to previous surgery, or secondary to long-standing TI. The data from this series appears to help answer this question. Of 23 OHS and NOHS patients without TI, 22 continue to have normal RV function at last follow-up. There were only 2 patients in whom RV dysfunction was clearly not associated with TV failure, and other explanations for RV deterioration were obvious in one of the two instances. It can be concluded that RV failure as a primary process leading to TI is uncommon but is a frequent sequelae after an abnormal TV fails.

The mean time from onset of TI, to documentation of RV failure in our patients was 5 years. This time frame is in contrast to patients with atrioventricular concordance, who often tolerate a significant degree of mitral insufficiency for decades before left ventricular failure ensues. In CTGA, the usual vicious circle occurs whereby the inability of the RV to cope with significant TI leads to decreased contractility and

![Figure 4. Kaplan-Meier estimate of survival A, from the time of diagnosis of TI, in 17 patients with CTGA, and B, after tricuspid valve surgery in the subset of patients with TI, who underwent either repair or replacement of the tricuspid valve. Note very high and continuing mortality rates within months of the diagnosis of TI, and dismal survival rates after tricuspid valve surgery.](image-url)
annular dilation that in turn exacerbate the degree of TI, but this occurs at an accelerated rate. Because the systemic RV in CTGA appears to be less tolerant than an anatomic left ventricle of similar degrees of valvular incompetence, the progression of TI and subsequent RV deterioration is often more rapid than in patients with mitral valve disease. The reason for this distinction between the right and left ventricles is not immediately apparent but is most likely related to geometric differences between the two ventricles and the design of the respective atrioventricular valves.\(^\text{19}\)

Repair or replacement of the TV has met with little success. In this series, survival 10 years after surgical intervention on the TV was only 14%. Similarly, Van Son et al\(^\text{20}\) reported 40% survival at a median follow-up of 4.7 years for 15 patients with CTGA undergoing TV repair or replacement before 1981. It would seem, therefore, that the high mortality rate for TV replacement for CTGA patients with severe TI and RV dysfunction would argue for different types of management. One approach would be to replace the TV earlier, before a significant depression of RV function occurs. Although this approach is theoretically attractive, most cardiologists are reluctant to recommend valve replacement in asymptomatic patients with abnormal but not severely regurgitant tricuspid valves without absolute proof of benefit. Furthermore, in the absence of obvious extreme RV failure, assessment of mild to moderate dysfunction by various imaging techniques hitherto has not been useful. There remain limitations in the quantitative assessment of RV function, especially in the setting of abnormal preload and afterload conditions that accompany systemic valvular insufficiency.\(^\text{21,22}\)

A “double switch” operation has been advocated for patients whose tricuspid valves are severely insufficient. An atrial switch, combined with an arterial switch in the absence of left ventricular outflow obstruction or with a Rastelli procedure have been successfully achieved. After surgery, the left ventricle and mitral valve are restored to the systemic circulation.\(^\text{23,25}\) Improvement in TV function in a low-pressure RV has been documented after these operations.\(^\text{24,25}\) This procedure carries significant risk, and late complications relating to the atrial switch component (baffle obstruction, sick sinus syndrome, and so forth) are of additional concern. Heart transplantation remains the final option for patients with CTGA, intractable TI, and RV failure.

Although the type of surgical treatment and timing for intervention for patients with CTGA remain difficult problems, the focus on TV anatomy and function as the major consideration in the decision-making process should allow rational management concepts to evolve. As surgical techniques improve and evaluation of RV function by new diagnostic imaging methods emerge, earlier and more effective interventions may become plausible in the not-too-distant future.

Study Limitations

The determination of TI severity by either angiography or echocardiography was carried out with the use of standard qualitative techniques. No attempt was made to calculate regurgitant fraction because there is to date no gold standard for grading atrioventricular valve insufficiency. The error intrinsic in the angiographic calculation of regurgitant fraction is quite significant,\(^\text{10}\) limiting its accuracy. Although recent echocardiographic methods\(^\text{26}\) may prove superior, the majority of our patients were studied before these technical developments. The rapidly progressive nature of TI in these patients, once it became more than mild, made for a clear delineation on clinical grounds between those with little TI and those with TI. This argues against a significant methodological error in the serial assessment of TI severity.

Similarly, RV function was determined qualitatively, there being no simple way to determine it quantitatively by the available methods. Such qualitative (or even quantitative) assessment can underestimate dysfunction in the presence of decreased afterload offered by a regurgitant atrioventricular valve. This problem was minimized in the assessment of RV function as a risk factor for development of TI, as only those patients in whom RV function was documented, albeit qualitatively, before the onset of TI, were analyzed. However, the number of patients with RV dysfunction at last follow-up may be underestimated because many had TI at this late time, and RV unloading could have masked dysfunction. Finally, the effect of older age on RV performance with or without TI may not be evident in this study because only 5 patients were followed beyond 40 years of age.

Several risk factors for development of TI, were independently analyzed in this relatively small series from a single institution. Accurate times to development of TI, and larger numbers of patients would allow more extensive analysis not only of individual risk factors but of combinations of risk factors. For example, although neither VSD closure nor the presence of complete heart block individually were associated with TI, patients who undergo VSD closure complicated by complete heart block may be at higher risk. Because only 3 patients in this study had VSD closure and postoperative complete heart block, larger numbers would be needed to answer this question.

References


Progressive Tricuspid Valve Disease in Patients With Congenitally Corrected Transposition of the Great Arteries
Lourdes R. Prieto, Allan J. Hordof, Michelle Secic, Marlon S. Rosenbaum and Welton M. Gersony

*Circulation*. 1998;98:997-1005
doi: 10.1161/01.CIR.98.10.997
*Circulation* is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
Copyright © 1998 American Heart Association, Inc. All rights reserved.
Print ISSN: 0009-7322. Online ISSN: 1524-4539

The online version of this article, along with updated information and services, is located on the World Wide Web at:
http://circ.ahajournals.org/content/98/10/997

Permissions: Requests for permissions to reproduce figures, tables, or portions of articles originally published in *Circulation* can be obtained via RightsLink, a service of the Copyright Clearance Center, not the Editorial Office. Once the online version of the published article for which permission is being requested is located, click Request Permissions in the middle column of the Web page under Services. Further information about this process is available in the Permissions and Rights Question and Answer document.

Reprints: Information about reprints can be found online at:
http://www.lww.com/reprints

Subscriptions: Information about subscribing to *Circulation* is online at:
http://circ.ahajournals.org//subscriptions/