Presence of a Ventricular Septal Defect and the Mustard Operation Are Risk Factors for Late Mortality After the Atrial Switch Operation

Thirty Years of Follow-Up in 417 Patients at a Single Center

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Background—Survival and functional status of patients with transposition of the great arteries treated by atrial switch are reported to be reasonably good within the first 15 postoperative years. However, in some patients, the function of the systemic right ventricle deteriorates, leading to significant morbidity or even to late mortality. This study seeks to identify risk factors for late death.

Methods and Results—Records of 329 patients after the Senning operation and 88 after the Mustard operation at a single center were retrospectively reviewed for demographic, anatomic, and echocardiographic predictors and outcomes. Mean follow-up interval was 19.1±6.5 years and was 95% complete. Survival 25 years after the Mustard procedure was 75.9±4.8% and after the Senning procedure was 90.9±2.3% (P=0.002). Mustard patients died more often of arrhythmia than Senning patients (P<0.001) and needed more baffle-related reoperations (P<0.0001). Ventricular septal defect closure at the time of the atrial switch operation (hazard rate=2.3; 95% confidence interval, 1.1 to 4.7; P=0.025) and the Mustard operation (hazard rate=2.0; 95% confidence interval, 1.01 to 3.8; P=0.045) emerged as independent risk factors for late mortality in multivariate analysis. At follow-up, 85.8% of the patients led a normal life with full-time work, and 11.8% were able to do part-time work. Only 2.4% experienced noticeable limitation of activities.

Conclusions—Our patient data reveal satisfactory results at long term in this historic collective. Patients who had undergone ventricular septal defect closure at the time of the atrial switch operation and those who had undergone a Mustard operation are at higher risk for late death. Close follow-up, especially of these subgroups, is warranted.

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Key Words: follow-up studies ■ heart defects, congenital ■ surgery ■ transposition of great vessels

Transposition of the great arteries (TGA) was initially treated by palliative procedures, such as the surgical atrial septectomy in 1950 and the balloon atrial septostomy in 1966. By creating an atrial septal defect and allowing intra-atrial mixing of the pulmonary and the systemic circulations, these procedures were the first to permit survival of newborns with TGA and intact ventricular septum. After initial attempts of the arterial switch procedure had failed, atrial switch procedures with separation of the systemic and the pulmonary circulations were successfully established. The surgical technique, with the use of autologous tissue to create an intra-atrial baffle, was first described by Senning in 1958. In 1963, Mustard presented a similar approach using synthetic material. Until the mid 1980s, atrial switch procedures were the treatment of choice for TGA. Then this treatment was abandoned in favor of the arterial switch operation.

Clinical Perspective p 1913

Survival, functional status, and quality of life of patients after an atrial switch operation are reported to be reasonably good within the first 2 decades of life. However, in some patients the function of the systemic right ventricle deteriorates, severe tricuspid regurgitation develops, or the patients suffer from arrhythmia. Several strategies are proposed to handle those patients with failing right ventricle, such as tricuspid valve repair, conversion to arterial switch, or heart transplantation. In most of the cases, these procedures are performed after the right ventricular function has already
deteriorated, with the consequence of a high operative mortality.18–21

By assessing preoperative morphological and clinical data, operative details, perioperative course, and patient status during follow-up, this study seeks to analyze the long-term outcome of patients after the atrial switch procedure to identify risk factors for late mortality in a large group of patients with TGA up to 30 years after atrial redirection.

Methods
This study was approved by the ethics committee of the Technical University Munich.

Patients
All patients with TGA who underwent an atrial switch procedure between 1974 and 2001 were included in a retrospective follow-up study. Patients with atrioventricular and ventriculoarterial discordance and patients with pulmonary vascular disease from an associated ventricular septal defect (VSD) who were treated by an atrial switch procedure without VSD closure were excluded. Furthermore, 30 patients from non-German-speaking countries were excluded because follow-up data could not be generated.

Data Collection
All data were collected from medical records and from follow-up examinations at the outpatient facilities. Records were retrospectively reviewed for demographic, morphological, clinical, echocardiographic, and hemodynamic details. The congenital heart lesion was classified as simple TGA if the interventricular septum was intact and as TGA+VSD if there was a VSD. In cases of significant left ventricular outflow tract obstruction (LVOTO), it was classified as TGA+LVOTO or as TGA+VSD+LVOTO, respectively.

Follow-up was obtained by a written questionnaire or by telephone. The functional status was determined according to the New York Heart Association (NYHA) class and ability index.22 Patients were asked about the occurrence of cardiovascular events, such as arrhythmia, stroke, thrombosis, and reoperation, as well as about previous cardiac catheterization, pacemaker implantation, hospital admissions, concomitant diseases, and medication. In case of death, the relatives and the general physicians of the patients were contacted to determine the cause of death.

During long-term follow-up, patients underwent routine examinations including echocardiography and electrocardiography. Right ventricular function and tricuspid regurgitation (TR) were evaluated according to written notes of echocardiographic examinations from the outpatient clinics by 1 of the authors. Right ventricular function was graded as follows: 0, normal right ventricular function; 1, mild right ventricular dysfunction (RVD); 2, moderate RVD; and 3, severe RVD. TR was graded as follows: 0, no TR; 1, mild TR; 2, moderate TR; and 3, severe TR. Twelve-lead resting and 24-hour ambulatory ECGs were used for evaluation of cardiac rhythm.

Composite end point of RVD was defined as the first onset of moderately or severely reduced right ventricular function, death from right heart failure, and conversion to arterial switch, including banding of the pulmonary artery and heart transplantation. Conversion to arterial switch and/or banding of the pulmonary artery was performed only in patients who presented with moderately or severely reduced right ventricular function

Statistical Analysis
Descriptive data for continuous variables are presented as mean±SD or as median with range; categorical variables are presented as relative frequencies. Fisher exact test was performed to detect significant differences between groups. For comparison of continuous variables between 2 groups, the t test was used (2-tailed tests were used for all analyses). The probability of freedom from events was estimated according to the Kaplan-Meier method.23 Freedom-from-events curves were compared with the use of the log-rank test.24 Values of P≤0.05 were considered statistically significant. Hazard rates were estimated according to the Cox proportional model. Parameters that were statistically significant between the 2 patient groups receiving either the Mustard or the Senning operation and parameters that were statistically predictive for late mortality were entered into a Cox proportional hazard model. Analyses were performed with SPSS 12.0.2 for Windows.

The authors had full access to the data and take full responsibility for its integrity. All authors have read and agree to the manuscript as written.

Results

Preoperative Data
The study included 417 patients (Table 1). Simple TGA was diagnosed in 265 patients (63.5%), TGA+VSD in 102 patients (24.5%), TGA+LVOTO in 22 patients (5.3%), and TGA+VSD+LVOTO in 28 patients (6.7%). Preoperative balloon atrial septostomy was performed in 382 patients (92.0%). In 57 patients, 92 surgical procedures had been performed before the atrial switch operation. Patients with VSD presented with older age at the time of the atrial switch operation (P<0.001), with a higher left ventricular–to–right ventricular pressure ratio (P<0.001), and with a higher aortic oxygen saturation (P=0.001). Patients after a Mustard operation were significantly older at the time of the atrial switch operation (P<0.001), presented more often with a complex TGA (P=0.004), presented with a lower aortic oxygen saturation (P=0.008), and had more often undergone a palliative operation (P<0.001) than patients after a Senning operation.

Operative Data
The Mustard operation was performed in 88 patients from 1974 until 1982, and the Senning operation was performed in 329 patients from 1977 onward. The Mustard operation was performed with the use of a trousers-shaped Dacron baffle as described by Meisner and Sebening.25 Hospital mortality was 8.0%.

The Senning operation was performed as described by Senning.6 The originally recommended incision of the coronary sinus was not performed because of a potential injury to the atrioventricular (AV) node. The atrial suture line was placed posterior to the coronary sinus connecting it to the functional left side. In most of the cases, the suture line in the vicinity of the sinus node was placed close to the superior vena cava orifice.25 Hospital mortality was 4.6%.

VSD closure was performed in 94 of the 130 patients who presented with a VSD; in the remaining patients the VSD was considered to be hemodynamically irrelevant. The VSD was closed via a right atrial approach in all patients, except for 1, in whom it was closed through the aorta. VSD closure was performed by direct suture in 37 patients and with a patch in 57 patients. The septal leaflet of the tricuspid valve was left in situ during VSD repair in all cases.

Postoperative Hospital Data
Median time in the intensive care unit was 6 days (range, 1 day to 81 days), and median time on ventilation was 2 days (range, 1 day to 51 days). Thirty-two patients (7.6%) showed transient or permanent AV block postoperatively, which was
TABLE 1. Perioperative Variables of 417 Patients With TGA Who Underwent the Mustard or Senning Operation

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Missing</th>
<th>Overall Group (n=417)</th>
<th>Mustard (n=88)</th>
<th>Senning (n=329)</th>
<th>(P^*)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Operation before 1983, n (%)</td>
<td>0</td>
<td>213 (51.1)</td>
<td>88 (100)</td>
<td>125 (38.0)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Mean follow-up time,† y</td>
<td>22</td>
<td>19.1±1.6</td>
<td>22.7±8.1</td>
<td>18.2±5.7</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Gender, male, n (%)</td>
<td>0</td>
<td>293 (71.0)</td>
<td>65 (73.9)</td>
<td>228 (69.3)</td>
<td>0.434</td>
</tr>
<tr>
<td>Mean age at atrial switch, mo</td>
<td>0</td>
<td>14.8±1.4</td>
<td>32.4±29.1</td>
<td>10.0±15.8</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Mean weight at atrial switch, kg</td>
<td>2</td>
<td>6.7±4.2</td>
<td>11.3±5.3</td>
<td>6.5±3.1</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Morphology</td>
<td></td>
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<td></td>
</tr>
<tr>
<td>VSD present, n (%)</td>
<td>0</td>
<td>130 (31.2)</td>
<td>37 (42.0)</td>
<td>93 (28.3)</td>
<td>0.019</td>
</tr>
<tr>
<td>Small</td>
<td>0</td>
<td>36 (8.6)</td>
<td>6 (6.6)</td>
<td>30 (9.1)</td>
<td>0.669</td>
</tr>
<tr>
<td>Moderate or large</td>
<td>0</td>
<td>94 (22.5)</td>
<td>31 (35.2)</td>
<td>63 (19.1)</td>
<td>0.002</td>
</tr>
<tr>
<td>LVOT, n (%)</td>
<td>0</td>
<td>50 (12.0)</td>
<td>13 (14.8)</td>
<td>37 (11.2)</td>
<td>0.360</td>
</tr>
<tr>
<td>LV/RV pressure ratio, n (%)</td>
<td>25</td>
<td>0.68±0.29</td>
<td>0.73±0.36</td>
<td>0.67±0.27</td>
<td>0.191</td>
</tr>
<tr>
<td>Aortic oxygen saturation, %</td>
<td>40</td>
<td>64.1±14.8</td>
<td>61.0±10.9</td>
<td>65.0±15.6</td>
<td>0.008</td>
</tr>
<tr>
<td>Palliative procedures</td>
<td></td>
<td></td>
<td></td>
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<td></td>
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<tr>
<td>Atrial septectomy, n (%)</td>
<td>0</td>
<td>26 (6.2)</td>
<td>21 (23.9)</td>
<td>5 (1.5)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Banding of pulmonary artery, n (%)</td>
<td>0</td>
<td>26 (6.2)</td>
<td>18 (20.5)</td>
<td>8 (2.4)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Ligation of patent arterial duct, n (%)</td>
<td>0</td>
<td>17 (4.1)</td>
<td>8 (9.1)</td>
<td>9 (2.7)</td>
<td>0.013</td>
</tr>
<tr>
<td>Shunt procedure, n (%)</td>
<td>0</td>
<td>11 (2.6)</td>
<td>5 (5.7)</td>
<td>6 (1.8)</td>
<td>0.059</td>
</tr>
<tr>
<td>CoA repair, n (%)</td>
<td>0</td>
<td>10 (2.4)</td>
<td>5 (5.7)</td>
<td>5 (1.5)</td>
<td>0.039</td>
</tr>
<tr>
<td>Brock’s procedure, n (%)</td>
<td>0</td>
<td>1 (0.2)</td>
<td>0 (0.3)</td>
<td>1 (0.3)</td>
<td>1.000</td>
</tr>
<tr>
<td>Balloon atrial septostomy, n (%)</td>
<td>2</td>
<td>382 (92.0)</td>
<td>75 (85.2)</td>
<td>307 (93.3)</td>
<td>0.013</td>
</tr>
<tr>
<td>Surgical</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean cardiopulmonary bypass time, min</td>
<td>7</td>
<td>105.7±33.7</td>
<td>105.3±33.7</td>
<td>105.8±33.7</td>
<td>0.907</td>
</tr>
<tr>
<td>Mean ischemic time, min</td>
<td>7</td>
<td>56.1±22.4</td>
<td>40.4±28.2</td>
<td>60.2±18.6</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Total circulatory arrest, n (%)</td>
<td>7</td>
<td>330 (79.1)</td>
<td>48 (54.5)</td>
<td>282 (85.7)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>VSD closure, n (%)</td>
<td>0</td>
<td>94 (22.5)</td>
<td>31 (35.2)</td>
<td>63 (19.1)</td>
<td>0.002</td>
</tr>
<tr>
<td>VSD closure with direct suture</td>
<td>0</td>
<td>37 (8.9)</td>
<td>12 (16.6)</td>
<td>25 (7.6)</td>
<td>0.091</td>
</tr>
<tr>
<td>VSD closure with patch</td>
<td>0</td>
<td>57 (13.7)</td>
<td>19 (21.6)</td>
<td>38 (11.6)</td>
<td>0.022</td>
</tr>
<tr>
<td>Left ventricular outflow tract procedure, n (%)</td>
<td>0</td>
<td>50 (12.5)</td>
<td>13 (14.8)</td>
<td>37 (11.2)</td>
<td>0.360</td>
</tr>
</tbody>
</table>

LV indicates left ventricular; RV, right ventricular; and CoA, coarctation of the aorta.

*Level of significance for comparison between the Mustard and Senning groups.

†Follow-up time was calculated excluding the 22 early deaths and including the 21 patients lost to final follow-up. Six Mustard patients could be followed up for a mean of 16.4±10.5 years, and 15 Senning patients were followed up for a mean of 10.2±7.8 years.

not significantly more frequent in patients in whom a VSD had been closed \((P=0.117)\).

**Subjects’ Progress During Long-Term Follow-Up**

Follow-up was conducted between June 2003 and July 2004. Follow-up was available for 332 patients and was achieved by a written questionnaire in 77.9% of the patients and by telephone in the remaining patients. Twenty-one patients could not be contacted and were lost at a mean of 12.0±8.9 years after the atrial switch operation. There were 42 late deaths. Hence, follow-up, including the late deaths, was available for 94.7% of the hospital survivors. The details of the subjects’ progress for the Senning and the Mustard groups are depicted in Figure 1. Mean follow-up time was 19.1±6.5 years (7553 patient-years). Mean age of the patients at final follow-up was 21.8±4.9 years.

**Late Reoperations**

After hospital discharge, 75 reoperations were performed in 63 patients (15.9%). In 12 patients (3.0%), 2 reoperations were performed. Frequently, several procedures had to be performed during 1 reoperation, resulting in 133 procedures performed on 75 reoperations (Table 2).

Baffle-related complications were the main indication for reoperation. Enlargement of the venous tunnel and/or closure of a baffle leak accounted for 80 of the 133 procedures (60.2%). Twenty-four procedures (18.0%) were performed because of RVD or severe TR.

One patient died 13 years after the Senning operation after going reoperations and 0.8% in relation to the whole group. Estimated freedom from reoperation of hospital survivors was 95.1±6.1% after the Mustard operation and 87.7±2.1% after the Senning operation (Figure 2A). Reoperations were significantly more frequent in patients after the Mustard operation \((P<0.0001)\). Estimated freedom from
reoperation for baffle-related complications at 25 years was 66.5±5.9% after the Mustard operation and 93.6±1.7% after the Senning operation (Figure 2B), the difference between the 2 groups being significant ($P<0.0001$).

**Rhythm Disturbances**

ECG at final follow-up could be obtained from 85% of the long-term survivors. Accordingly, 78.3% of them were in sinus rhythm, 13.3% presented with atrial or junctional rhythm with good chronotropic response, and 8.3% presented with poor chronotropic response, significant enough to require permanent pacemaker implantation. Among patients who presented with sinus rhythm, a right bundle branch block (RBBB) was observed in 19 patients (8.1%). The incidence of a RBBB was significantly higher in patients in whom a VSD was closed ($P<0.0001$). Pacemaker implantation was required in 35 patients. Indications for pacemaker implantation were sick sinus syndrome ($n=16$), complete AV block ($n=6$), atrial fibrillation with marked bradycardia ($n=4$), long-QT syndrome ($n=1$), and unspecified conduction disturbances ($n=7$). An implantable cardioverter/defibrillator was implanted in 1 patient suffering from recurrent atrial flutter with ventricular tachycardia. Estimated freedom from pacemaker implantation for all hospital survivors at 25 years was 86.1±2.7%, with no difference after the Senning and the Mustard procedure ($P=0.6$). However, freedom from pacemaker implantation was significantly lower in patients who received VSD closure at the time of the atrial switch operation ($P=0.008$).

**Late Deaths**

There were 42 late deaths (10.6% of the hospital survivors), 30 of which were cardiac related. Twelve patients died of

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**TABLE 2. Reoperations After Hospital Discharge by Operation Type**

<table>
<thead>
<tr>
<th>Procedure</th>
<th>Overall Group (n=395)*</th>
<th>Mustard (n=81)†</th>
<th>Senning (n=314)‡</th>
</tr>
</thead>
<tbody>
<tr>
<td>Closure of baffle leak</td>
<td>18 (24.0)</td>
<td>7 (18.9)</td>
<td>11 (28.9)</td>
</tr>
<tr>
<td>Enlargement of systemic venous tunnel</td>
<td>34 (45.3)</td>
<td>24 (64.9)</td>
<td>10 (26.3)</td>
</tr>
<tr>
<td>Enlargement of pulmonary venous tunnel</td>
<td>26 (34.7)</td>
<td>18 (48.6)</td>
<td>8 (21.1)</td>
</tr>
<tr>
<td>Left ventricular outflow tract procedure</td>
<td>12 (16.0)</td>
<td>2 (5.4)</td>
<td>10 (26.3)</td>
</tr>
<tr>
<td>Banding of pulmonary artery</td>
<td>9 (12.0)</td>
<td>2 (5.4)</td>
<td>7 (18.4)</td>
</tr>
<tr>
<td>Arterial switch and atrial redirection</td>
<td>5 (6.7)</td>
<td>0</td>
<td>5 (13.2)</td>
</tr>
<tr>
<td>Procedure of tricuspid valve</td>
<td>9 (12.0)</td>
<td>5 (13.5)</td>
<td>4 (10.5)</td>
</tr>
<tr>
<td>Closure of residual ventricular septal defect</td>
<td>8 (10.7)</td>
<td>5 (13.5)</td>
<td>3 (7.9)</td>
</tr>
<tr>
<td>Other procedures</td>
<td>12 (16.0)</td>
<td>4 (10.8)</td>
<td>9 (23.7)</td>
</tr>
</tbody>
</table>

*Data expressed as n (% of 75 reoperations in 63 patients).
†Data expressed as n (% of 37 reoperations in 30 patients).
‡Data expressed as n (% of 38 reoperations in 33 patients).
right heart failure, 15 of sudden death, and 3 during a reoperation. Five patients died of non-cardiac-related causes. The cause of death of the remaining 7 patients could not be determined. Estimated survival of all 395 hospital survivors at 25 years was 86.0±2.3%.

In univariate analyses, the risk factors for shorter time to late death in the overall study group were presence of a VSD (P<0.001), presence of a large VSD (P<0.001), prior operation (P=0.001), atrial septectomy (P=0.004), banding of the pulmonary artery (P=0.001), no prior balloon atrial septostomy (P<0.001), VSD closure (P<0.001), VSD direct suture (P=0.042), and VSD patch closure (P<0.001; Table 3). In multivariate analysis of these significant parameters, and with the parameters significantly different between the Mustard and the Senning groups, VSD closure at the time of the atrial switch operation (hazard rate 2.3; 95% confidence interval, 1.1 to 4.7; P=0.025) and the Mustard operation (hazard rate 2.0; 95% confidence interval, 1.01 to 3.8; P=0.045) remained significant.

Estimated survival at 25 years after the Mustard operation was 75.9±4.8% and after the Senning operation was 90.9±2.3% (P=0.002; hazard rate 2.6; Figure 3A). Patients after the Mustard procedure died significantly more often of sudden death (P<0.001; hazard rate 6.6; Figure 3B). Presence of a moderate or large VSD that was closed at the time of the atrial switch operation was the only parameter significantly associated with late death for the total atrial switch population (P<0.001; Figure 3C), as well as for the Mustard and Senning patients separately (Mustard: P=0.033; Senning: P=0.002; Figure 3D).

**Systemic Ventricular Failure**

Information concerning the composite end point of RVD was obtained from 91.4% of the hospital survivors. RVD occurred in 36 patients (10%), 12 of whom died of right heart failure. Conversion to arterial switch, pulmonary artery banding, or heart transplantation was performed in 12 patients. Twelve patients presented with moderately or severely reduced right ventricular function during follow-up. Estimated freedom from the composite end point of RVD for the whole atrial switch population at 25 years was 83.9±2.9%, with no difference after the Mustard and the Senning operation.

### Table 3. Predictors of Late Death by Operation Type

<table>
<thead>
<tr>
<th>Variable</th>
<th>Mustard (n=81)</th>
<th>No./Events</th>
<th>P*</th>
<th>HR (95% CI)</th>
<th>Senning (n=315)</th>
<th>No./Events</th>
<th>P*</th>
<th>HR (95% CI)</th>
<th>Overall Group (n=395)</th>
<th>No./Events</th>
<th>P*</th>
<th>HR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Morphology</strong></td>
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</tr>
<tr>
<td>VSD present</td>
<td>31/11</td>
<td>0.055</td>
<td>2.4 (1.0–5.9)</td>
<td>82/11</td>
<td>0.007</td>
<td>2.9 (1.3–6.6)</td>
<td>113/22</td>
<td>&lt;0.001</td>
<td>3.0 (1.6–5.5)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Moderate or large VSD (closed)</td>
<td>26/10</td>
<td>0.033</td>
<td>2.6 (1.0–6.3)</td>
<td>55/9</td>
<td>0.002</td>
<td>3.4 (1.5–8.0)</td>
<td>81/19</td>
<td>&lt;0.001</td>
<td>3.5 (1.9–6.4)</td>
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<tr>
<td><strong>Surgical</strong></td>
<td></td>
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<td></td>
<td></td>
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</tr>
<tr>
<td>Prior operation</td>
<td>28/10</td>
<td>0.058</td>
<td>2.3 (0.9–5.8)</td>
<td>22/3</td>
<td>0.217</td>
<td>2.1 (0.6–7.1)</td>
<td>50/13</td>
<td>0.001</td>
<td>3.0 (1.6–5.8)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Atrial septectomy</td>
<td>18/7</td>
<td>0.058</td>
<td>2.4 (0.9–6.1)</td>
<td>5/0</td>
<td>0.545</td>
<td>0.0 (0–11924)</td>
<td>23/7</td>
<td>0.004</td>
<td>3.1 (1.4–7.1)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Banding of pulmonary artery</td>
<td>14/5</td>
<td>0.290</td>
<td>1.7 (0.6–4.8)</td>
<td>5/2</td>
<td>0.003</td>
<td>6.8 (1.6–29.2)</td>
<td>19/7</td>
<td>0.001</td>
<td>3.6 (1.6–8.15)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No prior balloon atrial septostomy</td>
<td>11/8</td>
<td>&lt;0.001</td>
<td>7.4 (3.0–18.6)</td>
<td>16/1</td>
<td>0.923</td>
<td>0.9 (0.1–6.7)</td>
<td>27/9</td>
<td>&lt;0.001</td>
<td>4.3 (2.1–9.1)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>VSD closure</td>
<td>26/10</td>
<td>0.033</td>
<td>2.6 (1.0–6.3)</td>
<td>55/9</td>
<td>0.002</td>
<td>3.4 (1.5–8.0)</td>
<td>81/19</td>
<td>&lt;0.001</td>
<td>3.5 (1.9–6.4)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>VSD direct suture</td>
<td>12/5</td>
<td>0.095</td>
<td>2.3 (0.8–6.5)</td>
<td>23/2</td>
<td>0.710</td>
<td>1.3 (0.3–5.6)</td>
<td>35/7</td>
<td>0.042</td>
<td>2.3 (1.0–5.1)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>VSD patch</td>
<td>14/5</td>
<td>0.275</td>
<td>1.8 (0.6–4.9)</td>
<td>32/7</td>
<td>&lt;0.001</td>
<td>4.4 (1.8–10.7)</td>
<td>46/12</td>
<td>&lt;0.001</td>
<td>3.2 (1.7–6.3)</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

HR indicates hazard rate.
*Level of significance between the groups of dichotomous variables listed in the first column.
However, the incidence of RVD was significantly higher in patients who had undergone VSD closure at the time of atrial switch operation ($P<0.001$; hazard rate $=5.1$; Figure 4B).

During follow-up, 10 patients developed severe TR. The incidence of TR was not associated with VSD closure ($P=0.06$) and did not occur more often in patients in whom the sutures were placed through the annulus of the tricuspid valve.

**Figure 3.** A, Estimated survival of hospital survivors related to the procedure. B, Estimated freedom from sudden death of hospital survivors. C, Estimated survival for the combined atrial switch population related to VSD closure. D, Estimated survival of patients related to the procedure and to VSD closure.

**Figure 4.** A, Estimated freedom from composite endpoint of RVD of hospital survivors related to the procedure. B, Estimated freedom from RVD of hospital survivors related to VSD closure.
valve compared with patients in whom they were not \( (P=0.3) \).

**Functional Status**

Information concerning the functional status at the time of final follow-up could be obtained from 323 patients (91.5% of long-term survivors). Accordingly, 47.4% of the patients were in NYHA class I, 48.0% in class II, and 4.6% in class III, respectively. The majority (85.8%) of the patients led a normal life with full-time work (ability index class I), 11.8% were able to work part time (class II), and 2.4% experienced noticeable limitations on activities (class III). Only 9.4% of the patients were on medication for heart failure (angiotensin-converting enzyme inhibitors, diuretics, or digitalis), and 7.5% were on antiarrhythmics. RVD was significantly more frequent in patients assigned to NYHA classes II and III \( (P=0.018) \), in patients assigned to ability index class III \( (P=0.004) \), and in patients who presented with an RBBB \( (P=0.024) \).

**Discussion**

**Early Mortality**

In the 1970s and 1980s, the atrial switch procedure was the treatment of choice for patients with TGA. Initially, the Mustard procedure was exclusively performed at our institution with an early mortality rate of 8.0%, comparable to previous studies with mortality rates ranging from 8% to 12%.\(^{11,26,27}\) After Quaegebeur et al\(^{28}\) reported favorable results with the Senning operation in 1977, this operation was performed at the German Heart Center from 1977 until the end of the 1980s. Early mortality of the Senning operation was 4.6% and thus was also comparable to other reported series, ranging from 2% to 5.4%.\(^{11,12,29}\) However, during the transitional period, when practice changed from the Mustard to the Senning procedure, patients with complex TGA underwent preferentially the Mustard operation because surgeons felt more comfortable with this technique, whereas patients with simple TGA underwent the Senning operation, resulting in a significant difference in the relative number of complex TGA between the 2 groups. In addition, the surgical learning curve may have been a reason for the differences in mortality between the 2 groups because the Mustard operation was performed at the beginning of the series.

**Reoperation**

Baffle-related complications were the most frequent cause of reoperation and accounted for 30.7% of reoperations in the Mustard group and for 5.4% in the Senning group. This difference has been described previously by others.\(^{10,14,30}\) In the present group, the curves for freedom from baffle reintervention, as depicted in Figure 2B, were only slightly different within the first 15 years but began to diverge clearly after that time span. The reason for a higher incidence of baffle-related complications in the Mustard group may be seen in the use of synthetic material, potential peel formation at the site of the tissue-to-baffle anastomosis, or folding of excessive baffle material. In contrast, the study published by the Congenital Heart Surgeons Society in 2000\(^{16}\) found no difference in the incidence of baffle-related complications between 108 Mustard and 173 Senning patients. This might be due to the relatively short follow-up time of only 12 years. Furthermore, in the present group there was no death in patients undergoing reoperation for pathway obstructions, whereas Wells and Blackstone\(^{16}\) reported an operative mortality of 42%.

Surgery for RVD was the second most frequent indication for reoperation and accounted for 2 of the 3 late deaths in the present study. One patient underwent a heart transplantation 21 years after the Mustard operation and is currently in good condition 3 years after the procedure.

Mortality associated with reoperations in general has been described to be as high as 36% in a previously published series.\(^ {16}\) In the present study, mortality associated with reoperations was 4.0%, mainly because of the high operative mortality of conversion to the arterial switch operation.

**Rhythm Disturbances**

Loss of sinus rhythm at long term has been described in patients after atrial baffle procedures,\(^ {11,13}\) with the incidence being the same after the Senning or the Mustard procedure.\(^ {30}\) However, in the present study sinus rhythm was present in 80.8% of the patients 17.4 years after the Senning procedure, which is higher than in other reported series.\(^ {10,12,13}\) Freedom from pacemaker insertion was still \(91\%\) at 10 years. At 20 years, freedom from pacemaker insertion was still \(>90\%\). This might be related to the fact that in our patients the coronary sinus was not incised as originally described by Senning\(^{a}\) and the atrial suture line was placed posterior to the coronary sinus.\(^ {25}\)

**Late Death**

In the present series, 25-year survival of the patients was \(90.9\%\pm2.3\%\) after the Senning procedure and \(75.9\%\pm4.8\%\) after the Mustard procedure and thus was significantly different in univariate analysis. The Mustard procedure remained a significant risk factor for late death in multivariate analysis fully adjusted for all variables that were statistically significant between the 2 groups. This difference in late survival between the 2 operative procedures is not confirmed in all investigations. Whereas Sarkar et al\(^ {30}\) observed a significantly better survival of patients after the Senning operation \(94\%\) versus \(77\%\) at 15 years), Wells and Blackstone\(^ {16}\) reported the Senning operation to be a risk factor for late death. In contrast, Moons et al\(^ {10}\) did not observe a difference in survival between the 2 procedures in a nationwide multicenter study in Belgium \(79.3\%\) at 30 years for both procedures), and Oechslin and Jenni\(^ {14}\) reported a similar long-term outcome for the Toronto Mustard group and the Zurich Senning group, with \(\sim75\%\) survival after 25 years. However, they found a difference in the mode of death between the Mustard group and the Senning group. Similar to the results of the present study, relatively more Mustard patients died of sudden death compared with the Senning patients, who died preferentially of progressive congestive heart failure.

Irrespective of the type of atrial baffle procedure, patients with previous VSD carry a higher risk of late death than patients with intact ventricular septum.\(^ {10,16,30}\) Sixteen years...
after the Mustard procedure, Helbing et al\textsuperscript{32} found that 91% of the patients with simple TGA but only 60% of the patients with complex TGA were alive. The same was shown by Kirjavainen et al\textsuperscript{11} after the Senning procedure: 90% of the patients with simple TGA but only 78% of the patients with complex TGA were alive 15 years after the procedure. Our data confirm the finding that presence of a VSD is a significant risk factor for late death because VSD closure emerged as an independent risk factor for late death in multivariate analysis.

The question remains of whether the surgical procedure of VSD closure or rather the hemodynamic consequences of a previous VSD account for the intrinsic risk of late mortality. Potential complications of VSD closure that may also lead to late RVD and consecutively to late death,\textsuperscript{11,13} such as iatrogenic postoperative AV block or tricuspid insufficiency, were not more frequent in patients after VSD closure. However, freedom from pacemaker implantation was lower in patients who received VSD closure at the time of the atrial switch operation. The incidence of RBBB, which has been associated with late development of RVD,\textsuperscript{33} was increased. Hence, the surgical procedure of VSD closure may have an influence on mortality in the long term.

In the present study the hazard rate for late death was higher in patients in whom a VSD was closed with a patch (hazard rate=3.2) than in patients in whom a VSD was closed by direct suture (hazard rate=2.3). This finding suggests that the size of the VSD may also play an important role for late mortality. Hemodynamically, a large VSD leads to volume load of the right ventricle before the initial operative procedure and thus may predispose patients to RVD in the long term.\textsuperscript{13} According to multivariate analysis, VSD closure emerged as an independent risk factor for late death in the total study population. However, in our opinion, the key question of whether the preoperative presence of a VSD or its closure represents the intrinsic risk factor cannot be solved by performing a multivariate analysis because these variables are highly correlated.

Systemic Ventricular Failure

Deterioration of the function of the systemic ventricle is a major concern in patients after atrial switch procedures. The incidence of moderate or severe RVD shows a wide variation in the literature from 8% at 12 to 18 years\textsuperscript{34,35} to 20% and 18% at 20 and 28 years,\textsuperscript{12,17} respectively. Kirjavainen et al\textsuperscript{11} found a rapid increase of RVD after 10 years and described the probability of normal right ventricular function to be only 52% and 39% 15 years after the Senning procedure in patients with simple and complex TGA, respectively. In the present study the incidence of RVD was 16.1% at 25 years. However, the great variability in assessing right ventricular function and the lack of a uniform definition restrict comparison. The incidence of RVD in the long term has been shown to be associated with the complexity of the heart defect,\textsuperscript{10–12,31} which we confirmed in the present study.

Functional Status

Functional status according to ability index in the present study group was comparable to that in the literature,\textsuperscript{10,30} with 85% of the patients being able to lead a normal life with full-time employment. However, only half of the patients were in NYHA class I, whereas other authors found 66% to 93% being assigned to NYHA class I.\textsuperscript{10,14,30} This obvious difference from our results may be due to the fact that NYHA class was assessed by a cardiologist in the latter studies as opposed to patient self-assessment in the present investigation. In the present group, RVD was significantly more frequent in patients assigned to NYHA class II and III and in patients assigned to ability index class III. However, a general coincidence of RVD and poor functional status has not always been found in previous studies.\textsuperscript{11,12}

Limitations of the Study

Some parts of the data collection were retrospective, and hence missing values were inevitable because some variables were not always documented. Changes in preoperative, operative, and postoperative management may have affected the outcome parameters in a way not covered by our analysis. Follow-up data, eg, of right ventricular function and tricuspid regurgitation, were heterogeneous because of the assessment in 61 outpatient clinics where some of the patients were followed up. It was impossible to assess ventricular function directly from the echo tapes because the investigations had not been saved on tapes. In the present study, it was essential to determine the first occurrence of RVD rather than the degree of impairment.

Conclusions

Our patient data compare favorably with the literature concerning survival and freedom from RVD in the long term in this historic collective. Patients who had undergone VSD closure at the time of the atrial switch operation and those who had undergone a Mustard operation are at higher risk for late death. Close follow-up, especially of these subgroups, is warranted.

Disclosures

None.

References


**CLINICAL PERSPECTIVE**

Since the first atrial switch procedures described by Senning in 1958 and by Mustard in 1963, atrial baffle procedures were the treatment of choice for many patients with transposition of the great arteries for >3 decades. Then this treatment was abandoned in favor of the arterial switch operation. Survival, functional status, and quality of life after an atrial switch operation are reported to be good within the first 2 decades of life. However, in some of the patients the function of the systemic right ventricle deteriorates or the patients suffer from arrhythmia. In the present study, records of 329 patients after the Senning operation and 88 after the Mustard operation at a single center were reviewed. Mean follow-up interval was 19.1 ± 6.5 years. Survival 25 years after the Mustard procedure was 75.9 ± 4.8% and after the Senning procedure was 90.9 ± 2.3%. The Mustard operation (hazard rate = 2.0; P = 0.045) and closure of a ventricular septal defect at the time of the atrial switch operation (hazard rate = 2.3; P = 0.025) emerged as independent risk factors for late mortality. Mustard patients died more often of arrhythmia than Senning patients (P < 0.001) and needed more baffle-related reoperations (P < 0.0001). Most of the patients are now grown, and 86% lead a normal life with full-time work. However, patients who had undergone ventricular septal defect closure and those who had undergone a Mustard operation are at higher risk for late death. Close follow-up, especially of these subgroups, is warranted.
Presence of a Ventricular Septal Defect and the Mustard Operation Are Risk Factors for Late Mortality After the Atrial Switch Operation: Thirty Years of Follow-Up in 417 Patients at a Single Center
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