Late outcome of Senning and Mustard procedures for correction of transposition of the great arteries


METHODS

This was a collaborative project between the general and paediatric cardiology departments coordinated by the Unit of Adult Congenital Heart Disease. It was a retrospective study of all patients followed up in our institution who were discharged after undergoing an atrial repair procedure (Senning or Mustard) for diagnosed TGA from 1973 to 1997. Patients were divided into two groups depending on their presurgical anatomy. Anatomy was considered to be complex if there was associated significant ventricular septal defect requiring closure, significant left ventricular outflow tract obstruction also requiring correction (20–40 mm Hg), or in case of palliative switch where the presence of important pulmonary vascular disease discouraged ventricular septal defect closure (two patients). Otherwise, patients were considered to have a simple anatomy. The simple group was divided into two subgroups (Mustard or Senning) according to the specific technique used in each case. The complex group was considered as a whole given the small number of patients of this cohort.

Of a total of 201 patients with diagnosed TGA in our institution during the studied period (171 in the simple group: Mustard 50 and Senning 121; and 30 in the complex group: Mustard 7 and Senning 23), 173 were discharged after undergoing an atrial switch procedure. The surgical mortality rate for the simple group was 11.1% (Mustard 20% and Senning 7.4%) and for the complex group, 30% (Mustard 57.1% and Senning 21.7%). A total of 147 surgical survivors were followed up at our institution (the remaining 26 were followed up at other institutions and were not enrolled in the study) with annual or biannual controls that included anamnesis, physical examination, ECG, radiography, Holter monitoring, and echocardiography. Ten patients were lost to follow up, so that the final study group comprised 137 patients: 118 in the simple group (89 Senning and 29...
Late outcome of Senning and Mustard procedures

RESULTS

Mortality

Among the 137 patients in the final cohort, seven died during follow up (5.1%, 95% CI 1.37% to 8.84%), four in the simple group and three in the complex group at an average (SD) of 10.7 (10.7) years (median 12.4 years) after surgical repair (range 1.2 months to 21.5 years). The most common cause was sudden death (42.8%). Postsurgical survival rate at 10, 15, and 20 years was 99%, 95%, and 91%, respectively, in the simple group (no significant differences between Mustard and Senning cohorts) and 89%, 82%, and 82%, respectively, in the complex group (fig 1).

None of the surgical variables studied had a significant influence on late mortality. The follow up variables related to mortality were severe tricuspid regurgitation (p = 0.015), advanced New York Heart Association (NYHA) functional class (p < 0.001), and tachyarrhythmias (p = 0.048). Two additional variables nearly reached significance in the univariate analysis (simple v complex, p = 0.056, and need for reoperation, p = 0.068).

Multivariate analysis showed that only tachyarrhythmias and advanced NYHA functional class were independent predictors of mortality (table 4).

Table 2 Follow up variables

<table>
<thead>
<tr>
<th>Type of intervention</th>
<th>Complex</th>
<th>Censored data</th>
<th>Senning</th>
<th>Censored data</th>
<th>Mustard</th>
<th>Censored data</th>
</tr>
</thead>
<tbody>
<tr>
<td>RV dilatation</td>
<td>98.9%</td>
<td>96.6%</td>
<td>100%</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>RV dysfunction</td>
<td>11%</td>
<td>24.1%</td>
<td>15.8%</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>NYHA class I–II</td>
<td>98.9%</td>
<td>96.6%</td>
<td>84.2%</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Tachyarrhythmia</td>
<td>10.1%</td>
<td>20.7%</td>
<td>15.8%</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Bradycardia</td>
<td>55.1%</td>
<td>48.3%</td>
<td>21.1%</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Parachute implant</td>
<td>9%</td>
<td>10.3%</td>
<td>0%</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Baffle obstruction</td>
<td>11.2%</td>
<td>31%</td>
<td>5.2%</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Severe TR</td>
<td>5.6%</td>
<td>6.9%</td>
<td>26.3%</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Reintervention</td>
<td>4.5%</td>
<td>10.3%</td>
<td>10.5%</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Medical treatment</td>
<td>10.1%</td>
<td>17.2%</td>
<td>42.1%</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pregnancy</td>
<td>1.1%</td>
<td>10.3%</td>
<td>0%</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sequelae</td>
<td>13.5%</td>
<td>10.3%</td>
<td>26.3%</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

NYHA, New York Heart Association; RV, right ventricular; TR, tricuspid regurgitation.

Figure 1 Cumulative survival (Kaplan-Meier).

Table 3 Sinus node dysfunction diagnostic criteria

1. Sinus bradycardia
   - Neonates and infants: <60 beats/min asleep and <80 beats/min awake
   - Children aged 2–6 years: <60 beats/min
   - Children aged 7–11 years: <45 beats/min
   - Adolescents and young adults: <40 beats/min
2. Severe sinus arrhythmia (variation in RR interval of >100%)
3. Sinus pause or arrest
4. Escape rhythms at slow rate
5. Sinoatrial exit block (second degree, type I and II)
6. Bradycardia/tachyarrhythmia

Statistical analysis

Baseline variables were compared by $\chi^2$ test or $t$ test when appropriate. Differences in time to death between groups were analysed by a two sided log rank test. The Kaplan-Meier method was used to estimate cumulative survivals and to construct life table plots. Variables that a priori were thought to have a potential impact on survival in these patients were included in a multivariate analysis of mortality data. Relative hazards and 95% CIs were calculated as hazard ratios obtained from Cox proportional hazard ratios.

### Table 1 Presurgical variables

<table>
<thead>
<tr>
<th>Surgical procedure</th>
<th>Senning</th>
<th>Mustard</th>
<th>Combined</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number</td>
<td>89 (65%)</td>
<td>29 (21%)</td>
<td>19 (14%)</td>
</tr>
<tr>
<td>Male sex</td>
<td>68%</td>
<td>41%</td>
<td>47%</td>
</tr>
<tr>
<td>Age (years)</td>
<td>0.8</td>
<td>1.3</td>
<td>2.7</td>
</tr>
<tr>
<td>95% CI</td>
<td>0.04 to 5.97</td>
<td>0.15 to 5.1</td>
<td>0.3 to 12.3</td>
</tr>
<tr>
<td>Weight (g)</td>
<td>6727 (1912)</td>
<td>8010 (3598)</td>
<td>9691 (6926)</td>
</tr>
</tbody>
</table>

Previous intervention
- Rashkind: 98% 93% 63%
- Hanlon-Blalock: 3% 10% 0%
- Waldhausen: 3% 0% 0%

Weight data are mean (SD).

*Combined procedures were atrial switch procedure plus other corrections in patients with complex transposition of the great arteries; subclavian flap repair of coarctation of the aorta.

CI, confidence interval.

The cardiac rhythm was classified into three groups: normal, sinus node dysfunction (according to criteria shown in table 3), and atrioventricular block.

Statistical analysis

Baseline variables were compared by $\chi^2$ test or $t$ test when appropriate. Differences in time to death between groups were analysed by a two sided log rank test. The Kaplan-Meier method was used to estimate cumulative survivals and to construct life table plots. Variables that a priori were thought to have a potential impact on survival in these patients were included in a multivariate analysis of mortality data. Relative hazards and 95% CIs were calculated as hazard ratios obtained from Cox proportional hazard ratios.
Repeat operations
After the initial procedure, seven additional operations were needed during follow up: two for baffle obstruction, one for baffle leak, one for superior vena cava obstruction, one interventricular septum defect closure (patient initially treated with a palliative switch), one tricuspid valve replacement for severe tricuspid regurgitation, and one mitral valve replacement for severe mitral regurgitation of iatrogenic surgical cause.

There were no surgical deaths during reinterventions. No significant differences were found between the simple and complex cohorts in terms of need for repeat operation.

Rhythm disturbances
Cardiac rhythm follow up was by ECG at every annual visit and by annual or biannual Holter recording. The most frequent disturbance registered was significant sinus rhythm dysfunction (according to diagnostic criteria shown in table 3) affecting 47.6% of the whole cohort at the end of follow up. The survival rate free of sinus node dysfunction at 5, 10, 15, and 20 years was of 82%, 82%, 63%, and 46%, respectively, in the Mustard cohort, 53%, 44%, 40%, and 40%, respectively, in the Senning cohort, and 94%, 70%, 70%, and 70%, respectively, in the complex group.

At the end of follow up, patients in the complex group presented significantly less sinus node dysfunction than patients in the simple group (p < 0.05). In the simple group, the Senning cohort developed sinus node dysfunction sooner than the Mustard cohort (accumulated incidence during first five years, 57% vs 7.6%). Hanlon-Blalock septectomy preceding atrial switch was the only factor significantly related to development of sinus node dysfunction (p < 0.01).

Pacemaker implantation was mandatory in eight patients (8.8%) requiring valve replacement in only one. The average (SD) time for development of severe tricuspid regurgitation was 12.0 (6.2) years after surgical repair (range 1.7 months to 20.0 years, median 12.8 years) with no cases detected before surgery. Factors significantly related to development of tricuspid regurgitation in univariate analysis were right ventricular dysfunction (p = 0.016) and a complex anatomy (p = 0.013).

Functional status and quality of life
During follow up, 96.2% maintained functional class I–II.

Among the female patients, 7.2% (four patients) gave birth to four healthy babies. In three cases, pregnancy and birth developed without problems but in the forth case, the patient died during the first 48 hours after labour due to cardiogenic shock secondary to refractory supraventricular tachyarrhythmia. This patient had no history of right ventricular dysfunction or tricuspid regurgitation but did have atrial flutter-fibrillation.

Sixteen per cent of patients were receiving medical treatment at the end of follow up (8.8% digitalis, 4.4% degree atroventricular block, all of them requiring pacemaker implantation. The average (SD) time of pacemaker implantation was 9.4 (5.2) years (range 1.3–17.7 years) after surgical repair.

The incidence of clinical tachyarrhythmias in the whole cohort was 13.1% (14 atrial flutter-fibrillation and four other supraventricular tachycardias) with an average (SD) time of appearance 8.7 (7.4) years (range 2.6 months to 21 years) after surgical repair.

Echocardiographic data
The great majority of patients had a dilated right ventricle (98%) but only 14.6% (20 patients) developed systolic dysfunction (average (SD) time 14.3 (5.4) years after surgical repair). That condition led to an indication for cardiac transplantation in three patients that was carried out without problems in two of them. The third patient died suddenly while on the waiting list.

The presence of baffle obstruction was also followed up by echocardiographic examination, with 2.9% severe obstructions (three pulmonary venous pathway stenoses requiring surgical repair and one systemic venous pathway stenosis) and 11.6% mild to moderate obstructions (11 pulmonary and five systemic venous pathway stenoses). Of note, up to one third of patients undergoing the Mustard technique had a baffle obstruction.

We observed severe tricuspid regurgitation in 12 patients (8.8%) requiring valve replacement in only one. The average (SD) time for development of severe tricuspid regurgitation was 12.0 (6.2) years after surgical repair (range 1.7 months to 20.0 years, median 12.8 years) with no cases detected before surgery. Factors significantly related to development of tricuspid regurgitation in univariate analysis were right ventricular dysfunction (p = 0.016) and a complex anatomy (p = 0.013).

Table 4
Multivariate analysis of mortality predictive factors

<table>
<thead>
<tr>
<th>Factor</th>
<th>Hazard ratio</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Severe TR</td>
<td>3.9</td>
<td>0.5 to 28</td>
</tr>
<tr>
<td>NYHA class I–II</td>
<td>6.16</td>
<td>1.15 to 32</td>
</tr>
<tr>
<td>Tachyarrhythmia</td>
<td>5.59</td>
<td>1.006 to 31</td>
</tr>
<tr>
<td>Surgical procedure</td>
<td>3.29</td>
<td>0.4 to 26</td>
</tr>
<tr>
<td>RV dysfunction</td>
<td>0.55</td>
<td>0.06 to 5.05</td>
</tr>
</tbody>
</table>

Table 5
Late mortality

<table>
<thead>
<tr>
<th>Patient number</th>
<th>1*</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>5</th>
<th>6</th>
<th>7*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age at surgery (years)</td>
<td>3.0</td>
<td>1.2</td>
<td>0.2</td>
<td>2.6</td>
<td>1.2</td>
<td>0.6</td>
<td>17.4</td>
</tr>
<tr>
<td>Age at death (years)</td>
<td>24.6</td>
<td>18.6</td>
<td>15.7</td>
<td>15.0</td>
<td>3.7</td>
<td>0.7</td>
<td>22.7</td>
</tr>
<tr>
<td>Surgical procedure</td>
<td>Mustard</td>
<td>Mustard</td>
<td>Senning</td>
<td>Combined</td>
<td>Combined</td>
<td>Senning</td>
<td>Combined</td>
</tr>
<tr>
<td>Cause of death</td>
<td>Cardiogenic shock</td>
<td>Sudden</td>
<td>Endocarditis</td>
<td>Sudden</td>
<td>Not cardiogenic</td>
<td>Sudden</td>
<td>Cardiogenic shock</td>
</tr>
<tr>
<td>Tachyarrhythmia</td>
<td>Flutter-AF</td>
<td>SVT</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>No</td>
</tr>
<tr>
<td>Bradyarrhythmia</td>
<td>SND</td>
<td>No</td>
<td>2° AV block</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>No</td>
</tr>
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<td>Pacemaker</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>No</td>
</tr>
<tr>
<td>Severe TR</td>
<td>No</td>
<td>Yes</td>
<td>No</td>
<td>Yes</td>
<td>Yes</td>
<td>No</td>
<td>No</td>
</tr>
<tr>
<td>Reintervention</td>
<td>No</td>
<td>Baffle leak</td>
<td>No</td>
<td>No TR</td>
<td>No</td>
<td>No</td>
<td>No</td>
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<tr>
<td>RV dysfunction</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>Yes</td>
<td>No</td>
<td>No</td>
<td>No</td>
</tr>
<tr>
<td>Treatment</td>
<td>No</td>
<td>Female</td>
<td>Female</td>
<td>ACEI, diuretics</td>
<td>No</td>
<td>No</td>
<td>Amiodarone</td>
</tr>
<tr>
<td>Sex</td>
<td>Female</td>
<td>Female</td>
<td>Female</td>
<td>Male</td>
<td>Male</td>
<td>Male</td>
<td>Male</td>
</tr>
</tbody>
</table>

*Two patients without a history of RV systolic dysfunction rapidly developed cardiogenic shock during an episode of refractory supraventricular tachyarrhythmia. ACEI, angiotensin converting enzyme inhibitor; AF, atrial fibrillation; AV, atrioventricular; SND, sinus node dysfunction; SVT, supraventricular tachycardia.
diuretics, 6.6% angiotensin converting enzyme inhibitors, and 4.4% antiarrhythmic drugs).

Neurological manifestations (seven cases of hemiparesis and eight cases of episodes) were found in 15 patients (10.9%). These manifestations were mostly assumed to be related to thromboembolic events during the polycythemic phase before surgical repair, since four of the cases of hemiparesis developed before surgery and two in the immediate postoperative period (information is lacking in the remaining case). All the epilepsy episodes appeared after surgery, generally with computed tomography suggesting prior silent stroke. Five other thromboembolic events were registered in other locations (renal veins, iliofemoral area, pulmonary thromboembolism) and all of them (neurological manifestations and other thromboembolic events) are incorporated in table 2 as sequelae.

**DISCUSSION**

Nowadays, the surgical technique of choice for correction of TGA is Jatene’s anatomical repair, leaving physiological repair only for cases in which the Jatene procedure is not feasible. Nevertheless, there is a large cohort of patients who underwent the Senning or Mustard procedure 20–40 years ago that need to be followed up to be aware of their natural history. Some studies have been published that summarise different centres’ experience and at the same time try to search for factors that may influence late outcome.

Clear differences appear in terms of late mortality when several series are consulted, which reflects more a different year for the beginning of the technique in each centre (and so, greater development of cardiac surgery conditions) than a real difference between institutional practices (that is, 5.1% in our centre with the first intervention in 1974: 22% reported by Sarkar et al in the Mustard cohort with the first intervention in 1965).

Sudden death is the most common cause of death in our series as it has been in previous ones, and the history of tachyarrhythmias was an independent predictive factor for mortality. Some authors have hypothesised a relation between supraventricular tachyarrhythmias and death based on a rapid ventricular response documented in Holter recordings (that is, atrial flutter 1:1). On the one hand, increasing attention is being paid to diastolic dysfunction because a rapid heart rate may exacerbate the limitation of ventricular filling that is intrinsic to the atrial repair circulation, compromising cardiac output. In fact, in our series two patients without a history of right ventricular systolic dysfunction rapidly developed cardiogenic shock during an episode of refractory supraventricular tachyarhythmia (table 5). One of them was a patient with complex TGA (severe pulmonary and subpulmonary stenosis) who was operated on at our institution at age 17 after other approaches (Blalock-Taussig fistula) due to a very adverse anatomy. On the other hand, some papers have reported cases of supraventricular tachyarrhythmias with rapid ventricular response degeneration into ventricular fibrillation and therefore sudden death.

The other independent predictive factor for mortality in our series is advanced NYHA functional class, which has yielded more information about our patients’ prognosis than right ventricular systolic function evaluation. This may mean that functional class identifies not only patients with a poor prognosis for systolic dysfunction but also those with impaired diastolic function. So even though it is a subjective parameter, it may have value from a clinical point of view. Another explanation for the lack of significance of right ventricular systolic dysfunction in our series is that the echocardiographic parameter used for its assessment was two dimensional quantification, which today is considered a poor method. Magnetic resonance is nowadays the ideal method for measuring right ventricular systolic function but, in the past few years, various studies assessed the value of several echocardiographic parameters based on tissue Doppler imaging or three dimensional echocardiography, which may also offer the possibility of evaluating diastolic function and are less expensive and time consuming than magnetic resonance imaging. The use of a poor diagnostic method for determining right ventricular function may also explain a real difference in the incidence of right ventricular systolic dysfunction reported by previous series (14.6% in ours, 28% by Kirjavainen et al, 0.3% by Sarkar et al, and 1% by Wells et al).

Previous studies have shown clear differences in terms of late mortality between simple and complex cohorts. In our series, although mortality differed greatly (3.3% for simple and 15.7% for complex groups), these differences were not significant. This is probably due to the small number of patients with complex disease (n = 9) and the small total number of deaths.

In our series the most frequent arrhythmia was sinus node dysfunction, affecting 47.6% of the whole group at the end of follow up. As seen in previous studies, in our series patients who underwent the Mustard procedure had a longer mean survival in sinus rhythm than the Senning cohort and the only predictive factor for the development of sinus node dysfunction was septostomy (Hanlon-Blalock procedure) previous to atrial correction. Nevertheless, sinus node dysfunction has never been found to be a predictive factor for mortality.

Lastly, in terms of quality of life (although our study did not specifically assess this complex parameter) we may say that the majority of patients enjoy a nearly normal life. Almost all of them (96%) are in NYHA functional class I–II (consistent with many previous studies and 4) and four of the women gave birth to healthy babies. However, we cannot ignore the 10.9% incidence of neurological sequelae (hemiparesis and epilepsy) and an undetermined number of learning disabilities and delay in psychomotor development that were not evaluated in the present study but are summarised in others.

It is noteworthy that this study has been possible thanks to a close relationship between members of General Cardiology and Paediatric Cardiology departments of our centre, under the necessary coordination of the Unit of Congenital Heart Disease in the Adult. Adult patients with congenital heart diseases operated on in infancy present with a new pathology necessitating the creation of specific working groups to increase knowledge lacking in this challenging field.

In conclusion, the overall long term outcomes of patients with atrial correction of TGA in the present era are encouraging in terms of late mortality and quality of life. Nevertheless, two challenging problems need to be solved. First is the development of right ventricular dysfunction (either systolic or diastolic) with the real need for improvement in diagnostic methods (magnetic resonance imaging is nowadays the ideal means of assessing right ventricular systolic function but it is an expensive and time consuming technique. Second is the development of supraventricular tachyarrhythmias, which have been found to be an independent predictive factor for mortality. The great development in the field of electrophysiology may lead to a solution in the near future.

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Magnetic resonance imaging of anomalous origin of the left coronary artery from the pulmonary artery (Bland-White-Garland syndrome)

A 37 year old woman without a history of any cardiac disease presented with an incidentally detected left precordial systolic murmur. There was an anterior wall hypokinesia on echocardiography but no signs of valvar or congenital heart disease. Exercise testing showed relevant anterior ST segment depression suggestive of exercise induced ischaemia. Cardiac magnetic resonance (MR) imaging demonstrated hypokinesia and an area of subendocardial late enhancement in the anteroseptal left ventricular myocardium indicating non-transmural myocardial infarction.

Contrast enhanced MR coronary angiography showed an anomalous origin of the left coronary artery from the pulmonary trunk (arrow), known as Bland-White-Garland syndrome. The right coronary is enlarged (arrowhead). Right coronary angiography confirmed the diagnosis with retrograde filling of the left coronary artery and connection to the pulmonary trunk.

REFERENCES
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