Comparison of Long-Term Outcomes of Atrial Repair of Simple Transposition With Implications for a Late Arterial Switch Strategy

David Sarkar, MRCP; Catherine Bull, FRCP; Robert Yates, MRCP; David Wright, PhD; Seamus Cullen, MRCP; Marc Gewillig, MD; Rebecca Clayton, ASCT; Adelaide Tunstill, RSCN; John Deanfield, FRCP

Background—We report the single-institution, long-term results of 358 patients with simple transposition of the great arteries surviving >30 days after a Mustard (n=226, 1965 to 1980) or Senning (n=132, 1978 to 1992) procedure.

Methods and Results—Outcome measures included late death, reintervention, ECG and ambulatory ECG rhythm, new arrhythmia, and functional status. Average follow-up was 13.4 (range 0.32 to 17.9) years for the Senning group and 11.7 (range 0.04 to 23.9) years for the Mustard group. The Senning group had a better survival rate at 5, 10, and 15 years (95% versus 86%, 94% versus 82%, and 94% versus 77%, respectively). In both groups, the majority of late deaths were sudden, without preceding ventricular dysfunction. Survival and survival free of reintervention were significantly better in the Senning group (relative risk [RR] 0.34, \( P = 0.06 \) versus RR 0.39, \( P = 0.027 \)). Loss of sinus rhythm was comparable and unrelated to death. After era correction, the incidence of atrial flutter was similar and strongly associated with late death in both groups. Clinical systemic ventricular failure was uncommon, and at last follow-up, 92% of the Senning group and 89% of the Mustard group were in New York Heart Association class I. In a model exploring the implications of elective arterial switch conversion, this would only be beneficial if the hazard late after switch was markedly reduced and/or the hazard after the Senning procedure increased with time.

Conclusions—Late outcomes after the Senning procedure are superior to those after the Mustard procedure. Both groups had late sudden deaths that were not associated with clinical systemic ventricular failure. Good functional status after the Senning procedure suggests that a strategy of elective switch conversion cannot be justified for patients with isolated transposition. (Circulation. 1999;100[suppl II]:II-176–II-181.)

Key Words: transposition of great vessels ▪ heart defects, congenital ▪ survival ▪ death, sudden ▪ atrial flutter

In 1958, Senning successfully introduced an atrial switch procedure for transposition of the great arteries (TGA) by using autologous atrial tissue to construct the atrial baffle.1 Despite excellent early outcomes, the procedure has been largely abandoned in favor of the arterial switch because of concerns about late systemic ventricular failure,2–4 impaired exercise performance,5,6 arrhythmia, and sudden death.7 It remains unclear whether these complications are inevitable or whether predisposing factors at surgery or during follow-up may identify patients most at risk. A surgical strategy involving conversion to an arterial switch has been developed8 and is advocated for patients with deteriorating late hemodynamics. The indications and timing of this approach will be influenced by the outcome after atrial repair and ability to stratify risk during long-term follow-up. Therefore, we studied our cohort of Senning patients to establish survival, rhythm, functional state, and the need for reintervention and compared their outcome with that previously reported for patients who underwent a Mustard operation at our institution between 1965 and 1980.9 The long-term outcome data have been used to develop a model that examines the survival implications of elective late arterial switch conversion.

Methods

A retrospective review of hospital case notes of all patients born in the United Kingdom who had a Senning operation at Great Ormond Street Hospital for Children, London, was performed. Patients with simple transposition were included as well as those with a small ventricular septal defect that did not require closure, a persistent arterial duct, or a left ventricular outflow tract gradient ≥20 mm Hg at initial cardiac catheterization. Of 141 Senning operations between August 1978 and September 1992, there were 9 early deaths ≤30 days after surgery, with the 132 late survivors constituting the study group.
Follow-up records were reviewed, including ECGs, 24-hour ambulatory ECG recordings (AECGs), videotaped echocardiograms, and chest roentgenograms. Patients not seen in the previous 18 months were asked to come in for reassessment. The duration of follow-up was defined as the period between the operation and their last clinic visit or completion of the study questionnaire. The advent of atrial flutter or nodal rhythm was diagnosed on the basis of 1 ECG, and onset was dated to that study.

Two hundred forty-three AECG recordings were performed, including 39 in the 56 patients who came in for reassessment, an ECG, and an echocardiogram. We investigated patients who had died during the study period for the circumstances of the event, and where possible, autopsy data were obtained.

The complete consecutive series of Mustard operations in our institution was reviewed in 1990 with the same methods and definition of “simple” transposition. Two hundred forty-nine cases were identified. The 226 >30-day survivors constituted the comparison group; follow-up on this group was not updated.

Operative Technique
The surgical technique for the Senning operation during the study period was standard. All operations were performed by 2 surgeons who had considerable previous experience with the Mustard procedure. Hypothermic cardiopulmonary bypass was used with aortic and bicaval cannulation and cold cardioplegia injection into the aortic root every 30 minutes. Care was taken to avoid damage to the sinus node, sinus node artery, and AV node during cannulation and surgery. Excessive resection in the superior part of the interatrial septum was avoided. The systemic and pulmonary venous pathways were constructed with atrial tissue. In most patients, the atrial septum was closed directly, although pericardium or Dacron was used in some cases. The description of the Mustard surgical technique has been published previously.9

Statistical Methods
Actuarial survival curves were prepared with the Kaplan-Meier method. The Mustard and Senning operations are strongly confounded with era (Figure 1); if the Mustard procedure looked inferior in comparison with the Senning procedure, it was difficult to know whether this was attributable to the choice of operation or other repercussions of the early years of cardiac surgery and bypass. Therefore, each patient was given a series number based on date of surgery. The separate effects of surgery type and series number could then be examined in a multivariate analysis by use of the Cox proportional hazards model. The effects of the advent of nodal rhythm on the advent of atrial flutter and the advent of atrial flutter on late death were examined by entering the advent of nodal rhythm and flutter, respectively, as time-dependent covariates.10 Patients who died without clinical or ECG evidence of previous atrial flutter were included in the analysis as flutter-free up to the date of death. A model was prepared that contrasted the survival implications of leaving the Senning repair in place with a policy of elective banding and switch conversion of all Senning procedure patients. First, an estimate of the hazard of late death was obtained from our own medium-term Senning procedure survival data (10 to 20 years); this hazard was assumed to remain constant. Survival data for the normal UK male population (1992) was also available; the corresponding hazard increases with age. The long-term outlook of a person who has had Senning repair is subject to both these hazards, and combining the 2 functions provided a curve that depicts the expected late survival pattern of Senning procedure patients left with an atrial repair under these assumptions. This pattern could be compared with survival estimates after switch conversion and prepared under a range of assumptions.

Results
The patient characteristics of the Mustard and Senning cohorts are shown in Table 1.

Survival
Of the original Senning cohort of 141 consecutive patients, 9 (6.4%) died ≤30 days after surgery. There have been 12 late deaths (9%) to date. For the 30-day survivors, the actuarial survival rate at 5, 10, and 15 years was 95%, 94%, and 94%, respectively. The Mustard group consisted of 249 cases with 23 early deaths (9.2%). There have been 50 deaths (22%) during follow-up; the actuarial survival rate (of 30-day survivors) at 5, 10, and 15 years was 86%, 82%, and 77% (Figure 2). Survival was significantly better for the Senning cohort (Mustard procedure RR 2.67, P=0.0024), and this difference remained after the surgical series number had been taken into account (RR 2.57, P=0.06).

As in the Mustard cohort, the distribution of deaths in the Senning group (Figure 3) occurred in a bimodal pattern, with
In the first 5 years, 1 at 10 years, and the remaining 4 at ≈15 years of follow-up.

Reintervention
After the initial procedure, only 5 Senning procedure patients (3.8%) required further surgery: 1 for baffle obstruction, 1 for a baffle leak, 2 for relief of left ventricular outflow tract obstruction (LVOTO), and 1 for pulmonary artery banding in a patient with severe systemic ventricular dysfunction with a view to switch conversion. Pacemaker insertion has also been infrequent, with 2 systems inserted for symptomatic tachycardia-bradycardia syndrome and slow nodal rhythm.

Among the Mustard group, reinterventions have been significantly higher (13%). There have been 3 tricuspid valve replacements and 27 procedures for venous pathway obstruction. Permanent pacing has been required in 8 cases: 3 for slow nodal rhythm, 2 for complete heart block, 2 for flutter with slow AV conduction, and 1 for tachycardia-bradycardia syndrome. The curves for survival free of reintervention (Figure 4) continue to diverge over the follow-up experience, with superior outcomes for the Senning group. The relative risk of death or reoperation in the Mustard group compared with the Senning group was 2.75 ($P=0.0003$) and even after correction for era was 2.58 ($P=0.027$).

Functional Status
At last follow-up, 110 (91%) of 121 Senning-procedure survivors had minimal or no functional impairment. All were involved in full-time work or study and participated in routine sports. As anticipated, many found strenuous physical activity difficult. Eight patients were in New York Heart Association (NYHA) class II, 5 of whom fatigued easily. Of the 2 NYHA class III patients, 1 was limited by right ventricular (RV) dysfunction and one by LVOTO and a severe neurological deficit sustained during a neonatal Senning procedure. Only 7 (5.8%) patients were taking medication; 4 were taking an ACE inhibitor (ACEI) alone, 1 ACEI with diuretics and amiodarone, 1 atenolol alone, and 1 atenolol, digoxin, and diuretics. No patients were taking antiplatelet or anticoagulant therapy. The comparable figures for the Mustard group have been published previously.9

Rhythm
The loss of stable sinus rhythm occurred progressively and to a similar extent after both Mustard and Senning operations. At 10 years, nodal rhythm had been documented in 29% of the Mustard group and 35% of the Senning group with no difference with respect to type of operation after correction for era (RR 0.78, $P=0.2$). Generally, nodal rhythm was intermittent, occurring particularly at night. For the group as a whole, the onset of nodal rhythm increased the risk of advent of atrial flutter (RR 2.95, $P=0.002$), with the effect mainly discernible in the Mustard cohort.

In the Mustard group, atrial flutter developed in 36 cases (16%) compared with 8 (6.1%) in the Senning group. At 5, 10, and 15 years, freedom from flutter was 89% (Mustard) versus 98% (Senning), 75% versus 91%, and 69% versus 88%, respectively, but the later Senning procedure data were distorted by 3 late cases of flutter occurring in the oldest patients (Figure 5). There is an element of ascertainment bias, with the late flutter dated to its documented occurrence, whereas absence of flutter was dated to the last routine ECG. Of the 8 Senning procedure cases with documented flutter, 2 were among the subsequent late deaths. The relationship between the advent of late flutter and late death previously documented in the Mustard group9 was even more evident in the Senning group. Documented atrial flutter resulted in a 10.4-fold increase in risk of late death ($P=0.004$) and a 21-fold increase in risk of late sudden death ($P=0.0005$).

ECG and Ambulatory ECG Rhythm
In the preceding 12 months, 110 patients had a resting ECG that showed 81% were in sinus rhythm, 16% nodal, 2%...
paced, and 1% low atrial (nonsinus). Fifty-nine percent of the 243 AECGs indicated predominant sinus rhythm and 37% nodal rhythm for $30\%$ of the study. The remaining 4% had paced rhythm, Mobitz type II and third-degree heart block, nonsustained ventricular tachycardia, and 1 recording of atrial flutter.

Echocardiographic Data
Echocardiograms were performed on 113 of the 120 current survivors within the preceding 18 months. One hundred two (90%) had normal or only mildly impaired RV function. Ten had moderate impairment but despite this were in NYHA class I. Only 1 case of severe RV dysfunction was identified. The chest roentgenogram showed a cardiothoracic (CTR) ratio of 53%, and the patient was clinically well, receiving medical therapy.

Eight cases of LVOTO $\geq 30$ mm Hg were found. Only 2 had recent chest roentgenograms, with CTRs of 50% and 59%, respectively. The latter patient was in NYHA class I. Eighteen patients had mild to moderate tricuspid regurgitation (TR), and all were in NYHA class I. Only 4 cases of severe TR were identified. Three had recent chest roentgenograms, only 1 of which showed an increased CTR, and all 3 were in NYHA class I.

Late Deaths
There were 12 late deaths in the Senning group (Table 2), distributed in a bimodal pattern with 7 in the first 5 years, 1 at 10 years, and a second peak of 4 deaths after 15 years’ follow-up. In the first peak, 3 deaths were sudden, presumed arrhythmic (R.G., C.W., and B.V.). One (T.H.) had documented nodal rhythm on AECG monitoring with a satisfactory echocardiogram, and the other (V.C.) failed medical follow-up during the previous 4 years but reportedly had been free of clinical symptoms. The other 2 deaths were the result of right middle cerebral artery occlusion (R.M.) and severe hemoptysis secondary to multiple pulmonary arteriovenous malformations (J.S.). In total, half the deaths occurred after an episode of sudden collapse in children who were previously healthy, 2 with a past history of documented flutter.

A comparison of the causes of late death in the Mustard and Senning groups is shown in Table 3.

Surgical Model
It is possible to construct a hazard model to illustrate the outcome of widespread implementation of an elective late switch strategy contrasted with conservative management (Figure 6). Such a model has many sources of variability and only serves as a framework for rational decision making. The hazard associated with a Senning operation is modeled as a constant (Senning I) with our data, with the addition of the risk associated with a normal age-matched population. Alternatively, the Senning risk may not be constant but may increase progressively; Senning II illustrates an increasing hazard beyond the age of 30 years (16 years of additional

### Table 2. Twelve Late Deaths in Senning Procedure Cohort

<table>
<thead>
<tr>
<th>No.</th>
<th>Patient</th>
<th>Age at Operation, d</th>
<th>Follow-Up Interval</th>
<th>Died</th>
<th>Flutter</th>
<th>Circumstances</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>R.M.</td>
<td>184</td>
<td>15 y 7 mo</td>
<td>0</td>
<td></td>
<td>Stroke, right middle cerebral artery occlusion. Confirmed on scan and autopsy.</td>
</tr>
<tr>
<td>2</td>
<td>T.H.</td>
<td>275</td>
<td>15 y 4 mo</td>
<td>0</td>
<td></td>
<td>Sudden collapse during physical activity. Previously well.</td>
</tr>
<tr>
<td>3</td>
<td>J.S.</td>
<td>376</td>
<td>15 y 4 mo</td>
<td>0</td>
<td></td>
<td>Severe hemoptysis from multiple pulmonary arteriovenous malformations.</td>
</tr>
<tr>
<td>4</td>
<td>V.C.</td>
<td>215</td>
<td>15 y 3 mo</td>
<td>0</td>
<td></td>
<td>Sudden collapse while arguing with a friend. No follow-up for previous 4 years.</td>
</tr>
<tr>
<td>5</td>
<td>A.W.</td>
<td>94</td>
<td>9 y 11 mo</td>
<td>0</td>
<td>flutter</td>
<td>Sudden collapse on school playground.</td>
</tr>
<tr>
<td>6</td>
<td>C.W.</td>
<td>119</td>
<td>3 y 11 mo</td>
<td>7/9/92</td>
<td></td>
<td>Sudden collapse while playing. History of baffle leak repair and permanent pacemaker.</td>
</tr>
<tr>
<td>7</td>
<td>J.H.</td>
<td>124</td>
<td>4.5 mo</td>
<td>4/27/92</td>
<td></td>
<td>Sudden death at home. Previously documented superior vena caval obstruction.</td>
</tr>
<tr>
<td>8</td>
<td>R.G.</td>
<td>229</td>
<td>4 y 2 mo</td>
<td>4/3/92</td>
<td></td>
<td>Sudden collapse while playing.</td>
</tr>
<tr>
<td>9</td>
<td>L.F.</td>
<td>123</td>
<td>1 y 2 mo</td>
<td>1/17/91</td>
<td></td>
<td>Death after history of failure to thrive.</td>
</tr>
<tr>
<td>10</td>
<td>B.V.</td>
<td>182</td>
<td>1 y 8.5 mo</td>
<td>3/6/96</td>
<td></td>
<td>Sudden collapse.</td>
</tr>
<tr>
<td>11</td>
<td>A.S.</td>
<td>4 mo</td>
<td>2/4/82</td>
<td>0</td>
<td></td>
<td>Circumstances unknown. Autopsy showed pulmonary hypertensive changes.</td>
</tr>
<tr>
<td>12</td>
<td>J.P.</td>
<td>202</td>
<td>1 y 3.5 mo</td>
<td>7/5/80</td>
<td></td>
<td>Death after febrile illness. Autopsy showed RV fibroelastosis.</td>
</tr>
</tbody>
</table>

### Table 3. Comparison of Causes of Late Death Among Mustard and Senning Procedure Patients

<table>
<thead>
<tr>
<th>Cause of Death</th>
<th>Mustard Procedure</th>
<th>Senning Procedure</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sudden death with good hemodynamics</td>
<td>27</td>
<td>6</td>
</tr>
<tr>
<td>Sudden death preceded by poor hemodynamics</td>
<td>10</td>
<td>2</td>
</tr>
<tr>
<td>Reintervention</td>
<td>4</td>
<td>0</td>
</tr>
<tr>
<td>Ventricular failure</td>
<td>2</td>
<td>0</td>
</tr>
<tr>
<td>Not directly cardiac</td>
<td>7</td>
<td>2</td>
</tr>
<tr>
<td>Pulmonary hypertension/infection</td>
<td>0</td>
<td>2</td>
</tr>
<tr>
<td>Total deaths</td>
<td>50 (22%)</td>
<td>12 (9.1%)</td>
</tr>
</tbody>
</table>
Figure 6. Model of late survival of current cohort: normal population (age-matched, derived from the UK Life Tables 1992). Senning I adds this “background” risk to a late constant hazard for the Senning operation (1.5% per year) estimated from our follow-up data. Senning II: same as Senning I but with a late hazard that increases with time (modeled by adopting the background risk as a “normal” 55-year-old). Switch: illustrates the consequence of switch conversion of all patients “now”; early mortality assumptions described in the text with a late hazard half of Senning I.

To model the switch conversion strategy, we used the following assumptions: initial mortality within 1 month after surgery was estimated from previous reports\(^11,12\) at 5% for age 0 to 4 years, 10% for 5 to 9 years, 15% for 10 to 14 years, and 20% for 15 to 19 years. The late hazard after successful switch conversion was assumed to be half that expected without surgery (Senning I). When Senning I is compared with Switch, the curves never cross but converge late in follow-up, adversely affecting survival. If the Senning hazard increases (Senning II), there would be a benefit for the cohort at the expense of some early surgical mortality.

Discussion

This study reveals a superior outcome for the Senning operation for simple TGA compared with the Mustard operation, with an actuarial survival rate of 94% at 10 and 15 years. However, there have been late deaths, mostly sudden, which were not anticipated by symptoms, with only atrial flutter identified as a risk factor. Symptomatic status was excellent, with most patients appearing to have good ventricular function.

Atrial repair with the Mustard and Senning operations revolutionized the management of babies with TGA. However, the arterial switch operation has become the treatment of choice because of concerns about late development of arrhythmia,\(^7,9\) baffle problems, and, particularly, progressive right (systemic) ventricular failure.\(^2–4\) In our study, the Senning operation is superior to the Mustard operation largely because of the lower need for reoperation for venous pathway obstruction. Progressive loss of sinus rhythm, which has been widely reported, was found at a similar rate after both procedures and did not have a major clinical impact. The majority of Senning procedure patients were healthy and did not require pacemaker insertion or medical therapy. Although the number of Senning procedure patients who had developed atrial flutter to date was small, it was a risk factor for both total late death and late sudden death. The rapid heart rate presumably exacerbates the limitation of ventricular filling that is intrinsic to the atrial repair circulation, compromising cardiac output. The incidence of flutter on AECG was extremely low, so that it is unlikely that systematic routine monitoring with AECG would be helpful in identifying patients at greater risk. Although the absolute incidence of atrial flutter appeared lower after the Senning operation, era correction suggests that the risk is comparable for both types of atrial repair. The excellent survival rate after a Senning procedure may therefore be due to superior baffle function compared with the Mustard procedure.

The key to long-term outcome after the Mustard and Senning procedures may be the fate of the right ventricle in the systemic circulation. It is still difficult to quantify RV function because of a lack of a suitable control group for comparison and the dependence on shape assumptions and loading conditions of most of the commonly used systolic indexes. Although RV dilatation was common, during a follow-up of \(\approx\)20 years, only a few patients developed evidence of symptomatic RV failure. Serial studies do not support an inevitable progressive deterioration with time.\(^5,13,14\) An early study by Graham et al\(^1\) indicated that in patients with postoperative RV dysfunction, preoperative abnormalities had already been identified. In a recent large study in which radionuclide indexes were used, systolic RV function did not deteriorate over an 8-year interval. Conversely, diastolic function was impaired in the majority.\(^13\) Because abnormal ventricular filling may be due in part to flow limitation by the atrial baffle, the prophylactic use of ACEIs may be counterproductive. These findings are important when one considers indications for late conversion to the arterial switch.

Restoration of the morphological left ventricle to the systemic circuit and reversal of the atrial repair has obvious attractions. When ventricular retraining by pulmonary artery banding with subsequent arterial switch was performed for patients with systemic ventricular failure,\(^11,12\) the results were considerably better in younger patients, with age a major risk factor for operative death. However, most younger patients are well, without clinical RV failure, and there is no evidence that ventricular function will necessarily deteriorate. Thus, early arterial switch conversion may only be indicated for the small number of patients with early symptomatic RV failure. For older patients in this category, the higher surgical risk with this approach must be considered relative to the risks of cardiac transplantation.

A late switch conversion could be considered if it improved systemic ventricular function and reduced the late arrhythmic hazard. Our model demonstrates that with current levels of operative risk, life expectancy would only improve if the late hazard after the switch was very low in relation to the continuing Senning procedure risk. However, reversal of the atrial repair and reseption involves considerable atrial disruption and may not reduce the risk of flutter, although this may be better tolerated with removal of the baffles. There are also uncertainties about long-term ventricular remodeling and coronary adaptation in adolescence. The decision also depends crucially on the magnitude and shape of the late Senning hazard curve, making continued collection of follow-up data essential.

Alternative lower-risk treatment options are available for isolated atrial flutter. Antitachycardia pacing has been effective in some cases but at the risk of accelerating atrial

Alternative lower-risk treatment options are available for isolated atrial flutter. Antitachycardia pacing has been effective in some cases but at the risk of accelerating atrial
tachycardia into atrial fibrillation. Electrophysiological techniques may be a means of predicting which persons are most at risk of future flutter. Identification of protected zones of slow conduction critical for the maintenance of tachycardia has allowed targeting of radiofrequency ablation in symptomatic patients. AV node ablation is a last resort for the treatment of intractable flutter. The impact of these strategies on the incidence of sudden death is unknown.

The limitations of this retrospective study must be recognized. Although we have introduced a statistical correction for the major confounding influence of era, this cannot preclude other influences. Routine follow-up was not standardized for investigations such as AECG, although the very low incidence of atrial flutter in the available studies suggests that routine testing is unlikely to be of value. The assessment of functional status was not exercise based. The reporting of symptoms is influenced by patient expectations and not necessarily representative of the maximum exercise capacity. As discussed, RV function is perhaps the most difficult factor to quantify, but what our data do show is that most patients enjoy a good quality of life with no obvious RV failure but predictable RV dilatation.

Conclusions

The majority of patients with simple TGA treated by a Senning operation remain functionally well during adolescence and early adult life. A comparison of survival and the need for reintervention shows superior outcomes with the Senning procedure over the Mustard procedure, even after adjustment for differences in surgical era. However, in both groups there has been an appreciable incidence of sudden death, with atrial flutter identified as a risk factor. Although in principle there may be a role for switch conversion for symptomatic patients, in well patients with atrial repair, ventricular retraining and switch surgery are not justified in view of the high operative risk and the uncertainty about the long-term postsurgical hazard.

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References


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