Mitral valve replacement with mechanical prostheses in children:
improved operative risk and survival

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Abstract

Objective: The purpose of this study was to assess the early and late outcome following mitral valve replacement (MVR) with mechanical prostheses in children. Patients and methods: Between 1981 and 2000, 44 consecutive children (mean age 6.8 ± 4.7 years, 2 months–16 years) underwent mechanical MVR in Southampton. Twenty-three children were less than 5-years-old and nine were infants. Disease aetiology was congenital in 37, rheumatic in four, infective in two and Marfan’s syndrome in one. Mitral regurgitation was present in 36 and mitral stenosis in eight. Concomitant procedures were performed in 13, including aortic valve replacement (AVR) in seven. Follow-up was complete (mean 6.4 ± 4.8 years, 1 month–18.1 years). Results: The overall operative mortality was 14% (six patients). Before and after 1990 operative mortality was 31 vs 3.6% (P<0.02). From 1990, operative mortality for infants was zero out of six, for children less than 5-years-old was one out of 16 (one death after emergency AVR and MVR) and for older children it was 0/12. Seven children experienced valve or anticoagulation treatment-related events and eight had a mitral valve re-operation. Ten-year freedom from thromboembolism, prosthetic valve infection, bleeding, paravalvular leak and a mitral valve re-operation was 92.8 ± 5.2, 97.3 ± 2.7, 97.7 ± 2.3, 97.2 ± 2.7 and 75 ± 9.7%, respectively. Overall 10-year survival was 78 ± 7% (four late deaths); for children under vs over 5 years it was 61 ± 11 vs 95.2 ± 4.6% (P = 0.02), for atrio-ventricular septal defect (AVSD) vs other pathology 55 ± 15 vs 89 ± 6.1% (P = 0.05) and for those operated before 1990 vs after 1990 it was 63 ± 8.1 vs 86 ± 8.2% (P = 0.04). Conclusions: Mechanical MVR, in the current era, carries a low operative risk across the spectrum of paediatric age. Late survival is better for older children and those having no-AVSD pathology but it has improved substantially during the 1990s irrespective of age and disease aetiology. © 2001 Elsevier Science B.V. All rights reserved.

Keywords: Mechanical mitral valve; Children

1. Introduction

Repair of the mitral valve in children is the preferred surgical option [1–3] but dysplastic valves and complicated pathology of the mitral apparatus may present technical difficulties and valve replacement may be necessary.

The selection of the most appropriate valve substitute in the mitral position has been debated in the past but following the disappointing results produced with bioprostheses [4,5], most surgeons would currently agree that, despite their drawbacks, mechanical valves are the most suitable option [6].

Until 1980, we used biological valves for their merits in avoiding the need for anticoagulation and reducing the risk of thromboembolism. From 1981, having, also, found that they undergo early calcification and degeneration, we have, with occasional exceptions, routinely implanted mechanical valves.

In this paper, we present an analysis of our 20-year experience with the use of mechanical prostheses to replace native irreparable mitral valves in children.

2. Patients and methods

Between October 1981 and September 2000, 44 consecutive children underwent mitral valve replacement (MVR) with mechanical prostheses in Southampton. There were 23 male and 21 female with a mean age (±standard deviation) of 6.8 ± 4.7 years (range 2 months–16 years). Twenty-
three children were less than 5 years of age (nine less than 1 year) and 21 were older than 5 years.

During the study period 29 additional children with isolated mitral valve lesions underwent mitral valve repair in our unit. Reparative mitral valve surgery was, also, performed in other children having atrioventricular septal defects and/or other complex congenital abnormalities.

2.1. Aetiology of the disease and indication for valve replacement

   The aetiology of the disease was congenital in 37 patients, rheumatic in four, infective in two and Marfan’s syndrome in one.

   The predominant haemodynamic abnormality necessitating a MVR was mitral regurgitation (MR) in 36 and mitral stenosis (MS) in eight patients.

2.2. Patients with mitral regurgitation

   In the patients with MR the disease aetiology was congenital in 31, rheumatic in three, infective in one and Marfan’s syndrome in one.

   Seventeen of the patients with congenital MR had an atrio-ventricular septal defect (AVSD) which was complete in 15 and partial in two. Of the remaining 14 patients, two had isolated MR and 12 had MR in combination with other problems. These were double outlet right ventricle and ventricular septal defect (VSD) in two, subaortic stenosis in two, tricuspid atresia and VSD in one, interrupted aortic arch with aorto-pulmonary window and subaortic stenosis in one, aortic coarctation and VSD in two, multiple VSDs in two, mitral stenosis in one and aortic coarctation in one patient.

2.3. Patients with mitral stenosis

   The disease aetiology in the patients with MS was congenital in six (commissural fusion in four and a parachute mitral valve in two), infective in one and rheumatic in one.

   Additional problems were present in five patients, aortic coarctation in three and subaortic stenosis in two.

2.4. Previous operations

   Thirty-four patients underwent 66 previous cardiovascular operations shown in Table 1. Thirteen of these patients had one, 10 patients had two, seven patients had three and three patients had four previous cardiovascular procedures.

   Of the 17 patients who had an AVSD, 16 underwent AVSD repair at a mean time of 1.9 ± 2.1 years (range 1 day–7.2 years) prior to MVR.

2.5. The operation and concomitant procedures

   The operations were performed through a median sternotomy using moderately hypothermic cardiopulmonary bypass, established with an ascending aortic and bicaval cannulae. The mitral valve was approached via a transatrial or a direct left atrial approach. Myocardial protection was provided by means of cold crystalloid or blood cardioplegia and topical myocardial cooling.

   A bi-leaflet prosthesis was implanted in 42 patients (Carbo-medics in 24, St. Jude Medical in 17 and an On-X in one) and a Bjork–Shiley single-disk valve, early in the series, in two. The mean valve size was 23.8 ± 3.3 mm (range 16–31 mm).

   In order to insert a bigger valve, an inverted aortic prosthesis was implanted in eight children by one of the senior authors (J.L.M.). The mean size of the inverted aortic valves was 20.9 ± 2.1 mm (range 16–25 mm). In two patients with severe mitral and aortic stenosis, the annuli were enlarged by incising down through the aortic ring and through the anterior leaflet of the mitral valve. Two mechanical valves, an aortic and a mitral, were then inserted side by side suturing part of the circumference of their sewing cuffs together in a ‘pair of spectacles’-like fashion. The size of the valves in the first patient was 19 and 23 mm and in the second patient it was 21 and 25 mm.

   Fifteen concomitant procedures were performed in 13 patients, including aortic valve replacement (AVR) in six patients.
and a composite graft-valve aortic root replacement for Marfan’s syndrome in one (Table 2).

2.6. Anticoagulation policy and follow up

Postoperatively all patients received oral Sodium Warfarin aiming to maintain an INR (International Normalised Ratio) within the range of 3.0–3.5.

Patients were seen regularly by the paediatric cardiologists. Echocardiography was performed before discharge from the hospital and during each outpatient visit.

Data on the patients preoperative clinical features, operations, postoperative course, late events and survival were obtained through a detailed review of hospital medical records. Additional information was sought from the referring physicians, family doctors and/or the patients families.

The mean follow up for the hospital survivors was 6.4 ± 4.8 years, ranging from 1 month to 18.1 years, with a total of 213 patient years. Follow up was complete.

2.7. Definitions and statistics

Operative mortality includes death within 30 days following the mitral valve replacement. Continuous data are presented as means (±standard deviation) and categorical variables as percentages. Means were compared with unpaired t-test and proportions with χ² or Fishers exact test as appropriate. The prediction of freedom from death and other untoward events (±standard error from the mean) was calculated with the Kaplan–Meier product limit method and the resulting curves compared with the log-rank test. In these calculations included were the operative deaths and other untoward events (i.e. thromboembolism, endocarditis, re-operation) occurring early postoperatively, before patient-discharge from the hospital. A P value of less than 0.05 was considered significant. Analysis was done with the statistical package SPSS PC (version 8.0) (Chicago, IL, 60611).

3. Results

3.1. Operative mortality

There were six operative deaths giving an overall operative mortality of 14% (11% for isolated MVR and 29% for MVR plus AVR, P = 0.2).

Operative mortality for children aged under 5 years was 22% (5 out of 23) and it was 4.8% (1 out of 21) for the older children (P = 0.2).

Operative mortality for the children having an AVSD was 19% (3 out of 16) and for the remaining patients this was 11% (3 out of 27) (P = 0.6).

Operative mortality was reduced significantly over the study period. Before 1990 it was 31% (5 out of 16 children with a mean age 7 ± 4.5 years) and thereafter it was 3.6% (1 out of 27 children with a mean age of 6.8 ± 4.7 years), (P = 0.02). This reduction was more pronounced among the youngest, aged less than 1 or 5 years, children (Table 3).

Three of the patients who died early underwent repair of an AVSD 2, 4 and 14 months earlier and developed severe MR necessitating urgent or emergency MVR. One died intra-operatively and two died on the first postoperative day, one from low cardiac output and the other following a sudden cardiac arrest refractory to treatment.

The other three operative fatalities occurred in children who had previously undergone surgery for complex congenital conditions. The first patient had repair of an interrupted aortic arch with aorto-pulmonary window, resection of subaortic stenosis and a homograft AVR. The second had resection of a subaortic stenosis, mitral valvotomy and a tissue MVR and the third had had a Fontan procedure for tricuspid atresia. All three presented, on this occasion, in poor condition and underwent emergency surgery, the first two a double valve replacement (AVR & MVR) and the third one a MVR. One patient could not be weaned from bypass and two died 8 and 12 days postoperatively from multiple organ failure.

3.2. Early postoperative complications

Eleven additional patients (26%) experienced severe early postoperative complications. These were low cardiac output syndrome due the narrowing of the outflow of the tricuspid valve by the newly inserted mitral prosthesis in one, myocardial ischaemia attributed to the pressure exerted by the mitral prosthetic valve on the circumflex artery in one, early Staphylococcal prosthetic valve endocarditis in one, mitral valve thrombosis in one, complete heart block requiring insertion of a permanent pacemaker in two, transient complete heart block in one, persistent hypotension in two, difficulty in weaning from the ventilator in one, recurrent laryngeal nerve palsy in one and pericardial effusion requiring re-sternotomy for drainage in one patient.

Table 3
Trends in the operative mortality following mitral valve replacement in children over the study period

<table>
<thead>
<tr>
<th>Time interval</th>
<th>All patients (%)</th>
<th>Up to 1 year old (%)</th>
<th>&lt; 5 years old (%)</th>
<th>&gt; 5 years old (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>All years</td>
<td>6/44 (14)</td>
<td>2/9 (22)</td>
<td>5/23 (22)</td>
<td>1/21* (4.8)</td>
</tr>
<tr>
<td>1981–1990</td>
<td>5/16 (31)</td>
<td>2/3 (67)</td>
<td>4/7 (57)</td>
<td>1/9* (11)</td>
</tr>
<tr>
<td>1991–2000</td>
<td>1/28 (3.6)</td>
<td>0/6 (0)</td>
<td>1/16* (6.2)</td>
<td>0/12 (0)</td>
</tr>
<tr>
<td>P value</td>
<td>0.018</td>
<td>0.083</td>
<td>0.017</td>
<td>0.4</td>
</tr>
</tbody>
</table>

*Denotes death following emergency mitral plus aortic valve replacements.
Echocardiography performed before discharge from the hospital has demonstrated satisfactory prosthetic mitral valve function in all cases.

### 3.3. Valve or anticoagulation treatment-related events

Seven patients experienced valve or anticoagulation treatment-related events. Two patients developed prosthetic valve endocarditis (PVE). The first had early PVE and the second had two episodes of late PVE and a paravalvular leak. Ten-year freedom from PVE was 97.3 ± 2.7% and the linearized rate was 0.9% per patient year.

Two patients sustained thromboembolic events. One had early prosthetic valve thrombosis and the other one, a transplant candidate with poorly contracting left ventricle, had a late thromboembolic event, despite her INR being 4.2, resulting in left hemiparesis from which she made a slow recovery. Ten-year freedom from thromboembolism was 92.8 ± 5.3% (0.9% per patient year).

Two patients bled after tooth extraction requiring blood transfusion. Ten-year freedom from bleeding was 97.7 ± 2.3% (0.9% per patient year).

Paravalvular leak occurred in two patients, in one of them, mentioned above, following repeat MVR for PVE in another unit. Ten-year freedom from paravalvular leak was 97.2 ± 2.7% (0.9% per patient year).

Kaplan–Meier 10-year freedom from any of these events (PVE, thromboembolism, bleeding and paravalvular leak) was 85 ± 6.5% (3.7% per patient year) (Fig. 1).

### 3.4. Re-operations

Eight patients underwent re-operations related to the mechanical mitral valve. Four of these patients had an early re-operation during the same hospital admission. One had a right atrial–right ventricular homograft inserted to relieve a low cardiac output state caused from the narrowing of the tricuspid valve outflow by the mitral prosthesis. Another patient had a previously inserted 23 mm valve replaced with a 21 mm valve to relieve myocardial ischaemia caused by pressure on the circumflex artery. The other two patients had a repeat MVR for PVE and for valve thrombosis, respectively.

The remaining four patients had late mitral valve-related re-operations. The first patient underwent two repeat MVRs for PVE in another unit and repair of a paravalvular leak in our unit and the second patient had repair of a paravalvular leak. The third had re-resection of a subaortic stenosis followed by two AVRs and two repeat MVRs to insert bigger size valves. The fourth patient had a repeat MVR to insert, also, a bigger size mitral valve. These two patients were the only ones to have a repeat MVR to replace an outgrown mitral prosthesis. Two patients had re-operations unrelated to the mitral prosthesis. Both had a normally functioning mitral prosthesis and received a heart transplant. One had rheumatic heart disease and the other had congenital mitral stenosis and MR with severe endocardial fibroelastosis.

Ten-year freedom from re-operation related to the mitral valve was 75 ± 9.8% (3.7% per patient year) and from re-
operation due to any cause it was 64 ± 11% (4.3% per patient year) (Fig. 2).

3.5. Late survival

There were four late deaths. Three patients, all of whom had initially repair of an AVSD and underwent a MVR aged 5, 5 and 25 months, died from cardiac and/or respiratory failure 3, 4 and 27 months postoperatively. Another patient who underwent double valve replacement for rheumatic heart disease died more than 10 years later from intractable cardiac failure.

Overall, Kaplan–Meier, 5 and 10-year survival was 81 ± 6% and 78 ± 7.1% and for the hospital survivors this was 90.3 ± 5.4% and 90.3 ± 5.4% (Fig. 3).

Ten-year survival for the children aged less than 5 years was 61 ± 11% and it was 95.2 ± 4.6% for the older children (P = 0.02) (Fig. 4).

Ten-year survival for those having an AVSD was 55 ± 15% and for the remaining patients it was 89 ± 6.1% (P = 0.05) (Fig. 5). Five and ten years survival for those operated before and after 1990 it 63 ± 12% vs 85 ± 8.2% (P = 0.04) (Fig. 6). Currently, 28 patients are in NYHA functional class I, five patients are in class II and one patient is in class III. At latest echocardiographical evaluation all patients had normally functioning mitral prostheses.

4. Discussion

We make every effort to repair native valves with a view to avoid or, at least, delay the need for replacement but in some children the valve may be grossly abnormal and valve replacement becomes the only surgical option. There is no ideal prosthesis for children and the use of valve is a compromise. Heterografts have provided poor results, particularly in the younger ages, and are now rarely used. Homografts have the problems of limited durability and availability but they do not require anticoagulation and they may be a reasonable option for children with absolute contraindication to Warfarin, and in countries where adequate monitoring facilities of the levels of anticoagulation are not readily available.

Owing to their good durability, availability and haemodynamic performance, mechanical valves are the most preferred mitral valve substitute in children. Conclusive evidence supporting the superiority of any particular type of mechanical prosthesis in children is lacking and our preference in using bileaflet mechanical valves (in 42 out of 44 children) reflects our practice in the adult population over the same period.

The special anatomical features, the severe associated defects and the frequently compromised haemodynamic condition of some children, particularly infants, can render MVR a challenging and hazardous procedure. The overall operative mortality of 14% (11% for isolated MVR and 29% for MVR plus AVR) compares favourably with previous
reports [3–8]. The 22% mortality for infants and children aged less than 5 years was relatively high but not dissimilar to early mortality rates of 17, 28, 35 and 36%, respectively, as previously reported for these age groups from major paediatric centres in Europe and USA [3,6–8]. The operative death rate in children older than 5 years was low, at 4.8%, with the
only death occurring in a patient with complex congenital problems undergoing an emergency AVR and MVR.

Our operative mortality has decreased from 31% (5 out of 16) in the 80s to 3.7% (1 out of 28) in the 90s. Gratifyingly, this was the result of a dramatic reduction in the mortality between infants and children aged less than 5 years. From

Fig. 5. Kaplan–Meier 10-year survival for the children having an atrio-ventricular septal defect (interrupted line) was 55 ± 15%, for the remaining children (continuous line) it was 89 ± 6.1% (P = 0.05).

Survival by time interval of the study

Fig. 6. Kaplan–Meier 5–10 year survival curve for the patients undergoing a mitral valve replacement after 1990 (continuous line) was 85 ± 8.2% and for those operated in the 80s (interrupted line) it was 63 ± 12% (P = 0.04).
of a valve, allowing the insertion of a larger prosthesis in the first years of life is becoming increasingly safer. This is likely to reflect the improvements made in all aspects of peri-operative care of the paediatric surgical patients over-time.

As discussed earlier, with the exception of two children, we have used low profile bileaflet valves. Their haemodynamic performance has been good and the valve-related complication rate low. The thromboembolic rate in this series (0.9% per patient year) compares with previously reported rates of 0.7–2% per patient year [6,8,11]. Milano et al. [12], however, described a thromboembolic rate of 4% per patient year for mechanical MVR and 0.7% for MVR with bioprosthetic valves, reminding us that the use of bioprostheses may reduce but does not eliminate the risk of thromboembolism.

In this unit experience, PVE after implantation of mechanical valves in children has been uncommon. None of the 56 patients having an AVR between 1974 and 1999 acquired prosthetic valve infection [13]. The two patients who developed endocarditis in the present series were treated with repeat mechanical valve replacement. One made an uneventful recovery and the other required further re-interventions. We have previously reported low operative mortality and satisfactory late survival, but a high re-operation rate following surgery for infected heart valves in children [14].

Small annular sizes in the aortic position can be adequately managed with several aortic root enlargement manoeuvres and an adult-size prosthesis can usually be implanted [13]. A small mitral annulus cannot be enlarged and other techniques need to be employed. Supra-annular valve placement is one of the options and excellent [3] and poor results [15] following its use in small numbers of patients have been achieved. We used this technique only in one of our patients who died early.

Our preference is to use an inverted aortic prosthesis as this facilitates the implantation of usually a one size bigger valve. Six of the eight children receiving these prostheses remain well without having a re-operation at a mean follow up of 4.7 ± 3.4 years (range 2 months–6 years). The other two patients required repeat MVR to replace their outgrown prostheses. The first had initially a 16 mm valve and 6 years later had a further MVR with a 21 mm valve. The second patient had originally a 19 mm valve and required two further MVRs, the first 6 years later with a 23 mm valve and the second in another 8 years with a 27 mm valve. The ability of the mitral annulus to grow, despite the implantation of a valve, allowing the insertion of a larger prosthesis at subsequent MVRs has been well-documented [16].
from 50–76% [6,8,11,12,21]. However, as these series cover a wide time-span, include patients of different ages and utilised a host of valve substitutes, comparisons should be undertaken cautiously.

5. Conclusions

In the current era, replacement of native mitral valves with mechanical prostheses carries a low operative risk across the spectrum of paediatric age. Patients aged over 5 years and those having no AVSD fare better, but the survival prospects have improved substantially over the last decade irrespective of age and disease aetiology. Further re-operations for a considerable proportion of these children over their lifetime are to be anticipated.

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References