Outcomes and associated risk factors for mitral valve replacement in children

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Abstract

Objective: We aim to report time-related outcomes following mitral valve replacement (MVR) in children and to identify factors affecting outcomes. Methods: Clinical records from 307 children who underwent MVR between 1985 and 2004 were reviewed. Competing-risks methodology determined time-related prevalence of three mutually exclusive end-states: death, mitral reoperation and survival without subsequent MVR, and their associated risk factors. Results: Mean age was 11.4 ± 5.6 years including 36 (12%) patients <2 years old. There were 154 (50%) males. Underlying pathology was rheumatic fever (n = 195, 64%), congenital (n = 83, 27%) and other (n = 29, 9%) with congenital pathology predominant in younger children while rheumatic fever predominant in older children. Hemodynamic manifestation was regurgitation (83%), stenosis (5%), or mixed disease (12%). One hundred and twenty-six patients (41%) had undergone a prior cardiac surgery including mitral surgery (n = 96, 31%). Initial mitral prosthesis was mechanical (n = 229, 75%), tissue (n = 71, 23%), or homograft (n = 7, 2%). Concomitant cardiac surgery was required in 141 patients (46%). Competing-risks analysis predicted that 20 years following MVR, approximately 17% of patients have died, 51% have undergone mitral reoperation and only 33% were alive and free from mitral reoperation. Risk factors for death without mitral reoperation included younger age <3 years [PE (parameter estimates): +1.66 ± 0.31, p < 0.001], longer cross-clamp time (PE: +0.11 ± 0.04/10 min, p = 0.005), postoperative complications (PE: +1.58 ± 0.31, p < 0.001), and higher prosthesis size/body surface area (BSA)-predicted mitral annulus ratio (PE: +0.48 ± 0.10, p < 0.001). Risk factors for mitral reoperation included implantation of homograft or tissue prosthesis (PE: +1.12 ± 0.23, p < 0.001) and smaller prosthesis size (PE: +0.06 ± 0.03/1 mm, p = 0.05). Fifteen-year freedom from pacemaker implantation, endocarditis, bleeding, and thromboembolism was 92%, 96%, 82%, and 92%, respectively. Conclusions: Mortality and mitral reoperation are common after MVR in children and outcomes can be predicted based on patient’s age, prosthesis size, and other associated factors. Some modifiable factors such as avoiding oversized prostheses may improve outcomes especially in the smallest children.

1. Introduction

Valve repair is the treatment of choice for mitral valve disease in children [1–3]. However, mitral valve replacement (MVR) may be required in a subset of children for whom the mitral valve cannot be repaired or following repair failure [4–11].

MVR in paediatric patients is associated with distinct clinical and technical problems. Many of those problems are related to the lack of proper-sized small prostheses, particularly in younger children. Placement of a relatively large prosthesis can cause compression to adjacent cardiac structures with subsequent morbidity and mortality [9,12,13]. In addition, adequate anticoagulation is difficult to attain in children. Non-compliance with medications and life style limitations may expose children to high valve-related complications [14]. The above, in addition to early degeneration of tissue prostheses in children, and failure of the fixed-size stented prostheses to grow to match the child’s development leading to inflow obstruction, can all lead to frequent requirement for mitral reoperation [5–13].

MVR is especially challenging in younger children with congenital mitral disease due to the small size of native valve annulus, atrium and ventricle that predisposes them to complications related to leaflet entrapment, development of left ventricular outflow tract (LVOT), pulmonary veins or tricuspid valve obstruction and conduction block [9,12,15–20]. The inferior outcomes for MVR in smaller children are well-documented in the literature [9,12,19,20].

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In the current report, we aim to examine factors associated with mutually exclusive time-related events of death and mitral reoperation in children who underwent MVR at our institution.

2. Patients and methods

2.1. Inclusion criteria

From 1985 to 2004, 307 consecutive children younger than 18 years of age underwent MVR at the King Faisal Specialist Hospital and Research Center in Riyadh, Saudi Arabia. Patients were identified using the hospital surgical database. Clinical, operative, and outcome data were abstracted from their medical records. Approval of this study was obtained from the Research Ethics Board at our institution and requirement for individual consent was waived for this observational study.

2.2. Operative details

All procedures were performed through a midline sternotomy. Cardiopulmonary bypass was established via standard aortic and bicaval venous cannulation. The left ventricle was decompressed by venting through the right superior pulmonary vein. Moderate hypothermia (28—32°C) was utilised. Myocardial protection was provided with cold blood cardioplegia. In very small infants, deep hypothermic circulatory arrest was occasionally briefly used to improve exposure (n = 3).

The mitral valve was approached directly via the left atrium through the interatrial groove. In certain cases, such as in patients with small left atrium, a trans-septal approach was used. Once decision was made to replace the mitral valve, the aim was to preserve the posterior mitral leaflet with supporting chordal apparatus. However, in the majority of patients, this was not possible due to severe deformity of the subvalvar structure or due to small space that did not allow insertion of adequate size prosthesis. The prosthesis was placed within the mitral annulus in all patients. Occasionally, the prosthesis was tilted at the posterior annulus level with sutures placed in the left atrium rather than the annulus to permit admittance of the large prosthesis (n = 2). None of the patients had complete supra-annular placement of the mitral prosthesis.

Following completion of the valve replacement, patients had intraoperative trans-esophageal echocardiogram to assess the prosthesis function. Patients received either a mechanical prosthesis (n = 229, 75%), tissue prosthesis (n = 71, 23%), or homograft (n = 7, 2%). Details of the implanted valves are listed in Table 1. Concomitant cardiac surgical procedures were carried out in 141 patients (46%). Those included aortic valve repair (n = 9), aortic valve replacement (n = 78), tricuspid valve repair (n = 58), tricuspid valve replacement (n = 3), closure of ventricular septal defect (VSD) (n = 10), common atrium repair (n = 2), pulmonary artery debanding (n = 2), relief of left ventricular outflow tract obstruction (LVOTO) (n = 2), and various other cardiac surgeries (n = 9).

Mean duration of cardiopulmonary bypass and aortic cross-clamp was 123 ± 73 min and 82 ± 37 min respectively.

| Demographics and clinical |
|---------------------------|
| Gender (male)             | 154 (50%) |
| Age at surgery (years)    | 11.4 ± 5.6 |
| Age groups                |            |
| <2 years                  | 36 (12%)  |
| 2—5 years                 | 25 (8%)   |
| 5—10 years                | 31 (10%)  |
| 10—14 years               | 76 (25%)  |
| 14—18 years               | 139 (45%) |
| Weight at surgery (kg)    | 31.9 ± 17.5 |
| Underlying pathology      |            |
| Rheumatic                 | 195 (64%) |
| Congenital                | 83 (27%)  |
| Myxomatous/degenerative   | 17 (6%)   |
| Endocarditis              | 10 (3%)   |
| Other                     | 2 (<1%)   |
| Previous surgery          | 126 (41%) |
| Mitral valve repair       | 93        |
| Mitral valve replacement  | 3         |
| Tricuspid valve repair    | 12        |
| Aortic valve repair       | 17        |
| Aortic valve replacement (prosthesis) | 7 |
| Aortic valve replacement (Ross) | 7 |
| AVSD repair               | 25        |
| Coarctation repair        | 7         |
| VSD closure               | 8         |
| ASD closure               | 5         |
| Pulmonary artery band     | 4         |
| Anatomic L-TGA repair     | 3         |
| Conduit                   | 3         |
| Resection of subaortic membrane | 3 |
| Pulmonary artery debanding| 1         |
| Hemodynamic manifestation |            |
| Regurgitation             | 253 (83%) |
| Stenosis                  | 14 (5%)   |
| Mixed                     | 36 (12%)  |
| Surgical                  |            |
| Type of prosthesis        |            |
| Mechanical                | 229 (75%) |
| Carbomedics               | 198 (65%) |
| Medtronic Hall            | 15 (5%)   |
| St. Jude                  | 9 (3%)    |
| Other                     | 7 (2%)    |
| Tissue                    | 71 (23%)  |
| Hancock                   | 56 (19%)  |
| Quattro stentless          | 6 (2%)    |
| Other                     | 9 (3%)    |
| Homograft                 | 7 (2%)    |

Valve size (mm) 27 ± 4 (16—33)
Prosthesis size/weight 1.26 ± 0.99 (0.84—1.65)
Prosthesis size/BSA-predicted 1.13 ± 0.13 (0.84—1.65)
MV size 0.99 0.86 (0.34—6.17)
CPB time (min) 123 ± 73 (108—373)
Cross-clamp time (min) 82 ± 37 (77—230)
Additional surgery 141 (46%)
Aortic valve repair 9
Aortic valve replacement 78
Tricuspid valve repair 58
Tricuspid valve replacement 3
VSD closure 10
Common atrium repair 2
Pulmonary artery debanding 2
Relief of LVOT obstruction 2
Other 9
2.3. Anticoagulation protocol and follow-up

Postoperatively, following adequate haemostasis, patients with mechanical prostheses were started on intravenous heparin maintaining the partial thromboplastin time ratio between 1.5 and 2 times baseline. In addition, they received oral sodium warfarin aiming to maintain an International Normalized Ratio (INR) within the range of 2.5–3.5. Patients were seen regularly by the paediatric cardiologists on an average one visit yearly and anticoagulation was followed by specialised local anticoagulation clinics with established anticoagulation protocols. Aspirin was not routinely prescribed but was given occasionally to patients in whom INR control was difficult.

Late outcomes were determined from recent office visits at King Faisal Specialist Hospital and Research Center or from direct correspondence with patients’ families. Mean follow-up duration was 8.5 ± 6.8 years and ranged between 1 day and 25.2 years.

2.4. Statistical analysis

Data are presented as means with standard deviation, medians with minimum and maximum, and frequencies as appropriate. Time-dependent outcomes (death and mitral reoperation) after MVR were parametrically modeled. Parametric probability estimates for time-dependent outcomes uses models based on multiple, overlapping, phases of risk (available for use with the SAS system at http://www.clevelandclinic.org/heartcenter/hazard). The hazard procedure uses maximum likelihood estimates to resolve risk distribution of time to event in up to three phases of risk (early, constant and late). Competing risk analysis was performed to model the probability over time of each of two mutually exclusive endpoints: mitral reoperation and death without mitral reoperation; the remainder of patients being alive and free from mitral reoperation. In addition, parametric survival models were created for the following endpoints: all-cause cardiac reoperation and freedom from valve-related complications such as endocarditis, thromboembolism, pacemaker implantation and anticoagulation-related haemorrhage. Variables potentially influencing the likelihood of outcomes in the competing risk models were sought in a stepwise multivariate regression model (p < 0.05 to enter) to obtain the final model for each outcome. Effects of covariates on the probability of outcomes in competing risk models are given as parameter estimates (change in hazard associated with change of 1 unit in the independent variable, positive estimates associated with increased risk and negative estimates with decreased risk). Clinical relevance of identified covariates on likelihood of selected outcomes was established by solving the regression equations for multiple ‘typical’ test patients. All statistical analyses were performed using SAS statistical software v9.1 (The SAS Institute, Cary, NC, USA).

3. Results

3.1. Patient characteristics

During the study period, 307 patients underwent MVR. There were 154 males (50%) and 153 females (50%). Mean age at MVR was 11.4 ± 5.6 years and mean weight was 31.9 ± 17.5 kg. Age distribution at time of initial MVR is shown in Table 1. Underlying cardiac pathology included rheumatic fever (n = 195, 64%), congenital valve disease (n = 83, 27%), myxomatous/degenerative disease (n = 17, 6%), endocarditis (n = 10, 3%), and other (n = 2, <1%). Among patients <5 years of age, 93% had underlying congenital pathology, whereas 84% of patients >10 years of age had underlying rheumatic fever.

Before MVR, procedures to address mitral valve lesions and/or other cardiac lesions were performed in 126 patients (41%). Other than correction of atrio-ventricular septal defects (AVSD), 93 patients had previous operative attempts at mitral valve repair, and three patients had a prior MVR. The hemodynamic MV dysfunction was known in 303 patients and was primarily regurgitation in 253 patients (83%), stenosis in 14 patients (5%), and mixed in 36 patients (12%). Complete patients’ demographic and operative characteristics at time of initial MVR are listed in Table 1.

3.2. Competing-risks analysis for death or subsequent mitral reoperation after MVR

Following the 307 initial MVR, 76 patients (26%) had subsequent mitral reoperation and 43 patients (14%) died without a further mitral reoperation.

The hazard function for time-related transition to mitral reoperation was characterised by the presence of a constant late hazard phase that increases as years since surgery progresses (Fig. 1A and B). The hazard function for time-related transition to death without mitral reoperation was characterised by a pronounced early hazard phase with high risk of mortality, mainly in the immediate postoperative period, and a low but constant death hazard that continues years following initial MVR (Fig. 2A and B). The competing risks for the two events showed that at 1 year following MVR, approximately 9% of patients have died, 2% have undergone mitral reoperation, and 89% were alive and free from mitral reoperation. After 1 year, the risk of death remains low, but the risk of reoperation increases. At 10 years following MVR, approximately 15% of patients have died, 24% have undergone mitral reoperation, while at 20 years following MVR, approximately 17% of patients have died, 51% have undergone mitral reoperation, and only 33% were alive and free from mitral reoperation (Fig. 3).

3.3. Factors associated with mortality

At last follow-up, there were a total of 48 deaths including 20 operative (6.5%) and 28 late deaths: 21 deaths prior to any cardiac reoperation, five following mitral reoperation, and two following nonmitral cardiac reoperation. Overall survival was 85% at 10 years and 74% at 20 years.

Factors associated with higher risk of death after MVR were sought and results are shown in Table 2. Significant risk factors for mortality were: younger age <3 years at time of MVR [parameter estimate PE: +1.66 (0.31), p < 0.001], longer cross-clamp time (PE: +0.11 (0.04)/10 min, p = 0.005), postoperative complications (PE: +1.58 (0.31), p < 0.001), and higher prosthesis size/BSA-predicted mitral annulus size (PS/MS) ratio (PE: +0.48 (0.10), p < 0.001).
Overall, 19% of patients had postoperative complications that included, although were not limited to, complete heart block (n = 19, 6%), bleeding (n = 18, 6%), and low cardiac output (n = 13, 4%). Those major complications were associated with diminished early and late survival.

Of importance, patients with underlying congenital mitral valve disease had worse survival compared to those with other pathologies, especially rheumatic fever (PE: +1.27 (0.31), p < 0.001) on univariate analysis only. However, congenital disease may be surrogate for younger age at time of MVR rather than effect of underlying pathology per se as congenital disease was not a risk factor on multivariable analysis. On univariate analysis, preoperative hemodynamic manifestation of mitral valve disease, previous or concomitant cardiac surgeries were not associated with diminished survival.

The higher hazard of mortality in patients receiving oversized valves as evidenced by increased PS/MS ratio is depicted in Fig. 1A and B and the higher hazard in younger patients is shown in Fig. 1C. In addition, Fig. 4D portrays the risk-adjusted survival adjusted for a hypothetical high-risk patient with a combination of unfavourable characteristics versus a hypothetical low-risk patient who does not have those characteristics.

### 3.4. Factors associated with subsequent mitral reoperation

During follow-up, 76 patients required mitral reoperations. Indications for reoperations included degenerated
bioprosthesis (n = 37), obstruction by pannus formation (n = 19, including 5 with thrombosis), paravalvular leak (n = 6), valve thrombosis without evidence of pannus (n = 4), endocarditis (n = 3), high gradients due to a relatively too small prosthesis (n = 2), and other miscellaneous reasons (n = 5). Overall freedom from mitral reoperation was 49% at 20 years.

At time of the first reoperation, 64 patients underwent a redo MVR while the remaining 12 patients had resection of obstructing pannus (n = 7), repair of paravalvular leak (n = 3), thrombectomy (n = 1), and early excision of papillary muscle that was causing subvalvar obstruction and interfering with the opening of the mechanical prosthesis disc (n = 1). Among the 76 patients who underwent mitral reoperations, 13 patients needed a second mitral reoperation, all were valve replacement.

At time of first redo MVR (mean 7.7 years following initial MVR), patients received a prosthesis that is on average 1.4 mm larger than that originally implanted. However, when initial MVR was performed in small children <20 kg in weight, at time of reoperation (mean 6 years following initial MVR), the new prosthesis was on average 3.9 mm larger than that originally implanted.

Factors associated with higher risk of mitral reoperation after MVR were sought and results are shown in Table 2. Significant factors for late phase reoperation were placement of a tissue/homograft prosthesis (PE: +1.12 (0.23), p < 0.001), and smaller initial prosthesis size (PE: +0.06 (0.03)/1 mm, p = 0.05). The risk of mitral reoperation stratified by the type of implanted prosthesis is depicted in Fig. 5.

Younger age at time of surgery was associated with more mitral reoperations on univariate analysis, more so for tissue prostheses (PE: +0.25 (0.09)/1 year, p = 0.005) than for mechanical prostheses (PE: +0.06 (0.03)/1 year, p = 0.05) (Fig. 6A and B). While higher PS/MS ratio was associated with a trend of increased mitral reoperation risk in patients who

Fig. 3. Competing-risks depiction of outcomes following MVR in children 1–18 years of age. The competing risks for the two events (mitral reoperation and death without mitral reoperation) showed that at 10 years following MVR, approximately 15% of patients have died, 24% have undergone mitral reoperation, while at 20 years following MVR, approximately 17% of patients have died, 51% have undergone mitral reoperation and only 33% were alive and free from mitral reoperation.

Fig. 4. Parametric models for survival following MVR in children stratified by: (A) PS/MS ratio. Valve oversizing with increased ratio was associated with lower survival. (B) PS/MS ratio in different age groups. The effect of valve oversizing is more evident in younger patients. (C) Age groups. Younger age was associated with lower survival. (D) Risk-adjusted survival after MVR, stratified according to either unfavourable risk-profile or favourable risk-profile.
received mechanical prostheses (PE: +1.06 (1.33), \( p = 0.43 \)),
the relationship was the opposite in tissue prostheses recipients with lower reoperation risk in those with higher PS/BS ratio (PE: −0.53 (0.28), \( p = 0.06 \)).

At last follow-up, 83 patients had cardiac reoperation (including mitral) and freedom from all-cause cardiac reoperation was 97% at 1 year and 48% at 15 years.

3.5. Valve-related complications

Seventeen patients required permanent pacemaker implantation for complete heart block. The majority of those were done in the early postoperative period. Freedom from pacemaker implantation was 96% at 1 year and 92% at 15 years. Univariate risk factors for complete heart block included younger age, lower weight, congenital diagnosis, prior cardiac surgery and larger PS/MS ratio.

Eight patients received treatment for endocarditis. Freedom from endocarditis was 98% at 1 year and 96% at 15 years. Three patients underwent redo MVR and all survived, five patients were treated conservatively and two of them expired due to root abscess, severe prosthesis dehiscence and cardiogenic shock (\( n = 1 \)) and sepsis (\( n = 1 \)). Univariate risk factors for endocarditis included prior multi-valve surgery.

Thirty-three patients had documented anticoagulation-related bleeding. Freedom from bleeding was 97% at 1 year and 82% at 15 years. Those included epistaxis (\( n = 18 \)), intracranial (\( n = 6 \)), gastrointestinal (\( n = 5 \)), genitourinary (\( n = 4 \)), and soft tissue (\( n = 2 \)) haemorrhage. Three of those episodes were fatal (all intracranial). Univariate risk factors for bleeding included placement of a mechanical prosthesis.

Thirteen patients had documented thromboembolic complications. Freedom from thromboembolic complications was 100% at 1 year and 92% at 15 years. Two patients had embolic infarcts: brain (\( n = 1 \)), multiple organs (brain, spleen, renal, \( n = 1 \)) while 12 had thrombosis (one patient had both). Mitral reoperation was required in 7/12 patients and all survived; nonsurgical treatment was attempted in the remaining 5/12 patients and four survived. Univariate risk factors for thromboembolism included younger age, lower weight, mechanical valves, prior cardiac surgery, and larger PS/MS ratio. Of importance, many of the late deaths were sudden in nature at home indicating that thromboembolic episodes were under-reported in our series.

4. Discussion

Our study reports a single institution’s experience with MVR in 307 children <18 years of age. Competing-risks analysis was chosen because these patients were simultaneously at risk for two most important mutually exclusive events: death and mitral reoperation.

4.1. Survival

Our study showed that there was a pronounced early mortality hazard in the first 6 months following surgery. We demonstrated that MVR can be performed in children with acceptable in-hospital mortality of 6.5%; however, survival was greatly influenced by patient’s age at time of MVR. For example, in-hospital mortality for children <2 years of age was 26% compared to 4% in those >2 years of age. This is analogous to other series in the literature where operative mortality in this age group was reported as high as 52% [19,20].
More importantly, there was a continuous attrition beyond the perioperative period that was also more prominent in younger children. At last follow-up, only 59% of patients who underwent MVR <3 years of age were alive compared to 89% of those >3 years of age. The age factor is further complicated in younger patients by the presence of associated variables such as frequent valve oversizing, surgical complexity and concomitant surgery necessitating longer bypass and ischemic durations, and higher post-operative complications rate; that were all significant contributors to increased early and late mortality risk.

Similar to other prior reports, valve oversizing was identified as an important risk factor for early death. Caldarone et al. noted that higher prosthetic valve size to patient body weight ratio impacted on operative mortality, and suggested that other surgical options, such as Damus—Kaye—Stansel connection or heart transplantation, be considered if the mitral valve could not be repaired in very young patients [12]. In a prior study from our institution, prosthesis size/patient weight ratio ranged between 1 and 6.3, higher in younger patients undergoing MVR, and was associated with a significant increase in mortality risk [9]. Many of those early deaths were consequent to significant geometric disparity between the prosthesis and the relatively small mitral annulus, left atrium and left ventricle with subsequent complications such as acute leaflet entrapment with thrombosis, LVOT, tricuspid valve and pulmonary vein obstruction, circumflex artery injury, cardiac rupture and conduction block [9]. In the current study, the ratio of prosthesis size/BSA-predicted mitral valve annulus size was utilised and again valve oversizing was more common in younger patients and was associated with lower survival. The effect was important for all age groups although it was more obvious in younger patients. Selection of a too-large prosthesis in small children with low body weight may be inevitable because of the lack of availability of smaller prosthesis. Nonetheless, surgeons may attempt to deliberately oversize the prosthesis in an effort to increase its longevity. Our data suggest that such a strategy is not advisable due to the higher mortality risk and the lack of any benefit in reducing further mitral reoperation need.

4.2. Mitral reoperation

Younger age and smaller prosthesis size, a proxy for younger age, were associated with increased mitral reoperation risk. Many factors may contribute to the more frequent reoperation in small children. Placement of a relatively large prosthesis can predispose to leaflet entrapment, generation of inflammatory/immunologic response that may all increase the risk of fibrosis and pannus formation with possible complications such as valve obstruction or thrombosis requiring early reoperation. In addition, as patients grow, those prostheses become too small resulting in inflow obstruction and clinical deterioration necessitating mitral reoperation.

Of importance, a larger prosthesis could generally be placed at time of mitral reoperation. In children who where <20 kg in weight at time of MVR, a prosthesis that is on average 4 mm larger could be placed at a mean interval of 6 years, indicating that the annulus of the mitral valve continues to grow despite the fixed size of the stented prosthesis sewing ring. That, in addition to the fact that hospital mortality at mitral reoperation was very low, and that oversizing was associated with a trend to increased reoperation need in younger children receiving mechanical prostheses; all support our recommendation not to oversize the prosthesis at initial MVR.

The use of tissue prostheses in children is debatable. Tissue prostheses in the paediatric population are linked to accelerated structural degeneration and therefore are used infrequently [21]. In addition, tissue prostheses are unavailable in small sizes and therefore cannot be used in smaller children. Kojori et al. reported 104 children who underwent at least one MVR and they found that the use of Ionescu—Shiley and other tissue prostheses was a significant risk factor for reoperation [7]. We have similarly found that tissue prostheses are associated with almost inevitable reoperation however it is important to note also that mechanical prostheses were not a ‘permanent’ solution in those children with only 50% freedom from reoperation at 20 years following MVR. In a previous study from our institution examining the role of homografts and tissue prostheses in paediatric patients; we identified 110 children who received 123 prostheses in the mitral or aortic positions. Overall 15-year freedom from reoperation was <20%; however, that was associated with 15-year survival of 84%, freedom from thromboembolic and bleeding complications of 100%, in addition to excellent functional classification with 95% of patients in New York Heart Association (NYHA) class I and II. Moreover, pregnancy was safely completed in many females in that series and mitral reoperation was associated with low operative and complications risk [22]. Therefore, it is important to individualise valve choice to patient’s anatomy, gender, size and social factors. Tissue prostheses are valid options in older children and should be considered in select patients such as in females in child-bearing age and those non-compliant with anticoagulation. Despite the necessity for reoperation, tissue prostheses may be superior to mechanical prostheses in this selected population especially that complications and the risk of sudden death is high in the setting of inadequate anticoagulation.

4.3. Valve-related complications

Late valve-related morbidity in our series was common. Freedom from anticoagulation-related bleeding was 82% at 15 years and was comparable to that reported in adults [23,24]. Similar to other series of MVR in children describing low embolic risk in children as compared to adults, we noted very few embolic events in our study population despite that many of them had double valve replacement [5—10,25]. That may reflect that other factors contribute to increased risk of embolism in adults such as atrial fibrillation, atrial dilatation, ventricular dysfunction, etc. Those factors may be less prevalent in younger patients.

On the other hand, the risk of valve thrombosis seems to be higher in children as compared to that in adults [23,24]. In addition to difficulty achieving adequate anticoagulation in children, local factors such as the relatively large prosthesis size compared to the left heart structures may predispose the patient to pannus formation, leaflet entrapment and
increase the risk of subsequent valve thrombosis. When detected early, reoperation for valve thrombosis was safe and associated with minimal morbidity.

Most importantly, it should be noted that there has been a steady attrition rate with increased follow-up after MVR and many of the late deaths at home were sudden in nature in patients in whom the last follow-up echocardiogram showed good prosthesiand systolic function. That most likely indicates that there were undetected valve-related complications and that thromboembolic complications may have been under-reported in our current series. Moreover, some of the bleeding events in our patients were trauma-related, including two young children who died from fall-related intracranial haemorrhage. All of that highlights the delicate problem of compliance with anticoagulation regimen and its implication on the child’s lifestyle that is especially difficult to control in paediatric patients.

Again, all thromboembolic and bleeding events in our series were in mechanical prosthesis recipients. This fact highlights the potential role of tissue prostheses in select patients, particularly those non-compliant with anticoagulation. In our series, one patient with poor compliance with anticoagulation developed frequent embolic episodes to the brain, kidneys and spleen and eventually underwent mitral reoperation using tissue prosthesis to prevent recurrent embolism.

5. Summary

Mortality and mitral reoperation are common after MVR in children and outcomes can be predicted based on the child’s age, prosthetic size, and other associated factors. MVR remains a significant challenge in the smallest children and attempts should be made by the surgeons to repair rather than to replace the mitral valve. When MVR is required, some modifiable factors such as avoiding oversized prostheses may improve outcomes especially in the younger children. Mitral reoperation is safer and generally larger size prosthesis can be placed demonstrating continued annular growth. While reoperation is inevitable in children receiving tissue prosthesis, associated low valve-related morbidity and good survival are indicative of a valid role for tissue prostheses in selected group of older children.

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Appendix A. Conference discussion

**Dr J. Fragata** (Lisbon, Portugal): When we address the issue of mitral replacement, we must tackle patient-related factors, prosthesis-related factors, and the nature of the prosthesis itself, mechanical or biological, as well as the issue of anticoagulation. Also technically related issues, such as preservation or not of the subvalvular apparatus, myocardial protection techniques and disease-related factors, namely the ones which influence LV function.

I realize in your series that more than 80% of the patients had mitral regurgitation, so this raises the issue of ventricular function in your patients that I could not see being discussed here.

You identified that risk factors for death were young age, congenital disease, small or oversized prostheses, although you achieved fairly good results with a survival of 87% at 15 years.

*My* major criticism concerns the fact that the baseline level of LV function was not included in your analysis, and that might have had an impact on mortality. In fact, and interestingly, even myocardial protection and cross-clamp time seemed to have no impact on your final results.

I think these should have been included, as well as whether or not you preserved the subvalvular apparatus, as these factors are known to influence LV geometry and LV function at late follow-up.

Finally, one interesting point is that postoperative complications in patients actually trigger a hazard trend that will eventually affect late prognosis, and this is a very hot topic issue that you may wish to comment on.

**Dr Alsoufi:** Unfortunately, the echocardiographic data with regard to LV function were largely unavailable, so that was not entered as one of the variables in our analysis.

We attempt to preserve subvalvular apparatus if possible at the time of mitral valve replacement. However, in our experience, patients in whom subvalvular apparatus preservation is possible can usually undergo mitral valve repair. On the other hand, those who require mitral valve replacement usually have extensive damage to their entire mitral complex and therefore preservation of the subvalvular apparatus is often not feasible. Moreover, smaller patients have limited room for mitral prosthesis placement. In those patients, preservation of the subvalvular apparatus may further compromise that space or interfere with the function of the prosthesis and therefore we are frequently unable to preserve it completely.

As shown in one of the slides, postoperative complications were associated with significant increase in overall mortality. Although their effect was more pronounced in the early risk phase, it was still noticeable in the late risk phase. It seems, as you stated, that postoperative complications such as heart block and low cardiac output, trigger a series of events that may affect not only early survival, but long-term survival also.

**Dr Fragata:** If I may still ask, what type of anticoagulation did you use in children? Because the data you report on either bleeding or thromboembolic complications are fairly low. Do you use warfarin treatment alone, what is your policy?

**Dr Alsoufi:** We anticoagulate patients who receive mechanical prostheses with oral warfarin. All of the patients are followed at specialized centers with established anticoagulation protocols.

We need to be cautious when we report a low thromboembolic risk in our patients. When we examined the survival, many of the late deaths were sudden in nature. When we looked at those patients’ echocardiograms prior to their demise, many of them had well functioning ventricles and prostheses. That indicates that some of the complications, especially thromboembolic complications, are under-reported in our series because of sudden deaths at home.

**Dr R. Hosseinpour** (Seville, Spain): One concern is what happens to the annulus in the presence of a prosthesis? In those who do need a reoperation because they have outgrown the valve, can one go back and put in a bigger prosthesis, or is the annulus going to be fibrosed because of the presence of a previous prosthesis and that is the size they have to live with forever?

**Dr Alsoufi:** This is an important question. The issue is obviously more significant in younger children. In patients who underwent mitral valve replacement at a weight under 20 kg, we were able in general to place a larger prosthesis, 4 mm on average, at the time of mitral reoperation. That indicates that the mitral annulus regularly continues to grow despite the fixed size of the prosthesis sewing ring. This fact supports our recommendation not to oversize the prosthesis at the time of first mitral valve replacement because of the possible annular growth and the lower mortality risk of mitral reoperation as compared to initial mitral valve replacement in a smaller child with an oversized prosthesis.