Evaluation of Thromboembolism and Valve Thrombosis in Patients with Rheumatic Heart Disease Undergoing Mitral Tissue Valve Replacement in the Presence of Atrial Fibrillation with or without Left Atrial Clot: Review of A 17-Years' Experience

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Abstract

Background and Aim: To evaluate the incidence of thromboembolism in patients implanted with tissue mitral valves and to evaluate the risks and benefits of left atrial appendage ligation.

Materials and Methods: Carpentier-Edwards perimount, pericardial bioprostheses were implanted in 168 consecutive patients between January 2000 and March 2017 in the mitral position due to rheumatic heart disease. The patient's ages ranged between 12 and 75 years (mean ± SD 34.2 ± 9.8 years). Sixty-eight (40.4%) patients had giant left atrium measuring more than 65 mm diameter. Sixty (35.7%) patients underwent surgical reduction of giant left atrium. The left atrial appendage was ligated in 110 (65.5%) patients.

Results: The hospital and late mortalities were 1.8% and 1.8% respectively. The total cumulative follow-up period was 1447.2 patient-years with a mean of 107.2 ± 56.4 months (range, 1-207 months). There were 7 events of thromboembolism (2 events per 100 patient-years) and two instances of left atrial clot requiring re-institution of warfarin therapy. The actuarial survival and actuarial event-free survival at 207 months was 95.04% (± 0.02%) and 88.1% (± 0.04%) respectively.

Conclusion: We conclude that anticoagulation may be discontinued after 3 months in the majority of patients undergoing bioprosthetic MVR. Low intensity anticoagulation with an INR between 1.5 and 2.0 should be continued lifelong in a select subset of patients with preoperative atrial fibrillation, thromboembolism, giant left atrium, and low left ventricular ejection fraction and bioprosthetic degeneration. Liberal left atrial appendage ligation and surgical reduction of giant left atrium during MVR is consistent with reduction of surgical mortality, low cardiac output syndrome, respiratory complications and risk of late systemic embolism.

Keywords: Mitral valve replacement; Carpentier-Edwards pericardial prosthesis; Bioprosthetic degeneration; Thromboembolism; Left atrial appendage

Introduction

The ideal prosthetic valve should have excellent hemodynamics (similar to a normal human valve in the same position), last a lifetime, be free of structural dysfunction or deterioration, and require no anticoagulation. Needless to say, such a valve is yet to be available [1].

Mechanical valves have a high incidence of thromboembolism. They also require life-long anticoagulation which disposes the patient to complication of anticoagulation related hemorrhage. For St Jude Medical mechanical prosthesis, the reported actuarial survival rate is 61.3 ± 3.3% at 19 years. Bleeding complications related to anticoagulation was 1% per patient-year. The valve thrombosis rate is 0.2% per patient year. The percentages of patients free of endocarditis and valve avulsion are 98.6 ± 1% and 90 ± 3%, respectively [2,3].

Figure 1: Bar graph showing the age distribution of patients undergoing bioprosthetic mitral valve replacement in the study group.

In our previous publications, we demonstrated similar problems of valve thrombosis, anticoagulation related hemorrhage and thromboembolic complications following mechanical Mitral Valve Replacement (MVR) using a St. Jude mechanical prosthesis (St. Jude Medical Inc., St. Paul, MN) [4,5].

Several investigators including ourselves have noted that 20% patients had persistently poorly controlled anticoagulation during a follow-up of 10 years [4-7]. This clearly reflects the difficulty in the practical management of this treatment, the constraints that anticoagulants can impose on these patients, and the possible alteration of their quality of life. The problem of anticoagulation and the complications induced by anticoagulation account for 80% of valve-related complications [5-7].

Thromboembolism is perhaps the most common complication of both biologic and mechanical mitral prostheses but is more frequent in patients with mechanical valves. Bioprosthetic valves have a lower incidence of thromboembolism even in absence of anticoagulation [1-9].

Thromboembolism in patients with MVR is lower in those with a small left atrium, sinus rhythm, and normal cardiac output. It is much higher in patients with large left atrium, chronic atrial fibrillation, and the presence of intra-atrial clot [6-8]. ACC/AHA Practice Guidelines recommend anticoagulation for life in patients with atrial fibrillation [11]. Left atrial appendage ligation has been shown to reduce the incidence of cardiovascular accident in high risk patients with prosthetic heart valves [12-16].
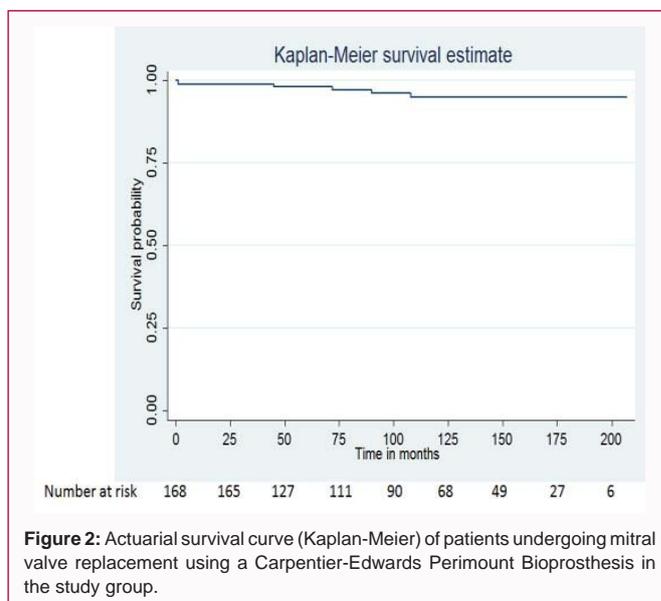
The aim of the present study is to evaluate the incidence thromboembolism in patients implanted with tissue mitral valves and to evaluate risk and benefits of left atrial appendage ligation.

Patients and Methods

Between January 2000 and March 2017, a total of 168 consecutive patients (69 males) with rheumatic heart disease undergoing bioprosthetic mitral valve replacement using Perimount pericardial bioprosthesis model 6,900-mitral (Edwards Life Sciences, Baxter Health Care Corporation, Irvine, CA, USA) at All India Institute of Medical Sciences, New Delhi, India, operated by the corresponding author (UKC) were included in the study. Selection of the porcine Carpentier-Edwards prosthesis was determined by patients' preference and surgeon judgement.

The indications for use of bioprosthesis in these patients were:

1.   Patients coming from remote rural areas where routine

Figure 2: Actuarial survival curve (Kaplan-Meier) of patients undergoing mitral valve replacement using a Carpentier-Edwards Perimount Bioprosthesis in the study group.
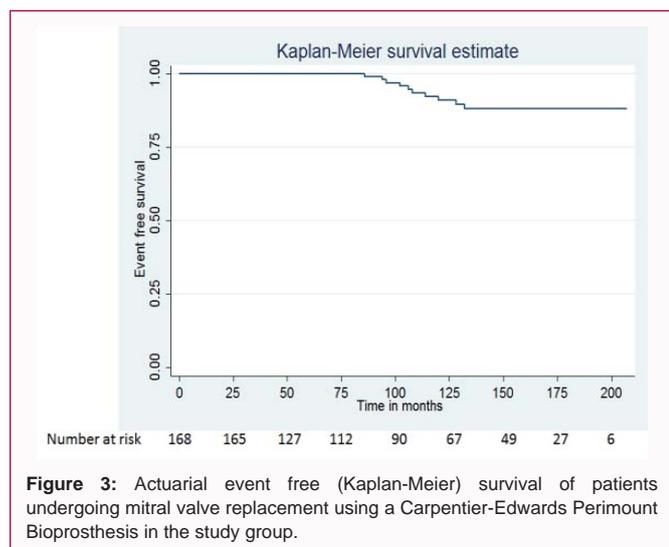
follow-up and anticoagulation monitoring is practically difficult,

2.   Contraindications to the use of anticoagulation,

3.   Young females desirous of pregnancy,

4.   Patients undergoing redo mitral valve surgery due to previous mechanical valve dysfunction/thrombosis, and

5.   Patient's choice because of lifestyle considerations.

Institutional review board approval for this study protocol was available and informed consent was obtained from all patients. Our institutional policy is to use tissue valves only after the bone growth and maturation completed that is after 18 years of age. There were two patients below 18 years of age. One patient, aged 12 years with prior mechanical valve replacement had prosthetic valve dysfunction due to thrombosed mitral prosthesis; hence the valve had to be replaced with a tissue valve. Other patient aged 13 years had thalassemia with hemolysis and a tissue valve was chosen over mechanical valve.

The mean age of the patients was 34.2 ± 9.8 years (range 12-75 years). The age distribution is depicted in Figure 1. One hundred and thirty-seven (81.5%) patients were in NYHA class III and 31 (18.5%) patients were in NYHA class IV. Thirty (17.8%) patients were on inotropic support and 10 (5.9%) patients were on ventilator in the preoperative period. Preoperatively, 5 (2.9%) patients required intra-aortic balloon counterpulsation for stabilization of hemodynamics. Ninety-seven (57.7%) patients had predominantly mitral stenosis (indexed mitral valve area <1 cm^2/m^2) and 64 (38.1%) patients had mixed mitral valve disease. Seven (4.2%) patients underwent redo mitral valve replacement due to thrombosed prosthetic mitral valve. Fifteen (8.9%) patients had undergone closed mitral valvotomy and 8 (4.8%) patients had previous balloon mitral valvotomy. Eight (4.8%) patients had previous mitral valve repair, 31 (18.5%) patients had clot within the left atrium/left atrial appendage and 8 (4.8%) patients had history of preoperative thromboembolism. One hundred and thirteen (67.3%) patients in the study group were in atrial fibrillation in the preoperative period and 96 (57.1%) patients continued to remain in atrial fibrillation in the postoperative period. Preoperatively, 68 (40.4%) patients had giant left atrium more than 65 mm in diameter and 41 (24.4%) patients had left ventricular ejection fraction between

Figure 3: Actuarial event free (Kaplan-Meier) survival of patients undergoing mitral valve replacement using a Carpentier-Edwards Perimount Bioprosthesis in the study group.

15% to 25% (Table 1).

Surgery was performed through a median sternotomy (n=163) or right anterolateral thoracotomy (n=5) with standard normothermic or moderately hypothermic cardiopulmonary bypass. Antegrade cold blood cardioplegic solution and topical cooling were used for myocardial protection in all patients. A trans-septal approach (n=54) was used in patients with a small left atrium and in cases of associated tricuspid valve or atrial septal defect. All efforts were made to preserve the chordo-papillary apparatus without causing prosthetic valve entrapment or left ventricular outflow obstruction. Total chordo-papillary apparatus was preserved using Miki's technique whenever feasible (n=45, 26.8%) [17]. In patients with calcified leaflets with annular extension and severe subvalvular fusion, the mitral apparatus was completely excised [n=14 (8.3%)]. The remaining patients had only posterior chordal preservation [n=109 (64.8%)]. The technical details of chordal preservation, annulus decalcification and reconstruction had been addressed in our earlier publications (Table 2) [4,5].

Mitral valve replacement was performed using Perimount pericardial bioprosthesis model 6,900 -mitral (Edwards's life sciences, Irvine, CA, US). Size of bioprosthetic valve ranged from 25 mm to 33 mm (median 27). Intra-operative trans-esophageal echocardiography was performed to confirm satisfactory prosthetic valve function immediately after surgery.

Patients (n=17) undergoing redo MVR for dysfunctional mechanical prosthetic valve (n=7) and degenerated bioprostheses (n=10) were subjected to a uniform surgical protocol standardized by the corresponding author. The redo operations were performed under moderately hypothermic cardiopulmonary bypass through femoral arterial cannulation (Medtronic Bio-Medicus Percutaneous Arterial Femoral, Medtronic Inc., Minneapolis, MN, USA) and bicaval venous cannulation through the femoral vein (Medtronic Bio-Medicus Percutaneous Venous Femoral) and superior vena cava. Redo sternotomy was performed under cardiopulmonary bypass in all these patients (n=17). Antegrade cold blood hyperkalemic cardioplegia was used in all patients for myocardial preservation. A mechanical heart valve [(Medtronic Open Pivot™ AP360° Apex and AP, Medtronic Inc., Mx, USA); size 24 mm, 5 patients; 26 mm, 5 patients] was used in patients undergoing explantation of the

Table 1: Demographic details of patients undergoing mitral valve replacement using Carpentier-Edwards pericardial bioprosthesis (n=168).

Variables	No. (%)
Males	69 (41.1)
Age in years(mean ± S.D), (range)	34.2 ± 9.8 (12-75)
Age distribution (years)	
- 10-20	6 (3.6)
- 21-30	63 (37.5)
- 31-40	63 (37.5)
- 41-50	25 (14.8)
- 51-60	7 (4.2)
- 61-70	3 (1.8)
- 71-80	1 (0.6)
Pre-operative NYHA class, n (%)	
- III	137 (81.5)
- IV	31(18.5)
Congestive cardiac failure (on inotropes and ventilation)	30 (17.8)
Predominant lesion, n (%)	
- Mitral valve stenosis	97 (57.7)
- Mitral valve stenosis + regurgitation	64 (38.7)
- Thrombosed mechanical prosthetic mitral valve	7 (4.2)
Preoperative left ventricular ejection fraction (mean ± SD, range)	55 ± 6.8 (15-70%)
Left ventricular ejection fraction, <0.25	41 (24.4)
Atrial fibrillation	
- Preoperative	113 (67.3)
- Postoperative	96 (57.1)
Left atrial size (65mm)	68 (40.4)
Clot within the left atrium/left atrial appendage clot	31 (18.5)
History of thromboembolism	8 (4.8)
Previous closed mitral valvotomy	15 (8.9)
Previous balloon mitral valvotomy	8 (4.8)
Previous mitral valve repair	8 (4.8)
Redo MVR due to bioprosthetic degeneration	8 (4.8)

degenerated bioprosthesis. Two patients undergoing redo MVR required left atrial thrombectomy in addition. Sixty-eight (40.4%) patients had left atrial size more than 65 mm. Sixty (35.7%) patients underwent surgical reduction of the giant left atrium. The left atrial appendage was ligated in 110 (65.5%) patients. No surgical procedure was performed for atrial fibrillation (Table 2).

Following MVR with or without chortal preservation, the disc movements were checked and left atrial volume reduction was done in patients with giant left atrium by a combination of para-annular and superior plication techniques. The postero-inferior wall of left atrium between the ostia of inferior pulmonary veins and mitral annulus was plicated in a semi-lunar fashion using interrupted 3-0 polypropylene mattress sutures over polytetrafluoroethylene pledgets.

The successive sutures were placed at a distance of 20 mm to 30 mm from each other, 15 mm to 20 mm from the pulmonary venous ostia and 10 mm from the annulus. The superior plication was done in the area between the right and left pulmonary veins. While closing the left atriotomy, the redundant left atrial wall above the right

Table 2: Operative and post-operative details of the study group (n=168).

Variables	No. (%)
Chordal preservation	
- Total chordal	45 (26.8)
- Posterior chordal	109 (64.9)
- Nil chordal	14 (8.3)
Valve size	
- 33 mm	9 (5.4)
- 31 mm	17 (10.1)
- 29 mm	48 (28.6)
- 27 mm	72 (42.9)
- 25 mm	22 (13.1)
Mean cardiopulmonary bypass time(min) (mean ± S.D, range)	63.3 ± 19.8 (range, 38-182 minutes)
Mean aortic cross clamp time(min) (mean ± S.D, range)	38 ± 17.6 (range, 27-131 minutes)
Giant left atrium (size >65 mm)	68 (40.4)
Left atrial appendage ligation	110 (65.5)
Surgical left atrial reduction	60 (35.7)
Thromboembolism	7 (4.16)
Transient ischemic attack	5 (2.97)
Reversible neurologic event	1 (0.6)
Peripheral embolic event	1 (0.6)
Redo MVR for bioprosthetic degeneration	8 (4.8%)

pulmonary veins was plicated in two layers using 3-0 polypropylene sutures. Subsequently, the base of the enlarged left atrial appendage was doubly ligated externally using no.3 (SUTUPAK) braided black silk (Johnson & Johnson Ltd) sutures.

The mean left ventricular ejection fraction was 55 ± 6.8% (range, 15% to 70%). Forty-one (24.4%) patients had left ventricular ejection fraction between 15% to 25%. Mean cardiopulmonary bypass time was 63.3 ± 19.8 min (range 38 to 182 min) and aortic cross-clamp time was 38 ± 17.6 min (range 27 to 131 min).

Patients were started on warfarin on first postoperative day maintaining an International Normalized Ratio (INR) between 2.0-2.5. After discharge, these patients were reviewed at one week, one month, 3 months, then subsequently at 6 months intervals. International normalized ratio was tested till 12 weeks after which anticoagulation was stopped. Warfarin therapy was re-instituted if there was a thromboembolic event or there was a newly formed clot within the left atrium or left atrial appendage, in patients with persistent atrial fibrillation, bioprosthetic degeneration with stiffened leaflets and increased transprosthetic gradients maintaining an INR between 1.5 and 2.0. All patients received Asprin life long, unless contraindicated.

Transthoracic two-dimensional (2D), color flow and Doppler echocardiography was performed using a Hewlett-Packard-Sonos-5500 with 2.7 or 3.5 MHz transducer. Prosthetic valve function was assessed on M-mode parasternal long-axis view and 2D apical four-chamber view. Left ventricular outflow tract obstruction was assessed on an apical five-chamber view, and by Doppler study. A Doppler velocity of greater than 2 m/s was considered significant for LVOTO. Echocardiographic data were measured according to American Society of Echocardiography criteria [18]. The ventricular

and prosthetic valvular function was assessed within first six months then annually.

Follow-up data included clinical history and assessment of NYHA class, occurrence of events such as thromboembolism, hemorrhage, infective endocarditis, congestive heart failure etc. Electrocardiogram was done at each review to assess the heart rhythm and screen for new onset of atrial fibrillation. A valve-related event was defined as any episode of thromboembolism, hemorrhage, congestive heart failure, infective endocarditis, structural deterioration, significant gradients or bioprosthetic valve dysfunction as per the published criteria [19].

Statistical analysis

Statistical analysis was performed using Intercooled STATA 9.0 software (College Station, Texas, USA). All variables were defined in compliance with the guidelines established by The American Association for Thoracic Surgery and the Society of Thoracic Surgeons [11]. Variables analyzed included valvular thromboembolism (including episodes of embolism, transient ischemic attacks, and valve thrombosis), anticoagulation-related hemorrhage (defined as episodes resulting in death, stroke, surgery, hospitalization, or transfusion), prosthetic heart valve thrombosis and valve-related mortality.

Interval related data were expressed as mean ± Standard Deviation (SD) and categorical variables were expressed as percentages. Mortality rates were calculated depending on the total number of years of follow-up. Freedom from valve related events and event free survival have been calculated using the Kaplan-Meier analysis. Statistical significance was set at $p < 0.05$.

Results

There were 3 (1.8%) early deaths. Two patients died due to low output syndrome. Both deaths occurred in patients who were in congestive cardiac failure preoperatively and underwent redo MVR for mechanical prosthetic valve dysfunction. One patient died in the immediate postoperative period secondary to acute biventricular dysfunction. Patients considered to have low cardiac output syndrome (n=79) required dopamine (4-10 $\mu g.kg^{-1}.min^{-1}$), epinephrine (0.01-0.1 $\mu g.kg^{-1}.min^{-1}$) and milrinone (50 $\mu g/kg$ IV bolus followed by 0.375-0.75 $\mu g.kg^{-1}.min^{-1}$) either isolated or in combination. Ten (5.9%) patients required intraaortic balloon counterpulsation as an additional support. Hospital morbidity included re-exploration for excessive bleeding within 12 hr in 6 patients. Four patients required tracheostomy and long-term ventilatory support. Three patients required hospital admission of 18th, 20th and 21st postoperative days because of deranged prothrombin time requiring pericardiocentesis.

All patients with normal renal function were administered oral angiotensin enzyme inhibitor (ACE) (0.5-1.0 mg/kg; every 8 hr) after extubation before weaning from inotropic agents. Digoxin, diuretics and ACE inhibitors were weaned at varying time intervals. Amiodarone was used for intractable atrial fibrillation. Hospital stay ranged from 5 to 52 days (median 8.8) Mean hospital stay was 8.8 ± 5 days.

Late Outcomes

There were three (1.8%) late deaths 45 days, 3 months and 9 months after surgery due to persistent left ventricular failure (n=2) and intractable ventricular arrhythmias (n=1). Out of 113 patients who were in atrial fibrillation in the preoperative period, 96 (84.9%)

Table 3: Details of patients who had thromboembolism in the postoperative period.

Patient	Age	Sex	Type of event	Heart rhythm	Pre-operative history of thrombo-embolism	Presence of left atrial clot pre-operatively	Size of the left atrium	Left atrial appendage ligation	Left ventricular ejection fraction	Chordal presser-vation
1	32	Female	Transient Ischemic Attack	Atrial fibrillation	No	No	40 mm	No	15%	Posterior
2	35	Female	Transient Ischemic Attack	Atrial fibrillation	Yes	Yes	45 mm	No	25%	Posterior
3	37	Female	Peripheral Thrombo-embolism	Atrial fibrillation	No	No	42 mm	No	22%	NIL
4	38	Female	Transient Ischemic Attack	Atrial fibrillation	No	Yes	47 mm	No	20%	Total
5	38	Female	Transient Ischemic Attack	Atrial fibrillation	Yes	Yes	40 mm	No	25%	NIL
6	45	Female	Transient Ischemic Attack	Atrial fibrillation	Yes	Yes	41 mm	No	17%	Posterior
7	48	Male	Reversible Neurological event	Atrial fibrillation	No	Yes	42mm	No	20%	Posterior

Table 4: Details of postoperative echocardiographic gradients (at one week) across the prosthetic valve in patients undergoing mitral valve replacement using a bioprostheis.

Valve size	End diastolic gradient (mmHg) Mean ± S.D	Mean diastolic gradient (mmHg) Mean ± S.D
25 mm	0.68 ± 0.47	2.54 ± 0.59
27 mm	0.69 ± 0.49	2.28 ± 0.63
29 mm	0.80 ± 0.57	2.36 ± 0.76
31 mm	0.75 ± 0.44	2.06 ± 0.44
33 mm	0.79 ± 0.52	2.15 ± 0.86

patients remained in atrial fibrillation and 17 (15%) reverted to sinus rhythm. No new onset atrial fibrillation was reported in any survivors of this study.

One hundred and sixty-two survivors (96.4%) were followed up in outpatient department. Follow up was 100% complete and yielded 1447.2 patient-years data with a mean follow up time of 107.2 ± 56.4 months (range, 1 to 207 months). The actuarial survival at a mean follow-up of 107.2 ± 56.4 months was 95.04 ± 0.02% (95% CI: 89.01-97.8) (Figure 2). The actuarial event free survival at 107.2 ± 56.4 months was 88.1 ± 0.04% (95% CI: 78.9-93.5) (Figure 3).

There were 7 events of thromboembolism (transient ischemic attacks, n=5; reversible hemiparesis, n=1; femoral thromboembolism, n=1). Preoperatively, these patients (n=7) were in atrial fibrillation with a left atrial size <40 mm and without any clot within the left atrium/left atrial appendage. They were without any oral anticoagulation and were on ecospirin alone. These patients were treated conservatively and recovered uneventfully. None of these patients required any surgical intervention. Echocardiographic evaluation in these patients demonstrated normal left ventricular function and there was no clot in any cardiac chambers. Details of patient profile who had episodes of thromboembolism are depicted in Table 3. In all patients, warfarin was restarted to maintain International Normalized Ration (INR) of 1.5 to 2.0. There was no recurrence of thromboembolic event or valve thrombosis. The left atrial appendage was not ligated in any patients.

Ten patients aged 43, 39, 50, 55, 36, 50, 52, 59, 60 and 65 years respectively developed severe bioprosthetic degeneration with predominant stenosis between 7 and 11 years (mean ± SD, 107.18 ± 56.4 months) after primary tissue valve replacement (Figure 3). Intraoperatively, two-dimensional and three-dimensional transesophageal echocardiography demonstrated severe prosthetic valve stenosis and no regurgitation. They underwent redo MVR using a Medtronic mechanical prosthesis and removal of the left

atrial thrombus (n=2) as stated above. These two patients with left atrial clot had unligated left atrial appendage with atrial fibrillation and was not on oral anticoagulation. Examination of the explanted bioprostheses revealed severely restricted mobility due to stiffening and calcification of the leaflets. Postoperatively, one patient undergoing redo bioprosthetic replacement required intra-aortic balloon counterpulsation in addition to inotropes for low cardiac output syndrome. Two patients undergoing redo-MVR due to degenerated bioprostheses had large left atrial clot. These two patients were without anticoagulation, in atrial fibrillation, had unligated left atrial appendage and calcific, stifeened, stenosed bioprostheses with excess transprosthetic gradients. These patients (n=10) survived the reoperation and are presently in NYHA class I. There were no structural failure among the remaining survivors (n=152) over the follow-up period.

Echocardiographically obtained hemodynamic measurements are detailed in Table 4. Valve leaflet thickening with mild prosthetic valve stenosis was seen in two patients at 32 and 40 months of follow-up.

Discussion

The procedure of choice for mitral valve disease is mitral valvular reconstruction wherever feasible [1-20]. For patients requiring MVR, the ideal valve is not yet available and surgeons need to choose between mechanical prostheses with the risk of anticoagulation-related hemorrhage and biologic valves with the risk of deterioration and reoperation [1-20]. Following bioprosthetic heart valve implantation, structural deterioration and the need for reoperation appear higher in mitral than in the aortic position, and many studies recommend its use in patients of older age [21-26].

Pericardial bioprostheses have been clinically used in human beings since 1970. The first generation of this type of valve has been

withdrawn from the market because of its poor clinical results [23-26]. The cause of deterioration was due to faulty design and tissue preparation failure [21,23-26].

The Carpentier-Edwards pericardial valve was designed with an original leaflet clamping technique which eliminates the retention suture and also abrasion risk [23,24-26]. Pericardium is carefully procured and treated with glutaraldehyde. With these characteristics, this pericardial bioprosthesis showed satisfactory intermediate results in both aortic and mitral positions, reestablishing pericardium as a good valve substitute [3,25,26]. These results especially in the mitral position, promise an interesting long-term follow-up.

Use of bioprosthetic valves confers an advantage over mechanical valve as no anticoagulation is required. Continuing with anticoagulation exposes the patient to increased risk of haemorrage whereas discontinuing the anticoagulation therapy may result in a higher incidence of thromboembolism. However, the duration of anticoagulation therapy following valve replacement with a bio-prosthesis remains controversial [6,7,9,16].

Due to increased risk of bleeding with anticoagulant therapy and the inability of appropriate prothrombin measurements indefinitely after operation, we decided to stop anticoagulation at 12 weeks and continue only with aspirin at a dose of 150 mg/day. This policy was continued even in patients who are in atrial fibrillation, had left atrial/left atrial appendage clot or preoperative history of thromboembolic episode. With this strategy, we observed comparable low rate of thromboembolism of 2 events per 100 patient years. Our actuarial event free survival at 207 months was 88.1% ± 0.04% (95% CI: 78.8-93.5) which is comparable to those reported by Akins and Jamieson [16,18]. Ruel and colleagues also showed that tissue heart valves have lesser incidence of anticoagulation related hemorrhage with no difference in actuarial survival, thromboembolism, infective endocarditis, paravalvular leak, structural deterioration and valve related dysfunction [15].

Ligation of the left atrial appendage during mitral valve surgery is still controversial [11,16]. Left atrial appendage is routinely ligated in patients undergoing closed mitral valvotomy for rheumatic mitral stenosis in an attempt to reduce the risk of thromboembolism [28]. Several investigators have shown that Left Atrial Appendage (LAA) ligation during surgery of MVR, performed in a high-risk population is consistent with a reduction of the risk of late systemic embolism. Several other studies have confirmed that the LAA plays a very important role in the formation of LA thrombus in patients with atrial fibrillation. In patients with rheumatic and non-rheumatic AF, at least 60% and 90% of LA thrombi, respectively, are located in the LAA. Therefore, it is likely that ligation of the LAA in patients undergoing cardiac surgery may greatly reduce the risk of stroke [11-16]. The utilization of this technique depends on the methodology and insight of the different surgical teams despite that it is a recommended procedure in the ACC guidelines [10].

Orszulak and colleagues evaluated the risk of stroke in elderly patients during the early postoperative period after MVR with a Carpentier-Edwards biological prosthesis and found a strong correlation between late stroke and left atrial appendage in patients undergoing MVR and CABG [29]. However, in the group of patients with isolated MVR and in the overall group, the only independent variable associated with a greater risk of late stroke was an advanced NYHA class [29].

Juratli and colleagues analyzed the effectiveness of LAA ligation during mitral valve surgery (50% underwent mitral valve repair and 23% received a mechanical prosthesis) as an alternative to anticoagulant treatment with warfarin [13]. Left atrial appendage ligation did not provide an adequate protection from thromboembolic events in the absence of effective anticoagulation treatment with warfarin [13].

In our study population, 67.3% (n=113) were in atrial fibrillation, 40.4% (n=68) had left atrial size >65 mm, 18.5% (n=31) were having left atrial appendage/left atrial clot, 4.8% (n=8) had preoperative history of thromboembolism, and 24.4% (n=41) patients had left ventricular ejection fraction <0.25. Two patients undergoing redo-MVR due to degenerated bioprostheses had large left atrial clot within the left atrium. These two patients were in atrial fibrillation, without oral anticoagulation, had unligated left atrial appendage and calcific stiffened, stenosed bioprostheses with excess transprosthetic gradients. Left atrial appendage ligation was done in 65.5% (n=110) patients, surgical reduction of left atrium was done in 35.7% (n=60) of patients with giant left atrium. Twenty-three (13.7%) patients had amputated left atrial appendage during previous surgery and in 58 (34.5%) patients, left atrial appendage was not ligated due to small size.

Currently, there is no consensus regarding the management of giant left atrium during mitral valve surgery. Most surgeons fix the mitral valve and do little to an oversized left atrium. Others occlude the left atrial appendage [30,31]. The co-existence of giant left atrium associated with mitral valve disease has been reported as a significant risk factor in mitral valve surgery with surgical mortality ranging from 8% to 23% [30,31]. Currently, high mortality rates following mitral valve surgery above 5% are not acceptable with improved operative techniques, modern anaesthetics and postoperative care.

In this study, 40.4% (n=68) patients had giant left atrium and 60 of 68 patients underwent left atrial volume reduction with three objectives: i) reduction of hospital mortality, ii) elimination of symptoms and alleviating the pressure effect to the left ventricle, bronchus and lung parenchyma, and iii) reduction of early postoperative complications related to low cardiac output syndrome and respiratory complications.

Importantly, significant reduction of hospital and late mortalities of 1.8% and other two above mentioned objectives were achieved by employing this strategy of surgical reduction of left atrial size in patients with giant left atrium and chordal preservation whenever feasible during MVR. We performed the simplest modality for size reduction by plicating the inferior and superior LA wall and ligating the base of the left atrial appendage. We avoided partial excision of the superior wall of left atrium because it carries greater risk for bleeding and atrioventricular node blockade.

A significant proportion of the study population was at high risk for thromboembolism. In our study, the incidence of thromboembolism was 2 per 100 patient years which is comparable to published results by other investigators [3,12]. In this study, using the anticoagulation management protocol as stated above, the incidence of postoperative thromboembolism was higher in females, those with atrial fibrillation, LA clot and preoperative history of thromboembolism and poor left ventricular function. Due to the occurrence of thromboembolic events in these high risk subset of patients as above and those presenting with bioprosthetic degeneration with high transprosthetic gradients,

we restarted low intensity anticoagulation in these high risk subset of patients maintaining an INR between 1.5 and 2.0.

Our data further suggests that the surgical LAA ligation and left atrial size reduction together with MVR reduces the incidence of low cardiac output syndrome and late strokes. Our data provides new information about potential impact of LAA ligation and surgical reduction of giant left atrium until new data of a randomized study with blinded event verification are available.

Study Limitations

Like that of other observational cohorts, the results of this study may not be generalizable globally to all patients undergoing bioprosthetic MVR with longer follow-up, the incidence of thromboembolism may raise further.

Conclusion

Our study shows that liberal LAA ligation and surgical reduction of giant left atrium during MVR is consistent with reduction of surgical mortality, low cardiac output syndrome, respiratory complications, risks of late embolism and supports this strategy if a MVR is indicated. Because of an increase in risk of thromboemboli in the first three months after implantation of a biological prosthetic valve, anticoagulation with warfarin is usually recommended. After 3 months, biological valve can be treated like native valve disease and Warfarin can be discontinued in over two-thirds of patients with biological valves. In the remaining patients with associated risk factors for thromboembolism, such as aneurysmal left atrium with atrial fibrillation, previous thromboembolism, poor left ventricular function, and bioprosthetic degeneration, life-long low dose warfarin therapy is indicated to achieve an INR of 1.5 to 2.0.

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