

Double Valve Replacement (Mitral and Aortic) for Rheumatic Heart Disease: A 20-Year Experience with 300 Patients

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ARTICLEINFO	ABSTRACT		
Article type: Original Article	Introduction: Rheumatic heart disease still remains one of the leading causes of congestive heart failure and death owing to valvular pathologies, in developing countries. Valve replacement still remains the treatment of choice		
<i>Article history:</i> Received: 31 Jul 2016 Revised: 22 Aug 2016 Accepted: 24 Aug 2016	in such patients. The aim of this study was to analyze the postoperative outcome of double valve replacement (Mitral and Aortic) in patients of rheumatic heart disease. Materials and Methods: Between 1988 and 2008, 300 patients of rheumatic		
<i>Keywords:</i> Double Valve Replacement Rheumatic Heart Disease Starr Edwards Valve St. Jude Valve	heart disease underwent double (Mitral and Aortic) valve replacement with Starr Edwards valve or St Jude mechanical valve prosthesis were implanted. These patients were studied retrospectively for preoperative data and postoperative outcome including causes of early and late deaths and the data was analyzed statistically. Results: The 30-day hospital death rate was 11.3% andlate death occurred in 11.6%. Anticoagulant regimen was followed to maintain the target pro- thrombin time at 1.5 times the control value. The actuarial survival (exclusive of hospital mortality) was 92.4%, 84.6%, and 84.4%, per year at 5, 10, and 20 years, respectively. Conclusion: In view of the acknowledged advantage of superior durability, increased thromboresistance in our patient population, and its cost effectiveness the Starr-Edwards ball valve or St. Jude valve is the mechanical prosthesis of choice for advanced combined valvular disease. The low- intensity anticoagulant regimen has offered suffcient protection against thromboembolism as well as hemorrhage.		

► Please cite this paper as:

Mishra P, Seth HS, Khandekar JV, Mohapatra ChKR, Ammannaya GKK, Raut Ch, Saini JS, Shah V. Double Valve Replacement (Mitral and Aortic) for Rheumatic Heart Disease: A 20-Year Experience with 300 Patients. J Cardiothorac Med. 2016; 4(3): 484-489.

Introduction

Chronic rheumatic heart disease (RHD) is characterized by repeated inflammation with fibrinous repair. The cardinal anatomic changes of the valve include leaflet thickening, commissural fusion, and shortening and thickening of the tendinous cords (1). It is caused by an autoimmune reaction to Group A β -hemolytic streptococci (GAS) that results in valvular damage (2). Valve replacement still remains the treatment of choice in such patients. Compared with single valve replacement, double valve replacement (mitral and aortic) represents a major technical challenge (3, 4). Mechanical prosthesis are better than biological prosthesis in terms of durability (5, 6). However, the long-term outcome of patients with double valve replacement is influenced by both prosthesisrelated complications and the severity of preoperative cardiac status of patients. Our clinical experience with patients who underwent double

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valve replacement with or without tricuspid valve repair over a period of 20 years forms the basis of this article. The aim of this study was to analyze the postoperative outcome of double valve replacement (Mitral and Aortic) in patients of rheumatic heart disease.

Materials and Methods

We analyzed a retrospective cohort of 300 patients in whom double valve replacement (Mitral and Aortic) was done in rheumatic heart disease patients at Lokmanya Tilak Municipal Medical College and General Hospital, Mumbai between 1988 and 2008

Inclusion Criteria: All patients who underwent valve replacement in the Aortic and Mitral area due to rheumatic pathology.

Exclusion criteria were applied: a) Patients who underwent valve surgery in only one area mitral or aortic. b) We did not include patients with incomplete data. C) Patients who had nonrheumatic causes of valvular heart disease. Demographic, epidemiologic, clinical, pre and post operative variables were analyzed. Echocardiography was the diagnostic modality, which was used.

Operative Technique

All patients were operated by establishment of bypass cardiopulmonary with moderate hypothermia and with the use of membrane oxygenator. Myocardial protection was offered by instillation of cold crystalloid cardioplegia given through the coronary ostia using modifed St. Thomas Hospital solution that was repeated every 20 to 25 minutes. Improved protection of the ventricles was provided by use of topical cold saline. In all patients either Star Edwards or St Jude Mechanical valve was used. The mitral valve was replaced first, but the aortic valve was excised as the first step through the aortotomy. The method invariably employed for both mitral and aortic valve implants used interrupted horizontal mattress sutures with Teflon pledgets. In those patients with dominant tricuspid incompetence a De vegas tricuspid annuloplasty was carried out (7). In patients with Tricuspid stenosis De Vegas commisurotomy was carried out. In 2 Patients

Table 1. Preoperative clinical data

with massive tricuspid incompetence valve replacement was carried out.

Postoperative Management

All patients were managed in the intensive care unit with monitoring of vitals, urine output and serial arterial blood gas analysis. Judicious use of inotropic agents provided further therapeutic support. Ventilatory support was provided for 24 to 48 hours for patients with pulmonary hypertension. Anticoagulation was initiated with Tab Warfarin from the day after surgery. A target INR of 2.5 to 3 was maintained.

Follow-up

Our patients were followed up monthly so as to review the INR status, which needed a close watch to be maintained in a therapeutic range. All patients were advised to take a shot of Injection Benzathine Penicillin 1.2 MU every three weekly till 45 years of age. All patients were advised regarding bacterial endocarditis prophylaxis prior to any dental treatment.

The completeness of follow-up was 80.2%; 19.8% of patients were lost to follow-up. Follow-up ranged from 1 to 20 years (median, 10.5 years).

Statistical analysis

Data analysis was performed in SPSS V.20 using MANOVA, Chi-square, and independent T-test. Moreover, numeral and classified demographic variables were compared using Chi-square, and distance variables were compared using the independent T-test. MANOVA was used for the comparison of the scores of study groups in terms of dependent variables. Additionally, effects of age and gender were controlled in variance analysis, and *P value* of less than 0.05 was considered significant.

Results

The mean age of the patients at the time of operation was 31.5 ± 10.25 years; 75% of the patients were less than 40 years, of which 15.2% were less than 20 years. There were 122 male and 178 female patients (Male/Female ratio 1:1.46). The preoperative characteristics of the study population are presented in Table 1. All patients

Variable	Number	Percent (%)
Age (y)	31.5 ± 10.25 *	
Male	122	40.66
Female	178	59.33
NYHA class III	204	68
NYHA class IV	96	32
Atrial fibrillation	123	41
Pulmonary hypertension (> 60 mm Hg)	100	33.33
Systemic cardiac index (1to 2 L.min ⁻¹ .m ²)	135	45
Previous closed mitral valvotomy	30	10

* Mean ± Standard deviation, Total number of patients:300, NYHA= New York Heart Association

belonged to either New York Heart Association (NYHA) class III or IV. The cause of valvular disease in our patients was rheumatic and this was manifested as tight calcific mitral stenosis (10.5%), severe mitral regurgitation (75.2%), calcific aortic stenosis (25.9%), and moderate to severe aortic regurgitation (84.6%). Seventy-three patients (24.33%) had associated tricuspid valve disease, of which 4 patients (5.4%) had dominant tricuspid stenosis and 69 patients (94.5%) had dominant incompetence. Severe pulmonary hypertension (> 60 mm Hg) was documented in 100 patients (33.3%). The systemic index was between 1to 2 L.min⁻¹ .m² in 45% patients. Patients more than 50 years old underwent coronary angiography and 1 patient had demonstrable coronary artery disease and underwent successful coronary artery bypass grafting (CABG) with double valve replacement. There were 30 (10 %) patients who had a previous closed mitral valvotomy.

The hospital mortality (defined as death occurring within 30 days of operation) was 11.3% (34 of 300), which decreased to 8.3% (15/180) in the last decade of our experience. The cardiac causes of hospital mortality were low cardiac output, refractory or anticoagulant-related bleeding and uncontrollable arrhythmias (Table 2).

 Table 2. Causes of early death after double valve replacement

Cardiac	Number	Percent (%)
Low cardiac output	11	32.3
Anticoagulant related	4	11.7
bleeding		
Refractory Arrythmias	3	8.8
Non- Cardiac		
Sepsis	8	23.5
Respiratory Insufficiency	8	23.5
Total Early Deaths	34	100

The noncardiac causes of death were sepsis, and respiratory insufficiency. Of patient deaths, 38.1% had severe pulmonary hypertension. In addition this subset also had low cardiac index. Late death occurred in 35 cases for mortality of 11.6% (Table 3). The most common cardiac causes of late death were congestive failure followed by anticoagulant related bleeding and valve thrombosis. Incidence of arrhythmias and endo- carditis related deaths were low in our

Table 3. Causes of late death after double valve replacement

Number	Percent (%)
10	28.5
6	17.1
6	17.1
2	5.7
1	2.8
2	5.7
2	5.7
6	17.1
35	100
	10 6 2 1 2 2 2 6

series. The noncardiac causes were renal failure, pneumonia, and unknown causes of death in 6 patients.

The actuarial survival (exclusive of hospital mortality) was 92.4%, 84.6%, and 84.4%, per year at 5, 10, and 20 years, respectively (Figure 1).

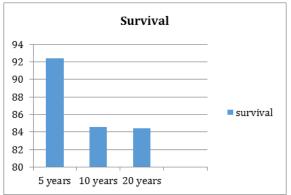


Figure 1. Actuarial survival of hospital survivors after double valve replacement

Valve replacement related morbidity-included thromboembolic events defined as a neurological deficit or peripheral thromboembolic phenomenon. Thromboembolic phenomenon was confirmed on basis of sub therapeutic INR. Anticoagulant related bleeding presented in the form of stroke and bleeding at other sites, which was confirmed by increased INR.

Thromboembolism

Thromboembolism occurred in 19 patients for a linearized rate of 1.18/100 patient-years. 1 patient had a fatal neurological thromboembolic event. 10 patients had thromboembolic complications with minimal residual neurologic deficit. The other 8 patients had minor thromboembolic episodes with total recovery.

Anticoagulant-Related Hemorrhage

Ten patients died of major bleed at varying periods of follow-up and died in the postoperative period for a linearized rate of 0.62/100 patient-years. Nonfatal bleeding events occurred in 3 patients for a linearized rate of 0.18/100 patient-years. These included a gastric bleed in 1 patient and Hemarthrosis of knee in 2 patients.

Prosthetic valve endocarditis occurred in 6 patients for a linearized rate of 0.37/100 patientyears. One patient died in the late postoperative period. Five of them underwent surgical procedures: 1 for re-replacement of an aortic prosthesis and 1 had a mitral prosthesis rereplaced. Three patients with gram-negative endocarditis were treated with appropriate long-term antibiotics and were asymptomatic during the study period.

Functional Class

At the end of this study follow-up information was obtained in 240 subjects; 65.8% were in NYHA class I, 30.8% were in class II, and 3.4% were in class III.

Discussion

Simultaneous double valve replacement (Mitral and Aortic) has been performed for many years. In most series of patients a combination of a mechanical and a bioprosthetic valve is used.9 Majority of our patients were under 40 years of age hence mechanical prosthesis was preferred, whereas in older patients bioprosthetic valves are preferred. In our study we used Starr Edwards ball cage valve or St. Jude Mechanical valve. It has been shown to be extremely durable in both accelerated fatigue testing and stress testing.¹⁰ According to Bortolotti et al mechanical prostheses perform better in the long term owing to their superior durability (11). The operative risk of mitral and aortic valve replacement has decreased considerably but remains between 5.1% and 12% (12, 13). The major predictor of risk still depends upon the advanced preoperative functional disability and higher incidence of valve related complications (13, 14).

Our hospital mortality of 11.3% compares favorably with other reported series. Bortolotti and associates cited hospital mortality of 19% in 221 patients having a dual mechanical prosthesis (11). Bernal et al from Spain reported a mortality of 10.7% after double valve replacement using the Carbomedics valve (15). Brown and coworkers from the NHLBI cited an in-hospital mortality of 14%.9The data for the United Kingdom heart valve registry over the period 1987-1997 estimates early mortality at 9.3% for double valve procedures inclusive of re-operations (16). Our review identified the association of pulmonary hypertension as a strong predictor of both morbidity and mortality. The operative mortality was high (38.1%) in those patients with severe pulmonary hypertension (> 60 mm Hg). Joseph et al also identified increased risk of mortality in patients of pulmonary hypertension with valve replacement (17). Galloway and colleagues in a large series of patients indicated that the operative mortality rose from 5.6% for those in whom the pulmonary artery systolic pressure was less than 60 mm Hg to a striking figure of 38.5% for those in whom the pulmonary hypertension was more than 60 mm Hg (18). We addressed the Tricuspid valve incompetence in our study by doing De Vegas annuloplasty. Grover and associates also have identified the association of tricuspid valve disease as a strong predictor of morbidity and mortality in their analysis (3).

In our series we have routinely preserved the

posterior mitral leaflet. As in a review by Talwar et al there was better long-term systolic function and LV performance both at rest and during exercise. They also demonstrated increased LV end-diastolic pressures after chordal transection and conventional MVR whereas these decreased after MVR with chordal preservation. It preserves LV geometry and function, reduces the operative mortality, improves early and long-term survival and reduces the risk of ventricular rupture (19).

In our study Thromboembolism occurred in 19 patients for a linearized rate of 1.18/100 patientyears. 1 patient had a fatal neurological thromboembolic event. 10 patients had thromboembolic complications with minimal residual neurologic deficit. The other 8 patients had minor thromboembolic episodes with total recovery. Another study by Kopf et al showed that St. Jude Medical valve has a low incidence of thromboembolism, hemorrhagic complications, and valve thrombosis in patients receiving modest doses of warfarin (20). Another report from India using the Björk-Shiley low-profile valve in young subjects cited a similar thromboembolic event occurrence (21).

We adhered to a regime of maintaining INR 1.5 times the normal, which provided sufficient protection against thromboembolic episodes, and bleeding. When and where available we opt to maintain the INR at 2.5 to 3.0. Furthermore, the low incidence of thromboembolic events is presumably related to factors such as inherent difference in coagulable states and competence of the individual managing the patient's anticoagulation. A modest degree of education and counseling to the patient has paid off in the follow-up. The importance of meticulous attention to anticoagulant therapy cannot be over-emphasized. The linearized occurrence of thromboembolic events in this review was 1.18/100 patient-years and anticoagulant-related hemorrhage occurred at a linearized rate of 0.62/100 patient-years. Ten patients on the lowintensity anticoagulant regime carried their pregnancy to term and bore normal children. The oral anti-coagulant therapy was substituted with subcutaneous heparin 5,000 units four times daily during the last trimester. Warfarin embryopathy and intracerebral hemorrhage in the newborn were not encountered in our experience. Salazar and colleagues emphasized that woman with cardiac valve prostheses should be counseled against pregnancy (22).

Corcos and colleagues reported that thromboembolism occurred at a linearized rate of 2.3% per year with Starr Edwards double valve replacement (23). The striking variability in the results using the same prosthetic devices is also known to occur from the experience of other centers. Armenti et al showed an actuarial survival of only 76% and 62% at 3 and 5 years, respectively, (24) using the St. Jude Medical prostheses. Furthermore they also stated that the freedom from combined thromboembolism and anticoagulant related hemorrhage at 15 years was only 40% using the Starr Edwards prosthesis (9). There was no instance of paravalvar leak in the present review. We used horizontal mattress sutures with Teflon pledgets. In 1986 Sethia and coworkers reported on a 14-year experience with the Björk-Shiley prosthetic replacement, noting a high incidence of paravalvar leak (2% per year) and suggesting along with other experts that horizontal mattress sutures provide better valve stability and may eliminate this adverse valverelated complication (25, 26).

The study results have demonstrated an excellent symptomatic improvement and favorable late survival after Double valve replacement, and have established the continued role for this procedure in patients with advanced rheumatic valvulopathy. In view of its remarkable long-term durability, superior thromboresistance and affordability, the Starr-Edwards were the valve of choice for the mitral position although, following its gradual withdrawal from the market, St. Jude mechanical valve was subsequently used. The choice of prosthesis should not be made on the basis of any unsupported promotional claims, but rather on the surgeon's experience, ease of insertion, availability, and cost. An advanced age, a higher NYHA class, preoperative congestive cardiac failure, pulmonary arterial hypertension advanced tricuspid regurgitation, poor left ventricular function, giant left atrium, gross cardiomegaly and associated procedures such as tricuspid annuloplasty or CABG negatively affect late survival. The operative mortality in patients undergoing DVR has improved remarkably over time, with the improvisation of extracorporeal circulation methods, myocardial protection techniques and postoperative management. However, based on the patients' quality of life, anticoagulation therapy represents the most serious problem when using mechanical valves. The development of a superior mechanical valve with an effective anti-thrombotic, and/or a refined bioprosthetic valve with a prolonged life span, would be expected to further improve the quality of the patients' life in the long term.

Limitations

In the present study, the majority of the data were collected retrospectively, and this may have reduced their validity in some cases. However, as they were acquired via personal and telephone enquiries, mailed questionnaires and outpatient clinical visit records, the data were considered satisfactory. An additional problem was the vastness of the Indian continent; the majority of the patients were from remote areas and neither reported back nor was followed up by local physicians in order to continue their prescribed medications. A third point was the inclusion of patients with different types of mechanical prosthesis.

Conclusion

In view of the acknowledged advantage of superior durability, increased thromboresistance in our patient population, and its cost effectiveness the Starr-Edwards ball valve or St. Jude valve is the mechanical prosthesis of choice for advanced combined valvular disease. The low-intensity anticoagulant regimen has offered sufficient protection against thromboembolism as well as hemorrhage.

Acknowledgments

I would like to thank my teachers, colleague's, and my family for their support.

Conflict of Interest

Author Harsh Sateesh Seth declares on behalf of all the contributing authors that we have no conflict of interest.

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