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RETROSPECTIVE ANALYSIS OF PATIENTS WITH RHEUMATIC HEART DISEASE FOLLOWING DOUBLE VALVE REPLACEMENT: OUTCOME AND LONG TERM FOLLOW UP OVER 15 YEAR PERIOD

Cardiology

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KEYWORDS

INTRODUCTION

Valvular heart disease in developing countries resulting from rheumatic fever is disabling and if untreated progresses rapidly and relentlessly leading to congestive heart failure and death. Therefore aggressive policy has been pursued and valve replacement has remained the procedure of choice for advanced valve diseases. Compared to single valve replacement combined mitral and aortic valve replacement represents a major technical challenge. Rheumatic valvulitis is the common cause of multiple valve disease in developing countries like India. Autopsy studies have shown that almost all patients with rheumatic heart disease have some involvement of mitral valve, although it is not always evident clinically (1). Long term follow up of children with rheumatic heart disease suggests that approximately 50% of patients have multivalvular involvement. Mitral and aortic valve disease is the most common combination in rheumatic valvular disease followed by mitral, aortic and tricuspid valve disease (2). Rheumatic heart disease can cause valve stenosis, regurgitations, or combinations of lesions. Mixed lesions producing stenosis and regurgitations are encountered most commonly in both aortic and mitral valves. Simultaneous development of important aortic and mitral valve disease usually results from severe and prolonged attacks and there may be florid myocarditis as well. Pathological changes in cardiac valves requiring surgical correction of more than one valve can result from rheumatic heart disease, age related degeneration and calcification, infective endocarditis, and connective tissue disorders like Marfan syndrome.

Further, the valve dysfunction may be primary, i.e. a direct result of a disease process, or secondary, caused by cardiac enlargement and/or pulmonary hypertension. Surgical management is influenced by the underlying cause of valve dysfunction and, when valves are secondarily involved, the anticipated response to replacement or repair of the primary valve lesion. The consequences the various combinations of diseased valves on left and right ventricular geometry and function frequently are different from that of a single valve disease. Multiple valve operations account for approximately 15% of all operations on cardiac valves; 80% of these operations involve the mitral and aortic positions. The challenges of multiple valve replacement and repair include not only the technical maneuvers of operation but also the identification of associated valve lesions and correct judgment in surgical management. The various etiologies of multiple valve disease occur in certain combinations, and understanding the pathophysiology and pathologic anatomy is necessary to select the best procedure and to optimize early and late postoperative results.When multiple valve replacement is confined to the left ventricle, replacement valves should be chosen from the same class with respect to the need for anticoagulation and projected longevity, valve-related morbidity or late death (3,4).

AIMS AND OBJECTIVES

In this **retrospective study**, we reviewed the patients with rheumatic heart disease, who had undergone **double valve replacement (DVR)** and associated surgeries in our department over the last **fifteen years**.

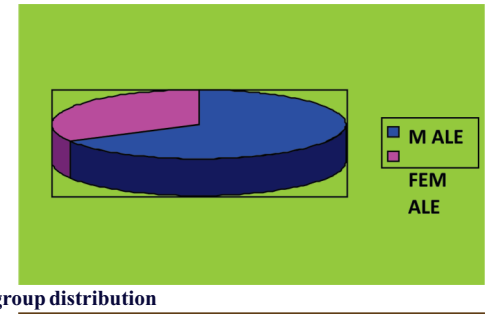
(1) To study the long term survival.
(2) To study the mortality and morbidity.
(3) To identify the risk factors influencing the late morbidity and survival.

STUDY DESIGN AND INCLUSION CRITERIA:

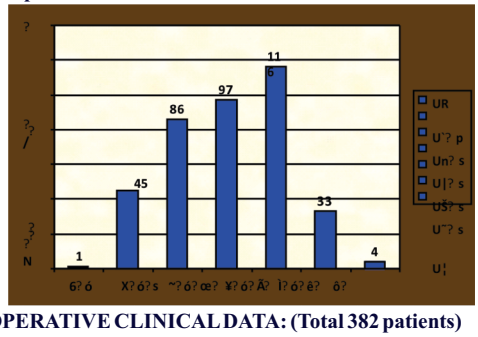
This is a retrospective study of rheumatic heart disease patients who underwent double valve replacement between January 2004 and December 2018 in the Department of Cardiothoracic Surgery, Madras Medical College, Chennai. Out of total 1581 patients with valve replacement surgeries, 451 were double valve replacement of which 398 patients underwent double valve replacement for rheumatic valvular disease. There were sixteen perioperative (30 day) deaths (4.05%). The rest of the 382 patients were evaluated retrospectively for late results, morbidity and mortality (See appendix for the proforma of data collection). Fifty patients were lost in the follow up.

The preoperative characteristics are summarized in **Table No-1** Echocardiography was the diagnostic modality in all the patients. Coronary angiogram was done in patients older than 40 years.

Gender distribution



Age group distribution

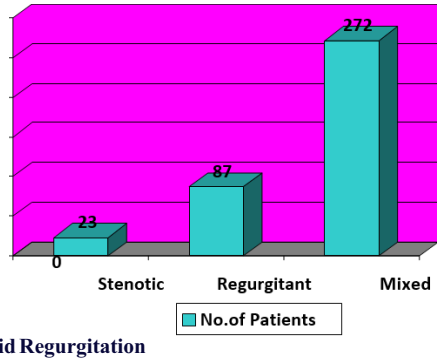


PREOPERATIVE CLINICAL DATA: (Total 382 patients)

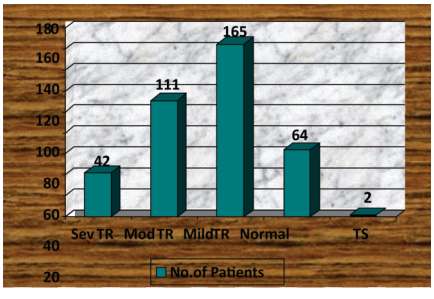
Sl. No	Variable	No. (Percent)
1.	Age	35.7 ± 11.81 (Range 8- 67 years)
2.	Gender Male Female	256 (67.01%) 126 (32.98%)
3.	NYHA class Class II Class III Class IV	108 (28.27%) 181 (47.38%) 75 (9.63%)
4.	History of Rheumatic fever	366 (95.8%)
5.	Penicillin prophylaxis	350 (91.62%)
6.	Duration of Penicillin prophylaxis	13.87 ± 7.51 years (Range 1-35 years)
7.	Type of lesion Purely stenotic Purely regurgitant Mixed	23 (6.02%) 87 (22.7%) 272 (71.2%)
8.	Tricuspid valve involvement Severe regurgitation Moderate regurgitation Mild regurgitation Normal valve Tricuspid Stenosis+ Regurgitation	42 (10.99%) 111 (29.05%) 163 (42.67%) 64 (16.75%) 2 (0.52%)

9.	Duration between onset of symptoms to surgery	53.71 ± 53.90 months
10.	Presence of CCF	53 (13.87%)
11.	Presence of PND	24 (6.28%)
12.	Preoperative Rhythm Sinus Atrial fibrillation	224 (58.63%) 157 (41.09%)
13.	Pulmonary artery hypertension	280 (73.29%)
14.	LA Clot	29/382 (7.59%)
15.	H/O Neurological Deficit	22 (5.75%)
16.	H/O Endocarditis	28 (7.32%)
17.	H/O Renal dysfunction	26 (6.8%)
18.	Previous Procedures Closed Mitral Commissurotomy Balloon Mitral valvotomy Open Mitral Commissurotomy Mitral Valve Replacement Balloon aortic valvotomy	39 (10.2%) 21 (5.49%) 2 (0.52%) 1 (0.26%) 4 (1.04%)
19.	Coronary artery Disease	12 (3.14%)

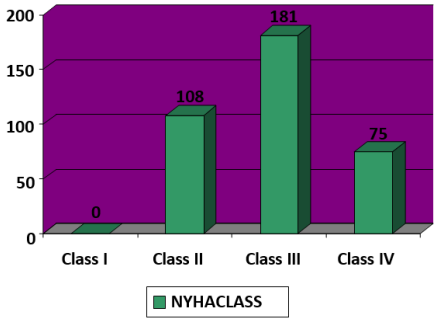
Type of lesion



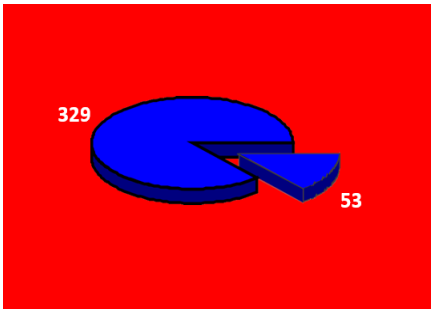
Tricuspid Regurgitation



NYHA class distribution



CCF in the study group



OPERATIVE TECHNIQUE: All the patients were operated by the same surgeon or his immediate associates. Cardiopulmonary bypass was instituted using membrane oxygenator. Moderate systemic hypothermia was employed routinely. Myocardial protection was offered by cold blood cardioplegia through the coronary ostia using modified St. Thomas solution that was repeated every 20-25 minutes. Improved protection of the ventricles was provided by the use of topical hypothermia with saline at 4°C or ice slush.

Aortic valve was excised as a first step through aortotomy. Starr Edwards valve (Model 6120) was used in mitral position in majority (97.9%) of the patients. In the remaining patients St Jude, Carbomedics, Medtronic Hall or Sorin mechanical prosthesis was used. Chordal apparatus was preserved whenever possible. Majority of the patients had Medtronic valve in the aortic position (52.87%) followed by St Jude valve (28.01%). Seventy-three patients had valves like Carbomedics, Omniscience, Omnicarbon, Starr Edwards, Sorin or Bjork- Shiley. Interrupted horizontal mattress sutures with Teflon pledgets were employed for both mitral and aortic valve implants **(Table no.-2).**

In patients with dominant tricuspid incompetence, De Vega's annuloplasty was utilized. In those patients, who had tricuspid stenosis, incisional tricuspid Commissurotomy with De Vega's tricuspid annuloplasty was carried out. Patients with coronary artery disease were offered coronary artery bypass grafting along with double valve replacement **(Table no.-3).**

VALVE DETAILS: (Total 382 patients)

Mitral Position	Patients	Aortic Position	Patients
Starr Edwards	374 (97.9%)	Medtronic Hall	202 (52.87%)
St Jude	5 (1.3%)	St Jude	107 (28.01%)
Carbomedics	1 (0.26%)	Starr Edwards	13 (3.4%)
Sorin	1 (0.26%)	Carbomedics	16 (4.18%)
		Omniscience	33 (8.63%)
		Omnicarbon	3 (0.78%)
		Sorin	4 (1.04%)
		Bjork Shiley	4 (1.04%)

OPERATIVE DATA :(Total patients = 382)

	Variable	No. (Percentage)
1	Type of Surgery DVR DVR+ TAP DVR+CABG DVR+ VSD Closure	345 (90.31%) 29 (7.59%) 7 (1.83%) 1 (0.26%)
2	Emergency Surgery	19 (4.97%)
3	Chordal Preservation Total Partial No	100 (26.17%) 200 (52.35%) 82 (21.46%)
4	CPB time	98.47 ± 22.78min (Range 55-193min)
5	Aortic Cross clamp Time	66.31 ± 12.84 min (Range 42- 123mn)
6	LA clot removal	29 (7.59%)
7	IABP support	5 (1.30%)

POSTOPERATIVE MANAGEMENT:
Judicious use of inotropic agents provided the required therapeutic support. Pressure controlled ventilation support was provided for 24 to 48 hours as per the clinical judgment and investigational parameters.Oral anticoagulation in the form of Acitrom or Warfarin was started from the second postoperative day with a target international normalized ratio of 2.5 to Ecosprin (150mg) was added from the fifth day for added antithrombotic status.

FOLLOW-UP:
Follow up was achieved by yearly out patient clinical visits, mailed questionnaires, telephonic survey and e-mail contact. The completeness of follow up was 86.91%. 13.08% patients were lost in the follow up. Follow up ranged from six months to fifteen years with a mean follow up of 64.78 ± 53.90 months. The total cumulative follow up was 1792.3 patient years. Most of our patients come from far away places in India as well as abroad, making the follow up studies little tedious.

STATISTICALANALYSIS:
All valve related morbidity and complication definitions follow the

guidelines proposed by the ad hoc Liaison Committee for standardizing definitions of prosthetic valve morbidity (57). Data was analyzed using SPSS Windows statistical software 11.0 version (SPSS Inc, Chicago III). All continuous variables are presented as mean ± standard deviation. Events were defined as death, valve related complications. Categorical data was analyzed univariately by Chi-square test. A probability value of less than 0.05 was considered significant. Long term survival and freedom from complications were calculated by the Kaplan-Meier method. Univariate analysis was carried out by log-rank statistics.The factors analyzed as predictors of mortality and late morbidity were age, sex, preoperative NYHA class, type of lesion, status of tricuspid regurgitation, pulmonary arterial hypertension, previous interventions (CMV, BMV), giant LA (>60mm), gross cardiomegaly (CTR>65%), preoperative renal dysfunction, LV dysfunction, type of surgery (DVR and associated procedures), type of aortic prosthesis used and chordal apparatus preservation. Linearized event rates were calculated from the number of events divided by the patient-years of follow up.

HISTORY OF SURGERY INVOLVING MULTIPLE VALVES:

Surgical treatment for combined aortic and mitral valve disease began during early 1950 by closed methods. Likoff and colleagues in 1955, reported about patients who had undergone simultaneous closed repair of aortic and mitral stenosis by Bailey and Glover in Philadelphia (5). Lillehei and colleagues, in 1958, were the first to report simultaneous repair of both valves by open techniques using cardiopulmonary Bypass (6). In 1963, Cartwright and colleagues, first reported simultaneous aortic and mitral valve replacement (7). Starr and colleagues, in 1964, reported patients with multiple valve replacement using mechanical aortic, mitral and tricuspid prostheses (8).

Morphology And Natural History Of Multivalvular Diseases:

In most patients, multivalvular diseases are rheumatic in nature. But, at the same time, each valve may manifest a separate pathologic condition. For example, in a patient of rheumatic aortic valve disease; the mitral regurgitation may be due to infective endocarditis, idiopathic chordal rupture or ischemic papillary muscle dysfunction. When combined aortic and mitral valve disease is caused by rheumatic fever, ten years or more may elapse before the development of significant murmurs and an additional decade or more may elapse before symptom becomes evident. Many patients with clinical evidence of combined disease of mitral and aortic valves have severe and progressive symptoms.

The effect of combined disease on the morphology of left ventricle is of great importance. At one extreme, combined aortic and mitral regurgitation imposes a large volume overload on the left ventricle and the LV size increases severely; the other being aortic and mitral stenosis which results in a small thick walled noncompliant left ventricle.The natural history of combined aortic and mitral valve disease is complicated by variability in dominance of one lesion over the other. When dominant aortic stenosis coexists with mitral stenosis prognosis becomes worse than that of isolated aortic stenosis. Survival is shorter with sudden death being a particular risk. But, when severe aortic and mitral regurgitations coexist, reduction of left ventricular afterload by mitral regurgitation provides a protective effect and patients tend to remain asymptomatic despite advances LV dysfunction (9).The mitral valve is involved almost universally, although the lesion may be so mild that operation is not required until many years after replacement of aortic valve. Double valve surgery in such a patient becomes sequential. Choudhary, et al followed patients with rheumatic heart disease who had mild aortic valve involvement at the time of mitral valve surgery. Freedom from development of moderate or severe aortic stenosis was 75 ± 6%, 62 ± 9%, and 46 ± 11% at 5, 10 and 15 years respectively. But freedom from development of moderate or severe aortic regurgitation was 100%, 97 ± 2% and 87 ± 5% at 5, 10 and 15 years (10).

In the presence of aortic and mitral valve disease repair of stenotic or regurgitant mitral valve can be accomplished with improved long-term survival. But, these results are not favorable in a rheumatic population (9).

CLINICAL FEATURES:

The clinical presentation and natural history of combined lesions is determined by the relative severity of each individual lesion and by the chronicity and order of development. Each lesion produces its characteristic effects on the heart and circulation. The physical findings, rontgenographic and electrocardiographic changes follow the major hemodynamic stress. One valvular lesion may protect a chamber from the full effects of a concurrent lesion. These neutralizing hemodynamic effects ameliorate and often confuse the clinical presentation. Medical, interventional and surgical management of the patient with combined valvular disease is guided by the relative severity of each individual lesion and by the severity of nonvalvular myocardial factors. Severity of all concurrent lesions must be fully appreciated before deciding for or against a specific form of therapy.

In general, the clinical criteria and noninvasive diagnostic tests are the same for mitral and aortic valve disease, whether they are combined or isolated; but additional cardiac catheterization is frequently needed when they are combined. One lesion is usually dominant and may modify the clinical signs of the less dominant one.A frequent problem is assessing the severity of the less dominant lesion; because, if it is mild or even mild to moderate it may not require simultaneous correction. Historically, it was sometimes possible to obtain reliable information on the second lesion during operation by palpating an atrial chamber to detect systolic pulsation by feeling the valve directly with finger before beginning cardiopulmonary bypass. Today, with 2D and colour Doppler echo, the status of aortic, mitral and tricuspid valves are well known before patient enters the operating room. Intraoperative use of transesophageal echocardiography confirms this.

INDICATIONS OF SURGERY:

The approach in a patient with double valve disease is more conservative than that with isolated mitral or aortic valve replacement, because of the higher early and late risks of double valve replacement and the probably increased late morbidity when there are two, rather than one artificial device in situ. Despite early and late risks, outcome of double valve replacement is superior to that which can be accomplished by nonsurgical means. Combined aortic and mitral valve replacement is required when the patient is

(1) Symptomatic (NYHA class III or IV) despite appropriate and intense medical regimen.
(2) Even though the patient is asymptomatic, if there is evidence of extreme left ventricular enlargement or LV dysfunction.
(3) Patients of active rheumatic carditis, with severe aortic and mitral regurgitation and critical heart failure, when the acute episode is not subsiding in spite of maximal medical therapy.

OPERATIVE MORTALITY AND RESULTS:

Current status of operative mortality for mitral, aortic and combined mitral with aortic replacements is 5.7%, 3.5% and 9.4% respectively (11). Double valve replacement with tricuspid annuloplasty increases the mortality rate to 14% (12). Valve replacement has high chance of prolonging the survival of patients with symptomatic mitral and aortic stenosis (13). But, it is difficult to show improved survival in regurgitant lesions.

Replacement of the diseased valve is not the cure. Majority of deaths in patients with prosthetic valve replacement are cardiac related; the predisposing factors being myocardial disease, other cardiac lesions and prosthesis related problems. Age and left ventricular function exert extremely important impact on the long term results. The myocardial damage due to long term pressure and volume overload with associated hypertrophy and fibrosis. Improvement of left ventricular function is more marked after correction of stenotic than regurgitant lesion. Myocardial dysfunction may occur as a result of surgery itself because of necrosis and fibrosis resulting from ischemia during surgery.

With Triple valve replacement, the operative risk rises up to 20%, but the long-term results are considerably better than the natural history of surgically untreated triple valve disease (14).

INFLUENCE OF TYPE OF PROSTHESIS ON LATE RESULTS:

In patients undergoing combined aortic and mitral valve replacement, the effect of different cardiac valve substitutes on late survival and the incidence of prosthesis related complications has not been fully evaluated. When employed for isolated aortic or mitral valve replacement, tissue valves are associated with a low risk of thromboembolism even without anticoagulation treatment. However, this consideration is not applicable for patients with combined double valve replacement. In fact, most patients with two bioprostheses are kept on anticoagulation, and as a result the incidence of thromboembolic episodes and anticoagulation related hemorrhages

are similar to the mechanical valve group. Furthermore, a greater incidence of major hemorrhages is paradoxically greater in bioprostheses group (4). If a patient needs antithrombotic therapy for any reason (i.e., atrial fibrillation or the presence of a mechanical valve in another position), the major advantage of a biological valve is reduced. The long term outcome of patients with double valve replacement is influenced by both prosthesis related complications and severity of preoperative cardiac status of the patient.

The final decision regarding a mechanical valve versus bioprosthesis is based on multiple factors; including patient age, overall longevity of the valve, patient's life style and relative contraindications to anticoagulation. When cardiac surgeons choose prosthesis for valvular replacement, they are required to make a compromise between the excellent durability of approved mechanical prostheses and the greater freedom from thromboembolism and diminished requirement for anticoagulation associated with current bioprostheses.

TYPE OF MECHANICAL VALVES:

Double valve replacements have been performed with various combinations of valves like two mechanical, two bioprostheses or simultaneous one mechanical and one bioprosthetic valve (3).

Starr-Edwards valve, a premier tool in the surgeon's armamentarium for the past three decades is gradually losing the role to new generation valves. Considering the problems of the S-E valves including cloth wear and prosthetic valve noise as described in the foregoing, the superiority of current mechanical valves is not deniable even though the S-E valves are considered to have fulfilled their role as the initial stage mechanical valves. There are still few reports comparing the Starr-Edwards valves and the St Jude Medical valves that are frequently used worldwide. Murday et al. conducted a prospective controlled trial in this regard using the S-E valves and the SJM valves. Excluding that prosthetic endocarditis occurred in the aortic position more frequently with the S-E valves in comparison with the SJM valves; they noted that there was hardly any difference between the two valves in terms of operative mortality and thromboembolism, etc (15). Their result is considered as a very valuable research result. On the other hand, there is another report on the inferiority of the S-E valves to the SJM valves in the prosthetic valve functions regarding thromboembolism, pressure difference in the prosthetic valves, etc. In other words, the opinions are divided as to the assessment of these valves (16).The bileaflet St. Jude and the tilting-disc Medtronic-Hall valves are the most common mechanical valve prostheses currently employed. The short- and medium-term results of patients after isolated aortic and mitral replacement have been analyzed and thus far the clinical and hemodynamic performance of these two prostheses has not been different. It has been suggested that the simultaneous implantation of two valves might magnify differences allowing for identification of a superior prosthesis. Survival itself usually is regarded as an insensitive measure of overall valve performance and relates mainly to the underlying disease and the perioperative status of the myocardium. Another measure of valve performance can be the incidence of thromboembolism, which is a major risk factor for patients having mechanical prostheses. The incidence of thromboembolic complications in the present valvular devices is very similar. This is predominantly due to improved hemodynamic design resulting in a better flow velocity profile, less turbulence, and reduction of stagnant areas; all of which are known to affect the thrombogenicity of the prosthesis. In the Medtronic Hall valve, a more central position of the disc in the open position enlarged the minor orifice, thus reducing stagnation of blood and turbulence. The central-flow design of the bileaflet SJ valve may contribute to its low incidence of thromboembolic events. The results of this study indicate that in the first years after simultaneous implantation in the aortic and mitral position, the performance of the St Jude and the Medtronic Hall prostheses are comparable.

Similarly follow-up of the Carbomedics bileaflet prosthesis demonstrates no structural deterioration, a low incidence of complications, and good hemodynamic performance. Additionally, it has the features of rotatability and protection against deformity of the valve housing, thus avoiding leaflet escape and binding of the leaflets (17).

The Omnicarbon mechanical prostheses are excellent with a low incidence of thromboembolism, no major hemolysis, no structural failure, good cardiac improvement, and a relatively high survival rate. These findings suggest that the Omnicarbon valve design characteristics are satisfactory and that the low incidence of thromboembolic complications may reflect certain design features unique to the Omnicarbon valve (18).

The operative risk is not dependent on the type of prosthesis selected. Presence of previous myocardial revascularization affects this negatively. No documented advantage exists comparing the various valves with regard to the actuarial survival, freedom from valve-related complications, and overall improvement in New York Heart Association functional class.

PREGNANCY:

Pregnancy poses a difficult problem. The disadvantages of the mechanical valves i.e. the complications of Warfarin or Unfragmented Heparin therapy, may affect the patient or the fetus. Warfarin is probably safe during the first 6 weeks of gestation, but there is a risk of embryopathy if Warfarin is taken between 6 and 12 weeks of gestation. Warfarin is also relatively safe during the 2nd and 3rd trimester of pregnancy, but needs to be discontinued and switched over to a heparin compound several weeks before delivery. Several studies strongly suggest that unfractionated Heparin or Low molecular weight Heparin therapy is safe for the fetus but poses a high incidence of thromboembolic complications, including fatal valve thrombosis. Thus, Warfarin is more efficacious than unfractionated Heparin for thromboembolic prophylaxis of women with mechanical heart valves in pregnancy, but with an increased risk of embryopathy. There are still insufficient grounds to make definitive recommendations about optimal antithrombotic therapy in pregnant patients with mechanical heart valves because properly designed studies have not been performed. The disadvantage of a bioprosthesis is the relatively higher rate of early structural valve deterioration. The final decision on the anticoagulation regimen requires discussion with the patient regarding the risks and benefits of each approach. For any anticoagulation, intensive monitoring is required (19).

OPTIMAL OF ANTITHROMBOTIC THERAPY FOR PROSTHETIC HEART VALVES:

All patients with mechanical valves require anticoagulation therapy. The risk of embolisation is greater with the valve in the mitral position than in the aortic position. Other risk factors for increased risk of embolisation include atrial fibrillation, LV dysfunction, clotting disorder, and prior embolic events. With either type of prosthesis or valve location, the risk of emboli is higher in the first three months after valve insertion, reflecting lack of endothelialization of the newly implanted valve and delay in achieving therapeutic anticoagulation in the early days after operation (20). In most patients with a mechanical prosthesis, the target international normalized ratio (INR) is between 2.5 and 3.5. Aspirin is recommended for all patients with prosthetic heart valves: Aspirin alone (75 to 100 mg per day) in patients with bioprostheses and no risk factors or aspirin (75 to 100 mg per day) combined with Warfarin in patients with mechanical heart valves and high-risk patients with bioprostheses. In high-risk patients who can not take Aspirin, the addition of Clopidogrel to Warfarin therapy should be considered (19).

INFECTIVE ENDOCARDITIS:

Surgery is indicated in patients with life-threatening heart failure or cardiogenic shock due to surgically treatable valvular heart disease with or without proven infective endocarditis, if the patient has a reasonable prospect of recovery with satisfactory quality of life after the operation. In the setting of acute infective endocarditis, surgery should not be delayed when heart failure exists. Indications for surgery for infective endocarditis in patients with stable hemodynamics are less clear. Surgery is recommended for patients with annular or aortic root abscess, those with infections resistant to antibiotic therapy, and those with fungal endocarditis. Prosthetic valve endocarditis and native valve endocarditis caused by *Staphylococcus aureus* are almost always surgical diseases. Early surgery in mitral valve endocarditis caused by virulent organisms (such as *Staphylococcus aureus* or fungi) may make repair possible. Whenever possible, mitral valve repair should be performed instead of MVR in the setting of active infection because of the risk of infection of prosthetic materials. Aortic valves may often be repaired as well if there are leaflet perforations, and this is preferable to AVR for the same reasons.

Incremental Risk Factors For Death After Surgery:

(1) DOUBLE VALVE REPLACEMENT :

Double valve replacement itself is an incremental risk factor for death

compared to isolated mitral or aortic valve (9). This is evident early after operation and particularly in intermediate and long term follow up, when many deaths occur because of increasing tricuspid regurgitation progressing to right atrial enlargement, hepatomegaly and finally, cardiac cachexia. The relative roles of decreasing LV performance, increasing pulmonary vascular resistance and decreasing RV compliance in this late deterioration after DVR are under consideration.

(2) Mitral Valve Replacement Rather Than Repair :
One stage aortic and mitral valve operations may not involve replacement of both valves. When they do not; the early risks is less and intermediate and long term results being better (21). According to Gillinov, et al hospital mortality is 5.4% with mitral valve repair in comparison to 7% with Mitral valve replacement. The 15 year survival is 46% with mitral valve repair, but 34% with MVR. Mitral valve repair with aortic valve replacement provides significantly better event-free survival than double valve replacement, but without a better actuarial survival. Reoperation rate is higher in the mitral valve repair and aortic valve replacement group whereas thromboembolic complications are more common in the double valve replacement group. Because of better event-free survival in patients undergoing mitral valve repair and aortic valve replacement, some surgeons favor the repair of mitral valve whenever possible, provided it is feasible and that the appropriate skill level and experience are available to perform this procedure successfully (19). Patients with pliable mitral leaflets without subvalvular disease should be good candidates for mitral valve repair in double valve replacement. However, moderately or severely deteriorated mitral valves, such as those with leaflet calcification, thickened leaflets, or mitral valves associated with severe subvalvular disease, should be replaced (22).

A higher INR is recommended for patients undergoing mitral valve replacement or DVR compared with isolated aortic valve replacement. It is also well known that long-term survival after prosthetic valve replacement is directly related to the hazards of anticoagulation. Also, the actuarial survival is not reduced despite a higher reoperation rate in these patients; because in the present era, the reoperations are safe and do not significantly increase the risk of death. Thus, in few subsets of patients who are unable to adhere to a more intensive anticoagulation regimen and do not come for regular follow-up or require lower INR, there may be a survival advantage of mitral valve repair and aortic valve replacement compared with DVR, despite a higher reoperation rate (23).

But according to Masaki, et al (24) although both DVR and aortic valve replacement with mitral valve repair resulted in good survival, DVR with mechanical valves should be the procedure of choice for the majority of patients, because of higher freedom from valve failure and similar rate of thromboembolic complications as compared with AVR with Mitral valve repair. Mitral valve repair should not be performed in patients with rheumatic disease because of the high incidence of late failures.

(3) PREVIOUS OPERATIONS:
About 15% patients undergoing first time simultaneous aortic-mitral valve replacement have previous valve operation. This does not increase the risk associated with DVR (9).

(4) CHOICE OF REPLACEMENT DEVICE:
This does not affect the long term survival. According to Caus, et al survival at 5, 10 and 15 years is similar (25). Although reoperations are more common in bioprosthetic group, the thromboembolic complications are more common in the mechanical valve group.

(5) AGE AT OPERATION:
With more patients now being operated in their eighth and ninth decades of life, old age is probably a risk factor for early post operative death in the current era. It is clearly a risk factor for death late postoperatively, especially for patients older than 70 years at the time of operation (26,27). Gillinov and colleagues have demonstrated 20% survival advantage for patients having operation at age fifty years versus those having operation at age 65 years.

6.left Ventricular Function And Preoperative Functional Status:
The more advanced the heart failure and thus the functionaldisability, the greater the early and late risks of death. Emergency operations are particularly high risk early postoperatively (27). Muller et al found that LVejection fraction less than 50% increased the risk of all deaths. Moderate and severe LV dysfunction was a risk factor for all deaths in late hazard phase (21,26).

(7) LEFT VENTRICULAR ENLARGEMENT:
Greater LV enlargement is a powerful risk factor for death late postoperatively. Because of large volume overload, combined severe mitral and aortic regurgitation has a strong tendency to produce marked LV enlargement. The outcome after operation for patients with severe LV enlargement and this combination of valve lesion is very poor with 5, 10 and 20 year survival of 64%, 37% and 9%, respectively.

(8) VALVE PATHOLOGY:
Patients having multiple valve operations for rheumatic heart disease have greater survival benefit than those having surgery for nonrheumatic heart disease. Stanley John reported survival of 85% at 15 years and 82% at 24 years in patients with mean age of 33 years having DVR for rheumatic heart disease (28). Gillinov reported that patients with rheumatic heart disease had greater predicted survival benefit than patients with nonrheumatic disease and repair of the mitral valve further improved the survival. Muller et al reported survival of 56% at 15 years and linearized death rate of 2.3% per year in a group of older patients (mean age 56 years).

(9) CARDIAC COMORBIDITY:
Early mortality is increased by the presence of tricuspid regurgitation, necessitating associated annuloplasty or valve replacement (29,30). Ischemic heart disease requiring concomitant coronary artery bypass grafting, especially left main coronary artery stenosis increases early mortality (27,31). Elevated preoperative pulmonary vascular resistance affects late survival (26). Atrial fibrillation is a risk factor for death in the late hazard phase because of added risk of embolism and heart failure related to atrial dysrrhythmia.

(10) NONCARDIAC COMORBIDITY:
Renal disease increases risk of death with elevated blood urea nitrogen adding risk in the early phase after operation. Dialysis at the time of operation increases the early relative risk by nine fold. Diabetes mellitus also increases the risk (26,27). Hepatic failure increases the risk of operation from 9.2% to 26% (26).

APPROACH TO TRICUSPID VALVE DISEASE IN PATIENTS UNDERGOING DOUBLE VALVE REPLACEMENT:
Tricuspid regurgitation may be present in 10% to 50% of patients with mitral or combined mitral and aortic valve disease (32). Despite this high frequency, criteria for the selection of patients requiring tricuspid valve surgery concomitant with left-sided valvular surgery remain controversial. Intraoperative assessment by digital palpation of regurgitant jet or by injection of saline into the right ventricle is unreliable, because hemodynamic conditions under anesthesia (lowered pulmonary and systemic vascular resistance) may cause apparent disappearance nonreversible tricuspid regurgitation (32). Intraoperative transesophageal echocardiography with 2D and color flow examination seems to solve this problem (33).There are two basic points about tricuspid valve interventions. First and the more important issue is when and how to decide on tricuspid valve repair or replacement. All conservative approaches should be first tried. After repair, 2 to 3+ tricuspid insufficiency is acceptable and does not necessitate tricuspid valve replacement, because the size of the tricuspid annulus decreases rapidly after valvular operations of left side of the heart.The second point concerns the selection of the prosthetic valve. According to the recent literature there is a trend toward new generation bileaflet mechanical valves because of their hemodynamic characteristics and durability, and some studies indicate that these valves have better long-term results in the tricuspid position. However, articles with no statistically significant difference between the two groups are also published. According to Kaplan, there is no significant difference between the two groups in terms of early mortality, re-replacement, and midterm mortality (34).

Functional Status After Double Valve Replacement:
Most surviving patients have considerably improved symptoms following DVR. But by 10 years after operation, only 51% are in NYHA class I and 34% are in class II. The proportion of surviving patients who are in NHYA class I gradually declines as follow-up becomes longer, reaching only 35% by 20years. Stanley John and colleagues reported 72% in functional class I, 25% in class II and 3.1% in class III at median 8.5 years of follow up after aortic and mitral valve replacement for rheumatic heart disease (28).

Causes Of Death After Double Valve Replacement:

Early Death	Late Death
(A) Cardiac	**(A) Cardiac**
- Low cardiac output	- Congestive failure
- Refractory arrhythmia	- Arrhythmia
- Endocarditis	- Endocarditis
- Anticoagulation related bleeding	- Anticoagulation related bleeding
(B) Noncardiac	- Acute Myocardial infarction
- Air embolism	- Valve thrombosis
- Sepsis	**(B) Noncardiac**
- Respiratory insuffiency	- Renal failure
	- Respiratory

COMPLICATIONS OF PROSTHETIC VALVES:

1) Hemorrhagic complications of anticoagulation
2) Systemic embolism
3) Endocarditis
4) Hemolytic anemia
5) Mechanical dysfunction
(a) Obstruction Thrombotic obstruction
(b) Insuffiency Valve stuck in open position
6) Paravalvular leak

COMPLICATIONS OF ANTICOAGULANT THERAPY:

Prevalence of hemorrhage related to anticoagulant therapy following double valve replacement is similar to that of mitral valve replacement. Freedom from bleeding events at 5, 10 and 15 years are 89%, 81% and 73% respectively in patients with mechanical prostheses. A recent meta-analysis shows the linearized rate of important hemorrhage to be 1-2% per year (35). Many hemorrhagic episodes are relatively minor and do not require hospitalization or transfusion. Miller and colleagues found that about one third of hemorrhagic events are fatal (36).

THROMBOEMBOLISM:

Thromboembolism is a common complication of prosthetic heart valves, especially for patients with mechanical heart valves. Stroke and other thromboembolic complications occur at the rate of 1-5% per year.Thrombosis and embolism may occur for several reasons. The prosthetic valve may cause turbulence, shearing stress, stagnation or eddy currents that may damage cellular elements and release factors that evoke the normal clotting reactions. Valve materials themselves may cause thrombosis. Atrial fibrillation adds to the risk. Obstruction of prosthetic heart valves may be caused by thrombus formation, pannus ingrowth, or a combination of both. The cause may be difficult to determine and requires knowledge of the clinical presentation and findings on echocardiography, including transesophageal echocardiography. Emergency surgery is indicated for patients with NYHA functional class III-IV heart failure or patients with a large thrombus burden. Fibrinolytic therapy for a left-sided prosthetic valve obstructed by thrombus is associated with significant risks (cerebral emboli in 12% to15%) but may be used in patients at high risk for surgery or those with stable hemodynamics and a small clot burden (19).

Bioprosthetic valves are inherently less thrombogenic than mechanical valves, particularly in aortic position. The thromboembolism incidence is low unless there is atrial fibrillation, large left atrium, left atrial clots at the time of surgery or history of prior thromboembolism. The incidence of thromboembolism for bioprosthetic valves appears to be highest in the first three months after implantation.

Freedom from thromboembolism after primary combined aortic and mitral valve replacement is similar to that after isolated mitral valve replacement (37). The use of bioprostheses in both positions does not eliminate late postoperative thromboembolic episodes (38). According to Muller et al, freedom from thromboembolism at 5, 10 and 15 years are 89%, 74% and 66% respectively (27). Meticulous attention should be paid to regulation of anticoagulation as 60% of the thromboembolic and 80% of the anticoagulation-related hemorrhagic events occur, when the prothrombin time is subtherapeutic and supratherapeutic, respectively (3).

HEMOLYSIS AND ANAEMIA:

With two mechanical prostheses, hemolysis and valve thrombosis are greater than with one. Chance of hemolysis is more in aortic position in comparison to mitral position. Caged ball valves cause more notorious than tilting disc ones in this regard; the causes being turbulent and eccentric blood flow as well as RBC compression by the ball when it comes in contact with the sewing ring. The risk of hemolysis is greater when the orifice through which the RBC traverses is small; example-paravalvular leak and stenotic valve.

The hallmarks of prosthetic valve hemolysis are hemosiderinuria, schistocytosis, reticulocytosis, increased levels of serum LDH and absence of serum haptoglobin. Valve replacement may be needed if the anemia is refractory treatment and causes high output failure.

HEMODYNAMIC FEATURES OF PROSTHETIC HEART VALVE:

Currently available prosthetic valve designs are such that there is minimal if any regurgitant flow, but all are stenotic as in vivo valve area is less than normal aortic and mitral valve. After implantation the effective orifice area further diminish secondary to tissue ingrowth and endothellialisation. The resting transvalvular gradient may not be severe, but with exercise severe gradients develop. Starr Edwards valve is intrinsically stenotic because of its design; with blood flowing around the occluder. Tilting disc valves have smaller transvalvular gradient because of their central flow design. The Doppler measurement overestimates pressure gradient compared with catheter assessment.

DURABILITY OF PROSTHETIC HEART VALVES:

Ideally, a substitute cardiac valve should last a patients life time. Mechanical valves last in to second to third decades after implantation. In Caged ball valves, the mechanical valve malfunction is caused by chemical and physical alteration in the occluder; such as increase or decrease in diameter, grooving, cracking, fragmentation, fluid lakes in the core of the occluder, ball variance. In Disc valve, the disc movement results in uneven distribution of stress on the contacting parts. If disc wears to such an extent that it can not cover the primary orifice, regurgitation occurs.

The durability of porcine bioprostheses has been shown to be influenced by patient age at operation, being considerably longer in patients older than 60 years age. Also the risk of reoperation for structural valve deterioration in patients with double valve replacement is greater than for those with single valve replacement (39). Recently Banbury from Cleveland clinic has demonstrated the maintenance of hemodynamics at up to 17 years follow up in patients with Carpentier Edwards Perimount bioprosthesis (40).

EVENTS CONSIDERED FOR CALCULATING EVENT-FREE SURVIVAL:

(1) Early death
(2) Late death
(3) Structural valve deterioration
(4) Significant stenosis or regurgitation
(5) Prosthetic valve thrombosis
(6) Paravalvular leak
(7) Hemolytic anemia related to valve lesion
(8) New focal or global neurologic deficit
(9) Transient ischemic attack
(10) Peripheral embolic event
(11) Bleeding events
(12) Infective endocarditis
(13) Reoperation

FOLLOW UP OF PATIENTS WITH PROSTHETIC HEART VALVES:

All patients with valve replacement need regular follow up. Patients with mechanical valves require life long chronic anticoagulation. This is accomplished by dosing oral coumadin to a desired INR. Intensity of anticoagulation is determined by the age of the patient, type and number of valves and position of the valve. Patients with bioprosthetic valves require anticoagulation for three months after surgery or longer if they have atrial fibrillation, history of systemic embolisation or intracardiac clot. To minimize both embolic and bleeding complications in patients with mechanical heart valves, the monitoring of coumadin treatment should be optimized, and the optimal intensity should be sought.

Each time a patient is seen; the physician should assess the overall medical status and seek evidence of prosthetic valve complications.He should auscultate for the valve click, if needed check in fluoroscopy for the rocking of the prosthesis or limitation of the occluder.

Two dimensional and Doppler echocardiography are the most reliable

techniques for evaluation of prosthetic heart valves. Scapira, et al found that M-mode echo provided a 67% diagnostic accuracy rate in patients evaluated for bioprosthetic valve dysfunction. But 2-D echo was significantly better with 97% diagnostic accuracy. Useful echo features include diastolic fluttering of the mitral leaflets, which suggests prosthetic aortic insufficiency. Normal septal motion suggests prosthetic regurgitation as the septum usually moves paradoxically for up to six years after implantation.

PATIENT PROSTHESIS MISMATCH:

Prosthesis-patient mismatch (PPM) is present when the effective orifice area of the inserted prosthetic valve is too small in relation to body size. Its main hemodynamic consequence is to generate higher than expected gradients through normally functioning prosthetic valves. PPM is common (20–70% of aortic valve replacements) and has been shown to be associated with worse hemodynamic function, less regression of left ventricular hypertrophy, more cardiac events, and lower survival (59). Moreover, as opposed to most other risk factors, PPM can largely be prevented by using a prospective strategy at the time of operation. The projected indexed effective orifice area should be systematically calculated at the time of the operation to estimate the risk of PPM and, if PPM is anticipated, alternative options should be considered in light of the patient's overall clinical condition and risk to benefit ratio.The best way to avoid PPM in the mitral position would be to repair rather than to replace the valve. Nonetheless, a significant proportion of mitral valves cannot be repaired and need to be replaced. Unfortunately, the options for preventing PPM in the mitral position are much more limited than in the aortic position. In particular, no alternative technique exists to implant a larger prosthesis, and the implantation of a homograft or of stentless prosthesis is technically more demanding and associated with poor long-term durability. Hence, the preventive strategy can be oriented only toward the implantation of a prosthesis having a larger EOA for a given annulus size (42).

Time Related Changes In Ventricular Size And Function Following Double Valve Replacement:

Following double valve replacement the left ventricular size and ejection fraction return to near normal level about one year after surgery. In the patients with regurgitant lesions, there is a period of early postoperative decline in ejection fraction. The role of chordal preservation in during double valve replacement for combined mitral and aortic regurgitation has never been properly investigated. But, according to Skudicky et al, chordal preservation does not have a significant impact in the outcome of rheumatic patients undergoing double valve replacement (43).

REOPERATIONS:

Any patient treated with a bioprosthesis may need reoperation for valve replacement if his or her life expectancy exceeds that of the valve. Need for reoperation is usually determined by the durability of repair or replacement device in the mitral position. Reoperation is done less frequently when mechanical prostheses are used. Freedom from reoperation at 15 years is more than 90% with mechanical device but only 25% with bioprostheses (9). The choice of replacement or repair of the mitral valve affects the procedure chosen for the aortic position.Patients requiring anticoagulant therapy for atrial fibrillation or deep vein thrombosis, derive greatest benefit from the durability of mechanical prostheses. Multivariate analysis has demonstrated that the risk of reoperative mortality after structural degeneration of bioprosthesis is three fold higher in patients older than 65 years (44). Bioprosthetic valves are reserved for older patients with limited life expectancy in view of the structural deterioration.

The age of the patients ranged from 8 to 67 years with the mean age at the time of operation being 35.7 ± 11.81 years. There were 256 males and 126 female patients (Male/Female ratio= 2.03:1). Sixty percent patients were younger than 40 years of age (229/382). 95.8% patients had history suggestive of rheumatic fever and 91.62% patients were on Penicillin prophylaxis. The mean duration of Penicillin prophylaxis was 13.87± 7.51 years.Sixty seven percent patients presented with NYHA Class III and IV symptoms. Either dyspnea or palpitation or both were the commonest presenting symptoms in the majority patients (73.29%). The valvular lesions were both stenotic and regurgitant in 71.2% patients (n=272). Forty percent patients had moderate to severe tricuspid regurgitation. Two patients had tricuspid stenosis.

Majority patients were in sinus rhythm with 41.09% patients being in atrial fibrillation. 73.29% patients had pulmonary arterial hypertension diagnosed either by echocardiography, cardiac cath studies or intraoperatively. 29 patients (7.59%) had left atrial clot detected by preoperatively echocardiography or intraoperatively. History of neurological deficit was present in 22 (5.75%) patients. Twenty-eight (7.32%) patients had history of infective endocarditis preoperatively detected by blood culture, echocardiography or positive culture from excised valve specimen. Renal dysfunction manifested by serum Creatinine was present in 26 patients (6.8%).39 patients (10.2%) had undergone previous closed mitral commissurotomy with 16.05 ± 6.11 years mean duration between closed mitral commissurotomy and double valve replacement. Three patients had multiple closed mitral commissurotomies. 5.49% (n=21) patients had previous Balloon Mitral valvotomy with mean duration between BMV and surgery being 5.8 ± 4.14 years. Two patients had Open mitral commissurotomy and one patient had previous mitral valve replacement. Four patients had previous balloon aortic valvotomy.The left atrial size was more the 6cm in 31.67% (n=121) patients. The cardiothoracic ratio was more than 65% in 36.64% patients. Coronary angiography was done in patients above more than 40years of age and 12(3.14%) patients were found to have coronary artery disease. 83.76% patients had normal left ventricular function, 13.87% were in moderate LV dysfunction and 2.35% were in severe LV dysfunction.

Most of the patients underwent elective surgery, but 29 patients were operated in semi-emergency basis. 345(90.31%) patients had double valve replacement only, 29 (7.59%)had both double valve replacement as well as tricuspid annuloplasty, whereas 7(1.83%) patents underwent double valve replacement with coronary artery bypass grafting. 52.35% patients had partial chordal preservation and 21.46% patients did not have chordal preservation. The mean cardiopulmonary bypass time was 98.47 ± 22.78 min and mean aortic cross clamp time was 66.31 ± 12.84 min. Five patients required intra aortic balloon pump support in the postoperative period.In the mitral position Starr Edwards was the valve of choice (97.9%). In the aortic position Medtronic Hall was the commonest valve (52.87%) followed by St Jude valve (28.01%). The less common valves in the aortic position were Starr Edwards (3.4%), Carbomedics (4.18%), Omniscience (8.63%), Omnicarbon (0.78%), Sorin (1.04%) and Bjork Shiley(1.04%). **(Table- 2)**

EARLY MORTALITY:

CAUSES OF EARLY DEATH (Total 16 patients) :

	Variable	No. (Percent)	
1	Cardiac		
	Low cardiac output	8	(50%)
	Refractory arrhythmia	2	(12.5%)
	Endocarditis	1	(6.25%)
	Anticoagulation related bleeding	1	(6.25%)
2	Non cardiac		
	Air embolism	1	(6.25%)
	Sepsis	2	(12.5%)
	Respiratory complications	1	(6.25%)

The hospital mortality (defined as death occurring within 30 days of operation) was 4.05% (n=16). Postoperative low cardiac output was the commonest cause, others being refractory arrhythmia, endocarditis and anticoagulation related bleeding. The noncardiac causes were air embolism, sepsis and respiratory complications. **(Table- 4).**110 patients had postoperative complications as presented in **Table- 5.** The commonest was rhythm abnormality (28.18%) including fast atrial fibrillation, ventricular arrhythmia, bradycardia and AV block. Twenty-three patients (20.9%) required pericardiostomy for pericardial effusion, whereas in eight patients (7.27%) it resolved with conservative management. Four patients required permanent pacemaker insertion for complete heart block. There were three incidences of postoperative blood culture positive incidences, but all resolved with long-term antibiotics treatment. Postoperative renal dysfunction was seen in three patients, all of whom recovered with conservative management. There were less common complications like Hepatic dysfunction (n=1), Gastrointestinal bleeding (n=3) and Respiratory complications (n=3).

Table No. 5: Post Operative Complications (total= 110):

	Name	No.(Percent)	
1	PE requiring pericardiostomy	23 (20.9%)	
2	PE with conservative management	8	(7.27%)

3	Neurological deficit	5	(4.54%)
4	Complete Heart block	4	(3.63%)
5	Rhythm abnormality	31 (28.18%)	
6	Endocarditis	3	(2.72%)
7	Wound infection	13 (11.81%)	
8	Renal dysfunction	4	(3.63%)
9	Hepatic dysfunction	1	(0.9%)
10	Respiratory complication	3	(2.72%)
11	Gastrointestinal bleeding	3	(2.72%)
12	Femoral pseudo aneurysm	1	(0.9%)
13	Urinary tract infection	11 (10%)	

The follow up ranged from six months to fifteen years with a mean follow up period of 64.78 ± 53.90 months. Total cumulative follow up period was 1792.3 patient years.The completeness of the follow up was 86.91%. 13.08% were lost in the follow up. There were 29 late deaths (8.73%) (Table- 6). The commonest causes of late death was found to be congestive cardiac failure; and arrhythmia as well as valve related causes such as endocarditis, anticoagulation related hemorrhage and valve thrombosis. The noncardiac causes such as renal failure, pneumonia and unknown reasons were responsible for death in four patients.

Table No.6: CAUSES OF LATE DEATH: (Total= 29)

Variable	No. of patients (Percent)	
(1) Cardiac		
CCF	15 (51.72%)	
Arrhythmia	4	(13.7%)
Endocarditis	3	(10.34%)
Anticoagulation related hemorrhage	2	(6.8%)
Valve thrombosis	1	(3.44%)
(2) Non cardiac		
Renal failure	1 (3.44%)	
Respiratory complications	1 (3.44%)	
Unknown	2 (6.8%)	

FUNCTIONAL CLASS:

At the time of the follow up study, 77.7% patients were in NYHA class I, 17.16% in class II, 2.71% in class III and 2.4% in class IV status. Thirty-eight patients (11.44%) had left ventricular dysfunction. Atrial fibrillation was present in 46.98% patients in comparison to the 41.09% patients of the preoperative status. Twenty-one patients (6.32%) patients had significant (more than 50mmHg) gradient across the aortic valve and 68 patients (21.79%) patients had gradient between 30-50mmHg. Moderate to severe tricuspid regurgitation was present in 21.08% of the follow up patients

Table No.7: FOLLOW UP DATA: (n=332)

Variable	No.(Percent)	
(1) Post op. functional class		
I	258	(77.7%)
II	57	(17.16%)
III	9 (2.71%)	
IV	8 (2.4%)	
(2) Rhythm		
Sinus	176	(53.01%)
Atrial Fibrillation	156	(46.98%)
(3) LV Ejection Fraction		
>50%	294	(88.55%)
35-50%	29	(8.73%)
<35%	9 (2.71%)	
(4) Aortic valve gradient		
< 30 mmHg	243	(73.19%)
31-50 mmHg	68	(21.79%)
>50 mmHg	21	(6.32%)
(5) Post op TR		
Severe	21	(6.36%)
Moderate	49	(14.75%)
Mild	187	(56.32%)
No	75	(22.59%)

ANTICOAGULATION RELATED HEMORRHAGE:

One patient died of major bleeding in the post operative period and two died in the varying period follow-up for a linearized rate of 0.16.per 100 patient years. Nonfatal major bleeding events requiring treatment occurred in six patients for a rate of 0.33 per 100 patient years. However, 35 patients had minor bleeding incidences not needing medical attention

(Table- 8 and Table-9).

THROMBOEMBOLISM:

One patient died due to valve thrombosis during the follow up for a linearized rate of 0.05 per 100 patient years. Two patients required thrombolysis of the Starr Edwards mitral prosthesis and another had redoreplacement of prosthetic St Jude aortic prosthesis. One patient with thrombosis of the Carbomedics mitral prosthesis declined any interventions and is in NYHA class III status at the time of follow up study. However, there were 19 minor thromboembolic episodes for a linearized rate of 1.06 per 100 patient years. Seven patients had thromboembolic episodes with mild residual neurologic deficit and 12 others recovered completely **(Table-8 and Table-9)**.

PROSTHETIC VALVE ENDOCARDITIS:

There was one death due to prosthetic valve endocarditis in the early postoperative period. Three patients died in the follow up period for a linearized rate of 0.16 per 100 patient years. Six patients (0.33 per 100 patient years) developed infective which was successfully managed with appropriate antibiotics and they are in NYHA class I status at the time of follow up study **(Table-8 and Table-9).**

Table No 8: FOLLOW UP COMPLICATIONS: (Total = 113)

	Variable	No. of patients	
1	Anticoagulation related hemorrhage	41	(36.28%)
	Minor	35	(30.97%)
	Major requiring hospitalization	6 (5.3%)	
2	Thromboembolic episodes	19	(16.81%)
3	Permanent disability	12	(10.61%)
4	Valve related complications		
	Valve thrombosis	4 (3.5%)	
	Anemia	31	(27.4%)
5	Post op Infective endocarditis	6 (5.31%)	

SURVIVAL ANALYSIS:

Survival curves (Kaplan- Meier) were constructed according to log rank Univariate analysis of significant variables. Parameters influencing survival and late morbidity were analyzed using Pearson Chi-square test.

Figure 1 depicts the survival trend over a follow up period of 15 years. The median survival was 170 months (95% Confidence Interval). **Figure 2** represented preoperative NYHA class on survival rate (p=0.001). **Figure 3** shows effect on age at the time of surgery on the long-term event free survival (p<0.05). **Figure 4** depicts the effect of preoperative congestive cardiac failure on survival (p=0.0008). **Figure 5** shows role of preoperative tricuspid regurgitation on long-term survival (p=0.0001). The role of pulmonary arterial hypertension on survival is demonstrated in the Figure 6 (p=0.0075). **Figure 7** shows the effect of preoperative left ventricular ejection fraction on survival (p<0.05). The effects of Previous CMV and BMV on the long-term results are shown in Figures 8 and 9 respectively (p=0.9089 and 0.9907). **Figure 10** represents the effect of preoperative large Left atrial size on late survival (p<0.05). **Figure 11** shows the effect of high cardiothoracic ratio on late survival (p<0.05).

The **figure 12** shows the late survival status after double valve replacement alone and with of associated surgeries (p<0.05). **Figure 13** represents the effect of chordal preservation on late survival (p=0.2335). The **figures 14 and 15** show the effects of preoperative renal dysfunction and infective endocarditis on late survival (p>0.05). The effect of type of aortic prosthesis on long-term survival is represented by **figure 16**. **Table-9** shows

the linearized rates of various complications in the follow up period. **Table no-10** shows cross-tabulation of the type of aortic prosthesis against the late development of aortic trans-prosthesis gradient. The Pearson Chi square test shows a significant association of transprosthesis gradient (p=0.008) in patients with aortic Starr Edwards, Carbomedics and Omniscience valves.

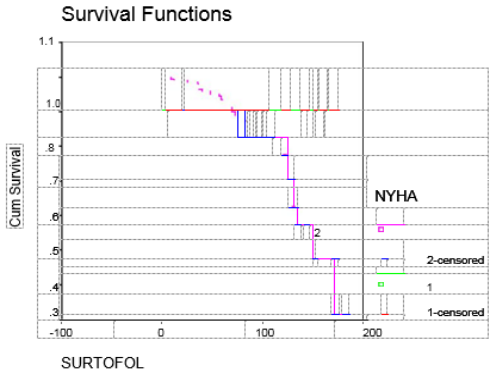


Figure 2) Effect of preoperative NYHA class on long term survival (1= NYHA class I and II,

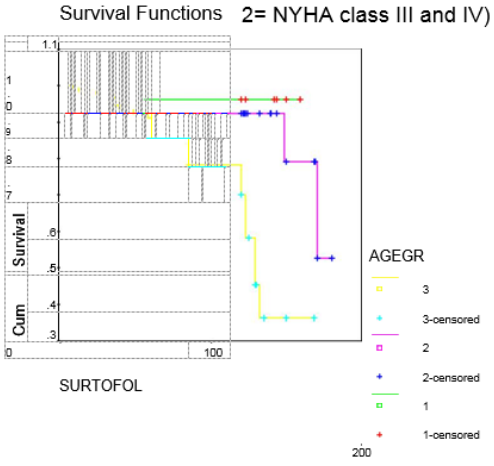
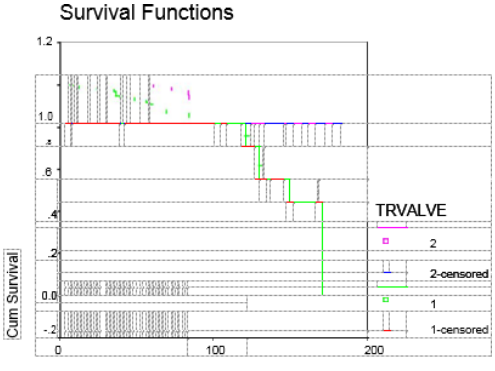
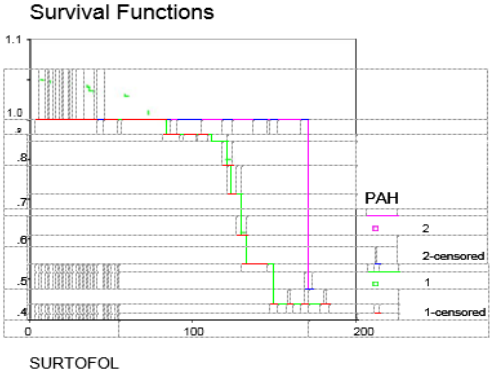


Figure- 3) Effect of age on event free long term survival (1= Less than 20 yrs, 2=21-40 years, 3= More than 40 years)



(Figure 4) Effect of preoperative CCF on event free long term survival (1= CCF, 2= Absent)



(Figure 5) Effect of preoperative tricuspid regurgitation in survival (1= Moderate to severe TR, 2= Mild or no TR)

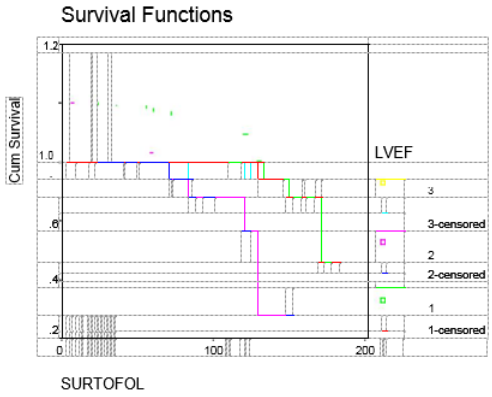
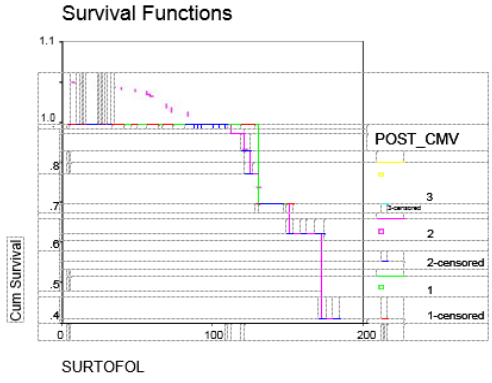
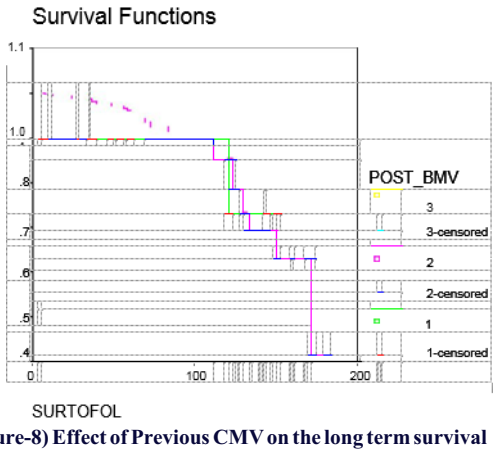


Figure-6) Effect of Pulmonary Arterial Hypertension on Survival (1= PAH, 2= Absent)



(Figure-7) Effect of preoperative left ventricular ejection fraction on survival (1= EF>50%, 2= EF 35-50%, 3= EF<35%)



(Figure-8) Effect of Previous CMV on the long term survival

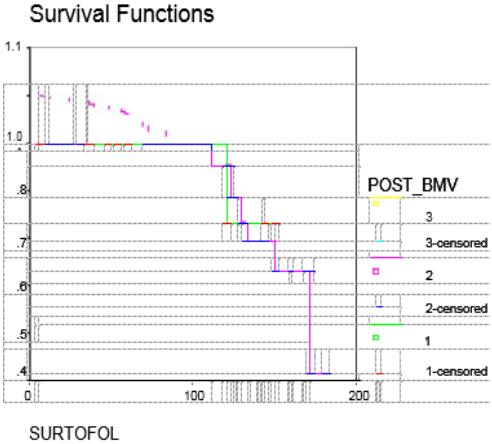


Figure-9) Effect of Previous BMV on the long term survival

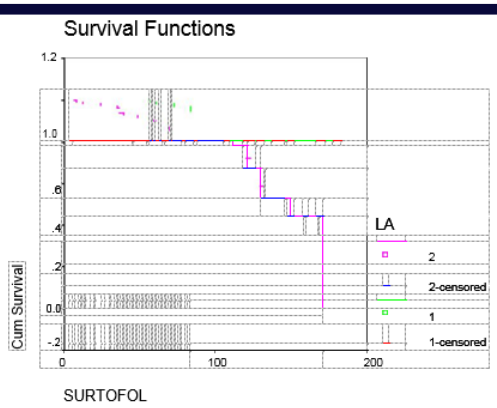


Figure-10) Effect of preoperative Left atrial size on late survival (1= LA size ≤ 60mm, 2= LA size > 60mm)

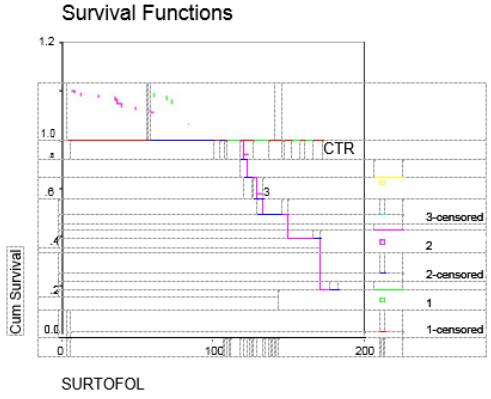
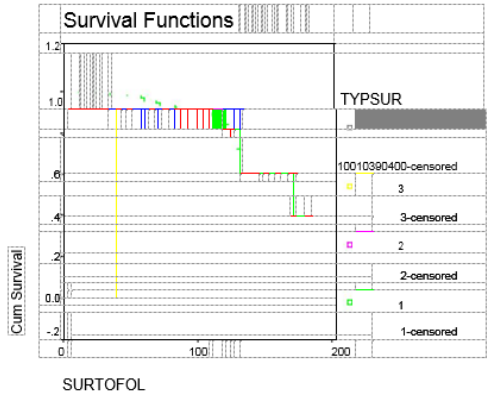
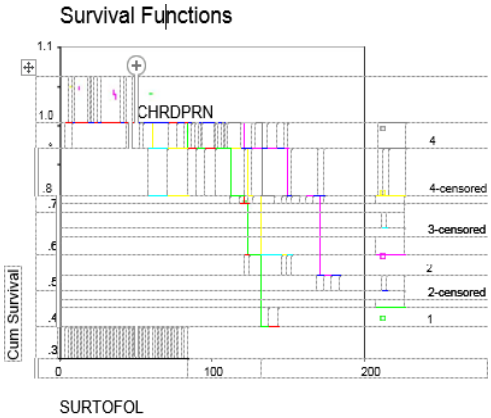


Figure-11) Effect of Cardiothoracic ratio on late survival (1= CTR < 65%, 2= CTR>65%)



(Figure-12) Effect of type of surgery on late survival (1= DVR, 2= DVR+TAP, 3=DVR+CABG



(Figure-13) Effect of chordal preservation on late survival (1= Absent, 2= Part, 3= Most, 4= Total chordal preservation)

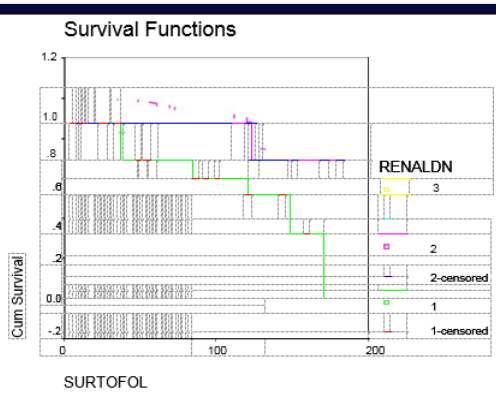


Figure-14) Effect of preoperative renal dysfunction on late survival (1= Renal dysfunction {Sr. Creat. > 1.6}, 2= Normal

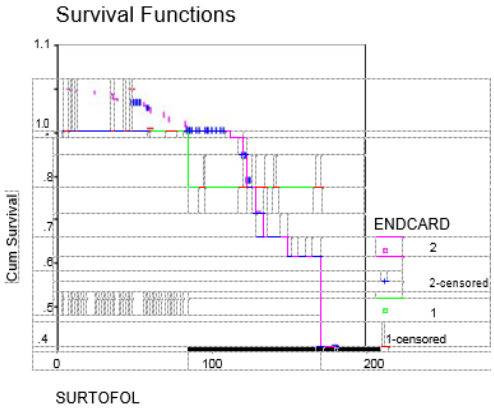


Figure-15) Effect of preoperative infective endocarditis on late survival (1=No endocarditis, 2= Endocarditis

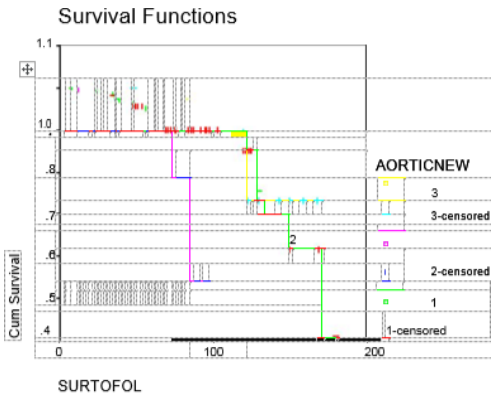


Figure-16) Effect of type of aortic prosthesis on long term survival (1= Medtronic Hall, 2= St. Jude, 3= Others

Table No. – 10: (Cross tabulation showing type of aortic prosthesis against Prosthetic aortic valve gradient)

	Ao. V. Grdt <30mmHg	Ao. V. Grdt >30mmHg	Total
Medtronic Hall	125 (51.7%)	47(52.2%)	172 (51.8%)
St Jude	83 (34.3%)19	(21.1%)	102(30.7%)
Others	34 (14.0%) 24	(26.7%)	58 (17.5%)
Total	242 (100.0%)	90 (100.0%)	332 (100.0%)

Operative risk of candidates for multivalvular operations is no longer substantially higher than that of patients with isolated valve replacement. Bioprosthetic valves are often reserved for older patients in view of their structural deterioration. We endorse the views of Bortolotti and associates that mechanical prostheses perform better in the long term owing to their superior durability (47). Majority of our patients were less than 40 years and cause of valvular disease was rheumatic in all. Hence our choice was for mechanical device, because of their better long-term performance owing to superior durability. In light of earlier experience from our institute (45,46,47) and with the acknowledged advantage of long-term durability and increased

thromboresistance; the Starr Edwards ball valve device was our choice in 97.9% of mitral positions.

For aortic position our choice was mostly low profile Medtronic Hall and St Jude prosthesis. Akins in 1996 has reported 10-year event-free survival with Medtronic Aortic prosthesis to be 72.4% (47). In a retrospective review of late results with Starr-Edwards, St. Jude Medical, Omniscience, Carbomedics, and Medtronic-Hall mechanical valves; the Medtronic-Hall valve had the best freedom from combined thromboembolic and anticoagulant-related bleeding complications (48). St Jude valves have remained a reliable asset for past 30 years with incidence of thromboembolism at 0.20–3.5% per patient-year, valve thrombosis at 0.06–0.12% per patient-year and hemorrhage related to anticoagulation therapy at 0.14–3.5% per patient year (49,50). According to Andrew et al, performance of both Medtronic Hall and St. Jude are equivalent and either can be recommended confidently for simultaneous double valve replacement (51).Although some studies have shown better event-free survival in patients with mitral valve repair with aortic valve replacement, there is no survival benefit (23). Since most of our patients belonged to younger age group, and reoperation was always a problem due to economic constraints, we did not attempt mitral valve repair with aortic valve replacement. In our study, the mean age of the study population was 35.7 ± 11.81 years and only four patients were aged more than 60 years.

The operative risk of double valve replacement has decreased considerably and remains between 5-12% (25). Our hospital mortality of 4.05% compares favorably with other reported series. Bernal in 1998 reported a mortality of 10.7% after double valve replacement using Carbomedics valve (52). Brown and coworkers cited an in-hospital mortality of 14% (3). The major predictor of increased risk continues to be the advanced preoperative functional disability and other valve related complications. Simultaneous insertion of two prostheses has also been demonstrated to be an incremental risk factor for late death (9).

In our study population late death occurred at 8.73%. The long-term standard survival (exclusive of hospital mortality) at 5, 10 and 15 years are 92%, 78% and 45% respectively with a mean survival of 153 months. In a review by Stanley john, the late death rate was 10.1% and the actuarial survival was 90.4%, 85.6%, 84.4%, and 82.4% per year at 5, 10, 20, and 24years, respectively (28). Brown in 1993 reported the 10-year survival of 50% following a mean 6.3 years follow up after double valve replacement with mechanical valves (3). Bortolotti reported 60% survival at 10 years follow up following double valve replacement and the actuarial survival at 14 years was 39% (4).

In our study 67% patients were in NYHA class III-IV functional class and it was found that high preoperative functional status was significantly associated with increased long-term mortality ($p<0.05$). Higher age at time of surgery was found to be significantly affecting the late survival ($p<0.05$), a finding that has been reported by Andrew in study population of 122 patients (51).

Preoperative pulmonary arterial hypertension was found to be significantly affecting the long-term survival ($p<0.05$). This corroborates with the findings of Galloway, who in a large series of patients indicated that pulmonary hypertension more than 60 mmHg adversely affects operative mortality as well as long-term survival (29). In our series, 40% (n=153) patients had moderate to severe tricuspid regurgitation, of which 29(7.59%) patients underwent De Vega's tricuspid annuloplasty. It was found that moderate to severe tricuspid regurgitation was associated with increased long-term hazard ($p<0.05$). Grover and associates have identified a similar association of severity of tricuspid valve disease as a strong predictor of mortality and morbidity in their analysis (53). Giant Left atrial size and cardiomegaly greater than 65% were found to be significantly affecting the late survival ($p<0.05$). Long-term survival is also significantly dependent on the preoperative left ventricular ejection fraction ($p<0.05$). Mueller has identified similar effect of ejection fraction on survival (27).

However, previous closed mitral commissurotomy or Balloon mitral valvotomy did not significantly affect the late results ($p>0.05$). We noticed that; need for coronary artery bypass grafting or tricuspid annuloplasty along with the double valve replacement adversely affects the long-term results ($p<0.05$). Akins, in their follow up study of patients of double valve replacement with coronary artery bypass grafting found the actuarial survival to be 60.7% at 72 months (31).In our patients, the chordal preservation policy was adopted as per the status of calcification and deformation of the mitral valve apparatus. We concur with Lillehei that the preservation of leaflet along with the chordopapillary attachment may be beneficial both early and in the long term (54). But, according to Skudicky, et al, chordal preservation does not have a significant impact in the outcome of rheumatic population undergoing double valve replacement (43). In our experience, chordal preservation did not significantly affect the late survival ($p=0.2335$).

The low occurrence of thromboembolic episodes at the linearized rate of 1.06 per 100 patient years in our patient population is noteworthy. A similar rate of thromboembolic events has been shown from our institute in a review of valve replacement in patients less than 20 years of age (46). In another report, Iyer cited similar thromboembolic event occurrence using Bjork-Shiley low profile valve (55). In a report, in 1986, Stanley John cited a low incidence of thromboembolism of 1.6/100 patient years in a follow up of aortic valve replacement patients utilizing Starr Edward prosthesis (47). Thromboembolism occurred at a linearized rate of 2.3% per year as reported by Corcos and colleagues with SE double valve replacement (32). We adhered to an anticoagulant regimen with a target international standardized ratio between 2.5 to 3.5. All patients as well as the relatives were explained about the importance of the anticoagulant and the role of regular INR check up with subsequent dose adjustment. The regimen was optimized to offer sufficient protection against thromboembolism on the one hand and bleeding on the other. In the last decade we have included Aspirin 150mg to all our patients of mechanical prosthetic valves. American Heart Association advocates the use of Aspirin or Clopidogrel in all patients of prosthetic heart valve.

The anticoagulation related hemorrhage requiring medical attention occurred at a linearized rate of 0.33 per 100 patient years. This compares favorably with the 2.6% linearized rate of bleeding events reported by Mueller in 1998 (58) and 0.8% rate as reported by Bortolotti and colleagues (4).Three patients on oral anticoagulation regime carried their pregnancy to term and delivered normal children. The oral anticoagulant was substituted with subcutaneous heparin in the last trimester. There was no incidence of Warfarin embryopathy in our experience. Salazar and colleagues have emphasized that women with cardiac valve prostheses should be counseled against pregnancy (56).There was only one episode of paravalvular leak in a patient with prosthetic mitral valve endocarditis. We believe that the interrupted horizontal mattress sutures with Teflon pledgets play an important role in its prevention. Bortolotti and colleagues noted an incidence of 0.67% ± 0.2% in a study of double valve replacement using mechanical prostheses (4).

At the end of this study with follow-up information from 332 patients, 77.7% were in NYHA Class I and 17.16% in class II symptoms. Only 5.1% were in class III-IV symptoms. These results are similar to that reported by Stanley John and colleagues (28).

LIMITATIONS OF THE STUDY:

(1) Most information were collected retrospectively, a process that may reduce the validity of some data. We used personal and telephone enquiry, mailed questionnaires as well as outpatient clinical visit records. In view of this and the high rate of follow-up, we believe our data to be satisfactory.

(2) Inclusion of patients with different type of mechanical prostheses. The risk factor analysis did not show valve type as a significant risk factor; thus the recruitment of patients appears to be more important than recruitment of one type of valve.

CONCLUSION :

Advanced age, higher NYHA status, preoperative congestive cardiac failure, pulmonary arterial hypertension, advanced tricuspid regurgitation, poor left ventricular function, giant left atrium, gross cardiomegaly and associated surgeries like tricuspid annuloplasty or coronary artery bypass grafting negatively affect the late survival. Post CMV and post BMV status, preoperative renal dysfunction or infective endocarditis, chordal preservation and type of aortic prosthesis do not significantly affect the late survival.

This study demonstrates the excellent symptomatic improvement and favorable late survival after double valve replacement and establishes a continued role for the procedure in patients with advanced rheumatic valvulopathy. In view of the remarkable long term durability, superior

thromboresistance and affordability; Starr Edwards valve had been our choice for mitral position. But, with its gradual withdrawal from the market, other valves are coming into picture. In aortic position, both St Jude Medical and Medtronic Hall valves reflect similar clinical and hemodynamic performances as well as valve related complications. The choice of prosthesis should not be made on the basis of unsupported promotional claims but rather should be based on surgeon's experience, ease of insertion, availability, and cost. The operative mortality in patents with double valve replacement has remarkably improved in the lapse of time with the improvisation of the extracorporeal circulation methods, myocardial protection techniques and postoperative control. However, in view of the quality of life of the patients, the anticoagulation therapy is the most serious problem after replacement with mechanical valves. The development of superior mechanical valves with antithrombotic features as well as newer bioprosthetic valves with prolonged life span is expected to further improve the quality of life in the long term.

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