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Ujjwal K. Chowdhury *

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Review Article

Long-Term Performance of Mechanical and Biological Prostheses in Young Rheumatics aged below 45 years undergoing Combined Mitral and Aortic Valve Replacements: A Propensity-Matched Study

Ujjwal Kumar Chowdhury [1*], Sushamagayatri B [2], Maroof A. Khan [2], Sundeep Mishra [1], Nagasai Manjusha [2], Shikha Goja [2], Shradha Gupta [2], Shweta Sharma [2]

[1] National Institute of Medical Sciences and Research, Rajasthan, Jaipur.

[2] All India Institute of Medical Sciences, New Delhi.

***Corresponding Author:** Dr. Ujjwal K. Chowdhury, M. Ch, Diplomate NB, Director Professor, Department of Cardiothoracic and Vascular Surgery, National Institute of Medical Sciences and Research, Rajasthan, Jaipur, Shobha Nagar, Jaipur-Delhi Highway, Jaipur-303121, Rajasthan, India.

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Abstract

Background and Aim: We compared 23-year composites of valve-related reoperation, morbidity, and mortality following combined mitral and aortic mechanical and bioprostheses in young rheumatics aged <45years.

Methods: Retrospective comparative analysis of valve-related reoperations and survival data were performed from 498 consecutive propensity matched patients undergoing either bioprosthetic MVR (Group I, n=249) or mechanical MVR (Group II, n=249) between 1998 and 2022.

Results: The median age was 33 (IQR: 27-40) and 33 (IQR: 28-39) years for Group I and II respectively. The median follow-up was 134 months (IQR: 99.5-178.5) with 5281.8 patient-years data in both biological and mechanical arm. Bioprosthetic arm exhibited lesser cumulative mortality (3.6% vs 4.8%, SMD= -0.18, p=0.01). Hazard regression for mortality included (HR, 95% CI) included preoperative CHF on inotropes and ventilator 9.84 (4.54, 18.64), p<0.001, renal failure requiring peritoneal/hemodialysis 11.64, (6.57, 20.64), p<0.001, atrial fibrillation 3.83 (1.63, 8.98), p<0.002, reoperation for thrombosed mechanical and degenerated bioprostheses 5.38, (3.09, 9.35), p<0.001, previous operation 3.53, (1.93, 6.45), p<0.001, poor left ventricular function 4.25, (2.29, 7.88), p<0.001, prolonged aortic clamp time 3.84, (2.19, 6.78), p<0.001, and prolonged CPB time 2.69, (1.84, 8.68), p<0.001. Propensity score matching did not exhibit any difference in reoperation between two groups (Group I vs Group II: 13.6% vs 17.6%, SMD= -0.110, p=0.21). At a median follow-up of 134 months (IQR: 99.5-178.5) months, actuarial survival was 92.3%±0.02% (group I vs 96.6%+0.01%) and there was no difference between the groups (p=0.90).

Conclusions: Bioprostheses are an acceptable alternative to mechanical prostheses in young rheumatics aged <45 years undergoing mitral and aortic valve replacements unwilling for mechanical valve, redo surgeries, life-long anticoagulation, and those desirous of pregnancy.

Keywords: bioprostheses; cerebral hemorrhage; mechanical prostheses; mitral valve replacement; propensity score matching; thromboembolism

Introduction

Current consensus guidelines of the American Heart Association and European Society of Cardiology, uniformly recommend either type of prosthetic valve for patients aged 60 to 70 years and mechanical prosthesis for patients less than 60 years. [1-6] These recommendations are based on

the results of 4 randomized controlled trials that demonstrated no significant difference in late survival. [5-9Two of these trials compared mechanical and bioprosthetic valve models implanted in 1970s and 1980s. – [8-10] The other 2 trials included patients undergoing aortic valve replacement. [4,5] Contemporary data are limited to small single center studies. [10-12]

Valve replacement in young adults entails a choice between a mechanical prosthesis with risks of anticoagulation-related bleeding/thrombosis versus bioprosthesis necessitating eventual reoperation. Over the last 20 years, there is a shift away from a clear cut age limit towards patients' wish and lifestyle considerations. [5-10] This may be related to the enhanced durability of new-generation bioprostheses, improved outcomes of redo surgery, or development of valve-in-valve transcatheter valve implantation. [5-10]

In patients requiring combined aortic and mitral valve replacements (MAVR), the valve prosthesis of choice in patients younger than 60 years has traditionally been mechanical prostheses. [11-23] Prosthesis selection is determined by several competing factors, including the elevated hazard for structural deterioration of biologic prostheses in younger patients, anticoagulation related complications with mechanical prostheses, complexity and difficulty in performing redo valve replacements for bioprosthetic failure and the growing trend towards avoidance of warfarin in younger patients. [11-23]

The results of bileaflet and Starr Edwards mechanical prostheses with single valve surgery have been extensively reported. [11-23] There is limited documentation, however, on the late (15 years) and very late (> 20 years) composites of complications, namely, valve-related reoperations, morbidity, and mortality following combined mitral and aortic valve replacements using mechanical and bioprostheses in young rheumatics. [11-31]

In 2018, we published our preliminary observations on the result of mitral valve replacement (MVR) using Carpentier-Edwards PERIMOUNT bioprosthesis in young rheumatics aged less than 40 years. [13] Subsequently in 2021, we published long-term propensity-matched outcomes after bioprosthetic MVR in 260 young rheumatics. [20] We also compared 22-year composites of valve-related reoperations, morbidity and mortality following mitral mechanical and bioprostheses in young rheumatics aged less than 45 years. [32]

The primary objective of this study was to compare the very late-term (20 years) outcomes of composites of valve-related complications in young rheumatics aged less than 45 years, undergoing combined bioprosthetic or mechanical mitral and aortic valve replacements (MAVR). The secondary objectives were to: i) compare the short- and long-term hemodynamic performance of prostheses and structural valve deterioration of multivalvular bioprostheses, and ii) ascertain the duration and intensity of anticoagulation required in bioprosthetic group in immediate and late postoperative period and before re-replacement of degenerated bioprostheses, and iii) determine whether the risk of reoperative mortality for structural deterioration of bioprostheses was greater than the cumulative rate of lethal thrombotic and haemorrhagic complications in patients with mechanical prostheses.

Materials and Methods

This retrospective study conforms to the principles outlined in the declaration of Helsinki and was approved by the Institutional Ethics Committee.

Patient selection criteria

Choice of prosthesis for MAVR was determined by patients' preference and surgeon's judgement based on patients' age and comorbidities, bleeding risk, life-style, and compliance to anticoagulation. Young rheumatics aged less than 45 years undergoing combined MAVR using either mechanical (St. Jude Medical or ATS Medical) or bioprosthesis (St. Jude Epic or Carpentier-Edwards PERIMOUNT) with or without tricuspid annuloplasty were included in this descriptive case series. Patients undergoing MAVR using prosthesis other than mentioned above, non-rheumatic etiology, and concomitant cardiac surgery were excluded. Young females desirous of pregnancy, patients coming from remote rural areas making follow-up and anticoagulant monitoring practically difficult, contraindications to use of anticoagulation, thrombosed mechanical mitral and/or aortic prosthesis, and patients' choice were indications for bioprosthetic MAVR (Figures 1A, 1B).

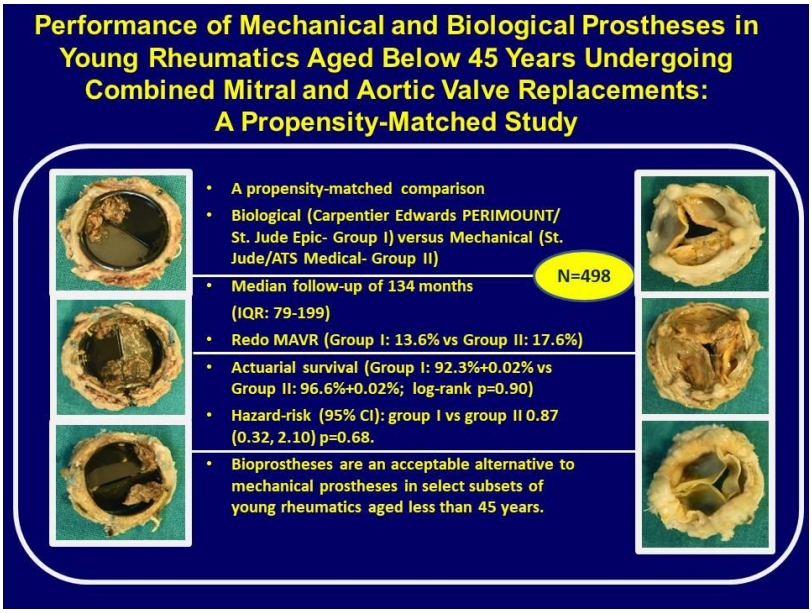


Figure 1A: Graphic display (n=498) showing long-term valve-related actuarial survival of Group I and Group II patients.

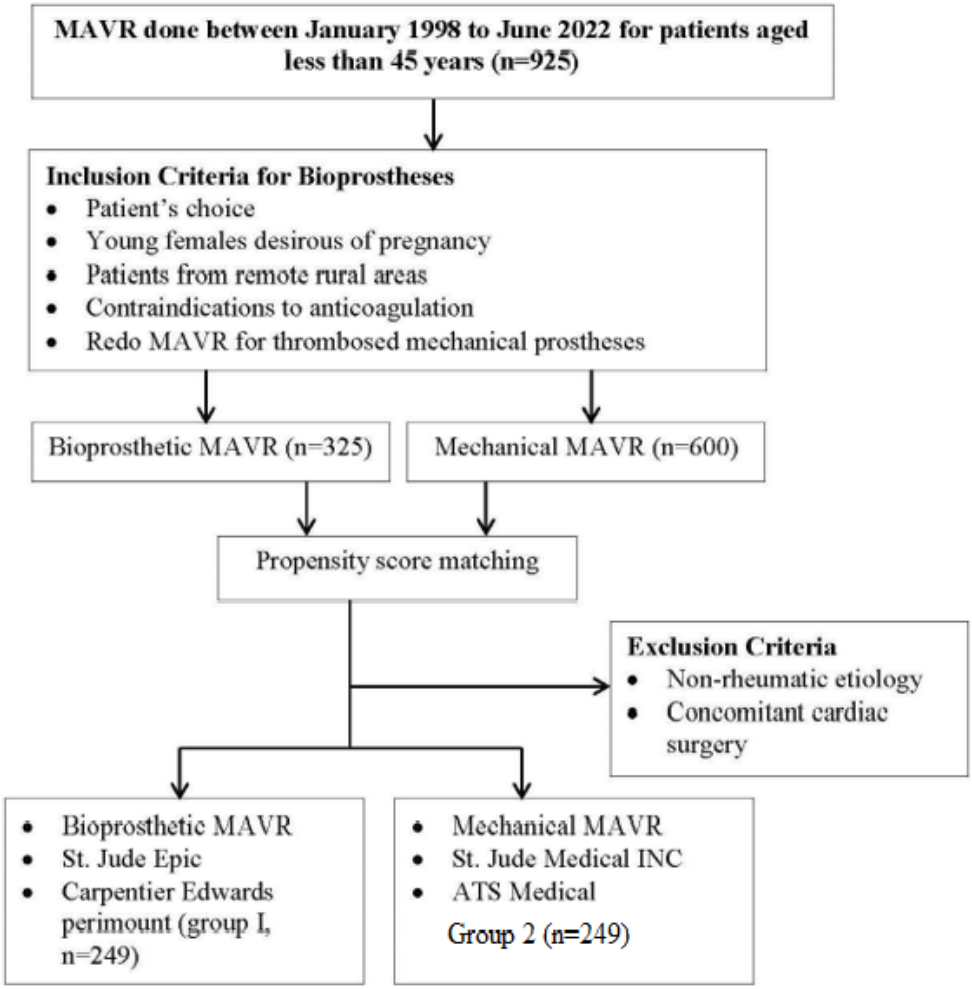
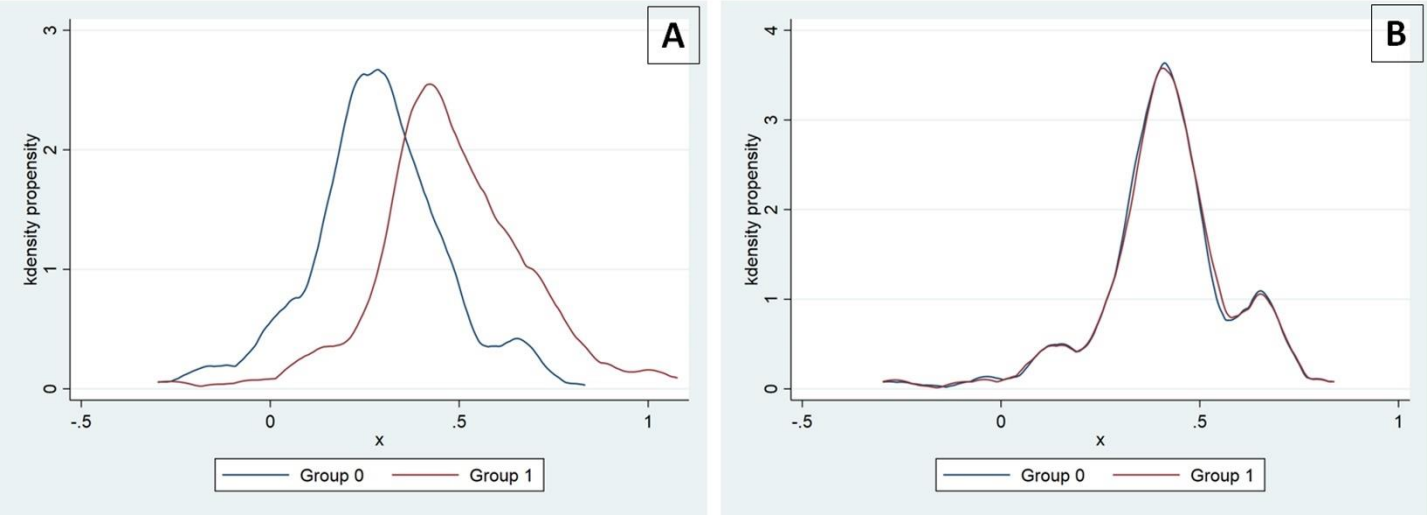


Figure 1B: Consort diagram showing inclusion and exclusion criteria for young rheumatics aged <45 years undergoing MAVR using either biological (Group I) or mechanical (group II) prostheses.

In patients with mitral stenosis and a small left ventricle, the low-profile Epic bioprosthesis was chosen over PERIMOUNT prosthesis. There were no specific criteria for selection of mechanical prosthesis. We retrospectively reviewed medical records of young rheumatics aged less than 45 years who underwent either a bioprosthetic (Group I) or mechanical (Group II) MAVR from January 1998 to June 2022 by the corresponding author.

A total of 925 aortic and mitral prostheses [325 bioprostheses; (Carpentier-Edwards PERIMOUNT model 6900 (Edwards Lifesciences, Baxter Healthcare Corporation, Irvine, CA, USA, n=105; St. Jude Epic Porcine bioprosthesis, n=220)] and 600 mechanical prostheses (St. Jude Medical, n=300; ATS Medical, n=300) were implanted.

Patients were matched one-to-one according to age, sex, preoperative thromboembolism, presence of atrial fibrillation (AF), advanced New York Heart Association (NYHA) status, preoperative congestive heart failure (CHF) requiring inotropes and ventilation, Left ventricular ejection fraction (LVEF) <0.25, size of left atrium (LA) >65 mm, and presence of LA clot according to optimal match technique. A power calculation estimated that approximately 233 patients per group were required to have a minimum of 80% power to detect a 10% difference in mortality between the two groups with a 2-sided of 0.05 Table 1, Figures 2A, 2B).



Figures 2A, 2B: Propensity density graph before (2A) and after (2B) propensity score matching.

Six-monthly follow-up data included clinical history, NYHA class assessment, and valve-related events. [33-35] If 6-monthly evaluation was not possible after repeated attempts to contact the patient, it was considered missing. If two consecutive evaluations were missing, the patient was considered lost to follow-up. Transthoracic two-dimensional (2D), colour flow and Doppler echocardiography was performed according to the American Society of Echocardiography criteria within first six months and then annually. [34,36]

In a developing country such as ours, where recognition of the need for information is a powerful asset in patient care, we spend time relating to three facets in the follow-up of patients: (1) instilling insight into the problem of chemoprophylaxis in preventing recurrent attacks of rheumatic fever (penicillin injections once every 3 weeks remain necessary until the age of 45 years); (2) advice regarding awareness about prevention of bacterial endocarditis particularly in relation to dental problems; and (3) education and counseling regarding low-intensity anticoagulation and the necessity for meticulous attention to its control. Follow-up was achieved by yearly outpatient clinic visits, mailed questionnaires, contact with the referring physicians, and use of social workers for direct patient contact.

Definitions

Outcome measures

Valve-related mortality included death caused by thrombosis, thromboembolism, hemorrhage, structural valve deterioration, non-structural dysfunction, or prosthetic valve endocarditis and death related to reoperation for a valve related complication including sudden unexplained, unexpected deaths. Valve-related mortality was defined either as early/perioperative (i.e. in hospital or within 30 days of operation) or late (after 30 days) attributed to the explanted valve. [6,33,34],

Valve-related morbidity was defined as permanent valve-related impairment as a result of permanent neurologic or other functional deficits caused by valve thrombosis, thromboembolism, hemorrhage, structural valve deterioration, non-structural dysfunction, prosthetic valve endocarditis, or reoperation.

Late reoperations were defined as reoperations that occurred more than 30 days after implant. Reoperations were defined as any subsequent mitral or aortic valve replacements. Reoperations that did not involve mitral or aortic valve replacement were excluded.[20]

Structural valve deterioration was diagnosed as clinically relevant valvular stenosis or insufficiency by Doppler echocardiography, reoperation, or necropsy. Examples included cuspal perforation, tear, thickening, calcification, stiffness, stretching, wear and abrasions, thinning, leaflet escape, stent creep, or stress fracture. Structural deterioration that resulted from endocarditis, paravalvular leak, or thrombosis was not included in the structural valve deterioration category. [4,6]

Stroke was defined as any cerebrovascular accident documented during the index hospitalization as well as any subsequent hospital admission in including transient ischemic attacks). [4,6]

A major bleeding event was defined as any subsequent hospital admission in which the principal diagnosis was intracerebral hemorrhage, hemopericardium/cardiac tamponade, gastrointestinal hemorrhage, hematuria, hemarthrosis, hemoptysis, or retinal hemorrhage. Bleeding events were classified as major (i.e. requiring hospital admission or transfusion, of intracranial location, or causing death), or minor (i.e. prospectively recorded but not major).4,6 Heart failure was defined as per previous publications as the composite end-point of (i) New York Heart Association (NYHA) functional class 3 or 4 for more than 4 consecutive weeks, corroborated with physical examination, chest X-Ray, ECG and echocardiography findings when available, or (ii) death where the primary or main contributing diagnosis was heart failure.[4,34,36]

Anticoagulation

Patients with bioprosthetic MAVR were started on warfarin and aspirin (100mg/day) on first postoperative day maintaining an INR between 2.0 and 2.5. After discharge, patients were reviewed at one week, one month, three months, then subsequently at six months interval. Anticoagulation was stopped in patients with bioprosthetic MAVR and normal sinus rhythm at 12 weeks of follow-up.

Patients with a preoperative LA/left atrial appendage (LAA) clot, history of recent thromboembolism, aneurysmal LA, AF, and degenerated bioprosthesis were maintained on anticoagulation with an INR between 1.5 and 1.8. All patients received aspirin life-long, unless contraindicated.

Patients undergoing mechanical MVR received life-long warfarin and aspirin (100mg/day) maintaining INR between 2.5 to 3.5. The three study end-points were the composites of valve-related complications (mortality, morbidity and reoperations), explantation due to thrombosed mechanical prosthesis and structural valve deterioration (SVD).

Selection of a balanced cohort

Table 1 shows the significant imbalances in baseline characteristics between patients treated with mechanical and biological mitral and aortic prostheses before matching. To assemble a balance cohort of patients with mechanical and biological mitral and aortic prostheses, we used propensity-score matching method on those with mechanical and biological prostheses on measured baseline characteristics. For this purpose, we estimated propensity scores for treatment (group) for each of the 925 patients using multivariable logistic regression model. Group was used as the dependent variable and baseline characteristics namely- LA reduction, aortic cross-clamp time, thromboembolism, dyspnoea, previous operation, LVEF, chordal preservation, type of mitral valve disease were included as covariates to find the best optimal match set. Here, model's effectiveness are not important because propensity-score based models are sample-specific adjusters and are not intended to be used for out-of sample prediction, discrimination or estimation of coefficients. The efficacy of propensity-score models is best assessed by estimating post-match absolute standardized differences between baseline covariates that directly quantifies the bias in the means or proportions of covariates across the groups. Therefore, we presented before and after propensity match standardized differences and its findings in Love plots (Figure 3).

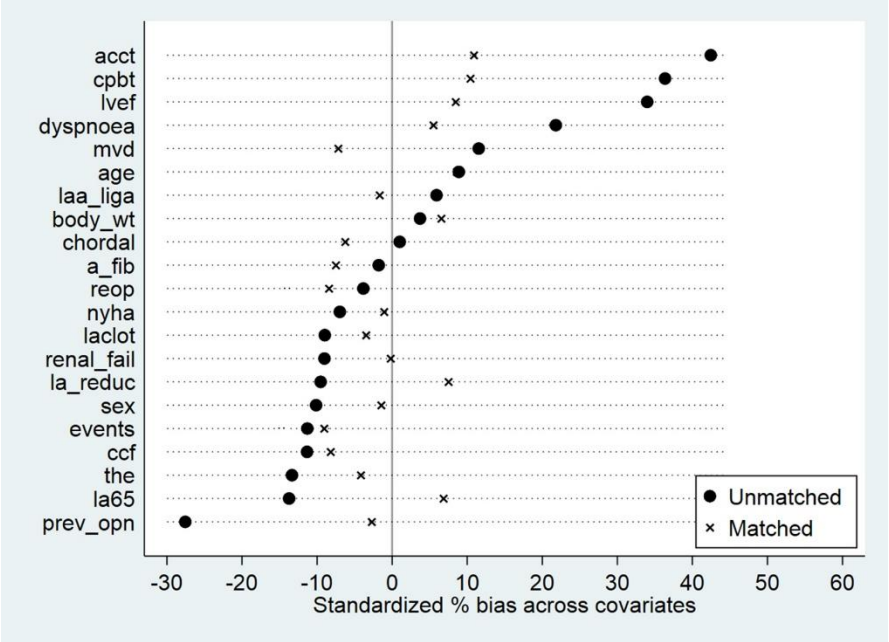


Figure 3: Love plot depicting standardized mean of difference (SMD) for covariates balancing before and after propensity score matching

An absolute standardized difference of 0% indicates no residual bias and less than 15% is considered of inconsequential bias. Greedy nearest neighbouring matching method was used for matching protocol with a caliper of 0.1 to match 1: 1 patients with mechanical and biological mitral and aortic prostheses. We were able to match 249 of the 325 biological prostheses and 249 of 600 patients of mechanical mitral and aortic prostheses.

Statistical Analysis

For descriptive analyses, we used Pearson Chi-square/Fisher's exact test and t-test/Wilcoxon rank-sum tests for before match and McNemar's test and paired sample t-test/sign-rank test for after match comparisons of baseline covariates between patients with mechanical and biological mitral and aortic prostheses. Kaplan–Meier curve with 95% confidence interval and matched Cox regression analyses were used to determine the associations of group with various outcomes during months of follow-up. All statistical analyses were done using STATA 14.0 Software (College Station, Texas, USA) and two-sided tests with a p-value of < 0.05 were considered statistically significant. The freedom from the composites of valve-related complications (mortality, reoperation and adverse postoperative events) were calculated by Kaplan-Meier actuarial methods and compared with log-rank statistic (Fig. 4A, 4B, 5A, 5B, 6A, 6B).

Results

Study population

After matching as described previously, our final study population consisted of a total of 498 patients aged between 11 and 70 (Group I: mean 33.32±7.80, median 33.0 (IQR: 27-40) years; Group II: mean 33.22±7.95, median 33.0 (IQR: 28-39) years (SMD 0.012, p=0.19). As presented in Table 1, after propensity matching, there were no differences among the 249 matched pairs in preoperative characteristics and both groups were fairly homogenous. Our institutional policy is to use bioprostheses beyond 18-years of age after bone growth and maturation are completed. In this study, one patient aged 12-years with a thrombosed mechanical prosthesis and another patient aged 13-year with thalassemia and hemolysis underwent bioprosthetic mitral and aortic valve replacements.

Covariates	Before propensity score matching		SMD	p-value	After propensity score matching		SMD	p-value
	Bioprosthetic MAVR (Group I, n=325) No. of patients (%)	Mechanical MAVR (Group II, n=600) No. of patients (%)			Bioprosthetic MAVR (Group I, n=249) No. of patients (%)	Mechanical MAVR (Group II, n=249) No. of patients (%)		
Sex								
- Male	120 (36.9)	240 (40.0)	-	0.340	90 (36.1)	95 (38.1)	-	0.643
- Female	205 (63.1)	360 (60.0)	0.066		159 (63.9)	154 (61.9)	0.104	
Dyspnoea								
- Yes	321 (98.8)	570 (95.0)	0.219	0.003	245 (98.4)	244 (97.9)	0.030	0.737
- No	4 (1.2)	30 (5.0)			4 (1.6)	5 (2.1)		
New York Heart Association								0.919
- Class IV	244 (75.1)	432 (72.0)	-	0.300	66 (26.5)	65 (26.1)	0.009	
- Class III	81 (24.9)	168 (28.0)	0.072		183 (73.5)	184 (73.9)		
CCF on inotropes & ventilator								
- Yes	46 (14.1)	110 (18.3)	-	0.100	42 (16.9)	47 (18.9)	-	0.559
- No	279 (85.9)	490 (81.7)	0.115		207 (83.1)	202 (81.1)	0.052	
Renal failure requiring peritoneal/hemodialysis								
- Yes	14 (4.3)	38 (6.3)	-	0.198	10 (4.0)	13 (5.2)	-	0.523
- No	311 (94.7)	562 (93.7)	0.091		239 (96.0)	236 (94.8)	0.057	
Mitral valve disease								
- Yes	219 (67.5)	370 (61.7)	0.115	0.096	178 (71.5)	179 (71.8)	-	0.921
- No	106 (32.5)	230 (38.3)			71 (28.5)	70 (28.2)	0.009	
Atrial fibrillation								
- Yes	215 (66.1)	402 (67.0)	-	0.821	179 (71.8)	174 (69.9)	0.044	0.622
- No	110 (33.9)	198 (33.0)	0.016		70 (28.2)	75 (30.1)		
Left atrial clot								
- Present	71 (21.8)	154 (25.7)	-	0.187	59 (23.7)	58 (23.3)	0.009	0.916
- Absent	254 (78.2)	446 (74.3)	0.092		190 (76.3)	191 (76.7)		
THE								
- Yes	26 (8.0)	72 (12.0)	-	0.057	25 (10.0)	21 (8.4)	0.055	0.537
- No	299 (92.0)	528 (88.0)	0.135		224 (90.0)	228 (91.6)		
Left atrial size > 65(mm)								
- Yes	119 (36.6)	260 (43.3)	-	0.043	87 (34.9)	80 (32.1)	0.059	0.507
- No	206 (63.4)	340 (56.7)	0.140		162 (65.1)	169 (67.9)		
LA reduction								
- Yes	115 (35.4)	240 (40.0)	-	0.157	84 (33.7)	71 (28.5)	0.113	0.209
- No	210 (64.6)	360 (60.0)	0.098		165 (66.3)	178 (71.5)		
Chordal preservation								
- Yes	229 (70.5)	420 (70.0)	0.012	0.859	184 (73.9)	188 (75.5)	-	0.681
- No	96 (29.5)	180 (30.0)			65 (26.1)	61 (24.5)	0.037	
Left atrial appendage ligation								
- Yes	288 (88.6)	520 (86.7)	0.051	0.466	217 (87.1)	226 (90.8)	-	0.198
- No	37 (11.4)	80 (13.3)			32 (12.9)	23 (9.2)	0.115	
Reoperation								
- Yes	34 (10.5)	70 (11.7)	-	0.568	34 (13.7)	44 (17.6)	-	0.218
- No	291 (89.5)	530 (88.3)	0.040		215 (86.3)	205 (82.4)	0.110	
Previous operation								

Covariates	Before propensity score matching		SMD	p-value	After propensity score matching		SMD	p-value
	Bioprosthetic MAVR (Group I, n=325) No. of patients (%)	Mechanical MAVR (Group II, n=600) No. of patients (%)			Bioprosthetic MAVR (Group I, n=249) No. of patients (%)	Mechanical MAVR (Group II, n=249) No. of patients (%)		
- Yes	96 (29.5)	256 (42.7)	-	<0.001	74 (29.7)	75 (30.1)	0.318	0.922
- No	229 (70.5)	344 (57.3)	0.276		175 (70.3)	174 (69.9)		
Low LVEF								
- Yes	103 (31.7)	224 (37.3)	-	0.080	90 (36.1)	62 (24.9)	0.246	0.006
- No	222 (68.3)	376 (62.7)	0.121		159 (63.9)	187 (75.1)		
Cumulative events								
- Yes	48 (14.8)	114 (19.0)	-	0.101	48 (19.3)	60 (24.1)	-	0.192
- No	277 (85.2)	486 (81.0)	0.115		201 (80.7)	189 (75.9)	0.117	
Cumulative mortality								
- Yes	10 (30.8)	42 (7.0)	-	0.013	9 (3.6)	12 (4.8)	-0.18	0.01
- No	315 (96.9)	558 (93.0)	0.181		240 (96.4)	237 (95.2)		
Age (years)								
- Mean±SD	33.51±7.7	32.79±8.35	0.091	0.190	33.32±7.80	33.22±7.95	0.012	0.192
- M (IQR)	34 (11-70)	33 (12-45)			33 (27-40)	33 (28-39)		
Body weight (kg)								
- Mean±SD	49.44±11.52	49.07±8.13	0.035	0.589	49.18±11.70	49.14±7.75	0.004	0.964
- M (IQR)	48 (24-85)	49 (30-80)			47 (24-85)	49 (30-74)		
Preoperative left ventricular ejection fraction								
- Mean±SD	50.06±19.87	43.59±18.16	0.344	<0.001	47.84±20.55	49.28±17.13	-	0.396
- M (IQR)	58 (15-72)	48 (16-76)			56 (15-72)	56 (16-74)	0.076	
ACCT (min)								
- Mean±SD	41.76±14.40	36.20±11.66	0.423	<0.001	40.50±14.16	41.91±14.39	-	0.272
- M (IQR)	36 (25-76)	32 (25-72)			42 (35-70)	46 (36-70)	0.098	
CPBT (min)								
- Mean±SD	56.80±15.09	51.57±13.66	0.363	<0.001	55.48±15.03	55.96±15.96	-	0.720
- M (IQR)	50 (36-94)	48 (36-118)			59 (46-86)	57 (47-84)	0.032	
Follow-up (months)								
- Mean±SD	133.12±51.42	138.18±75.23	-	0.279	132.30±51.85	143.24±76.04	-	0.061
- M (range)	131 (1-228)	142.5 (1-264)	0.079		129 (1-228)	140 (1-264)	0.168	

Table 1: Preoperative and intraoperative characteristics of patients undergoing mitral and aortic valve replacements (MAVR) before and after propensity score matching

Surgical techniques

The technical details of the surgical steps of combined mitral and aortic bioprosthetic and mechanical valve replacements have been enumerated in the video presentation (**Video Presentation**) as well as in our earlier publication.[20,32] Every attempt was made to preserve the chordopapillary apparatus ensuring implantation of an appropriate sized prosthesis without leaflet entrapment or left ventricular outflow tract obstruction (LVOTO).

In patients with predominantly stenotic lesions with severe chordopapillary fusion, MVR was performed without chordal preservation. Intraoperative transesophageal echocardiography was performed to confirm satisfactory prosthetic valve function immediately after surgery.

Total chordo-papillary apparatus was preserved using Milki's technique whenever feasible (Group I, n=149, 59.8%; Group II, n=160, 64.2%). In patients with calcified leaflets with annular extension and severe subvalvular fusion, the mitral apparatus was completely excised (Group I, n=40, 16.1%; Group II, n=39, 15.7%). The remaining patients had only posterior chordal preservation (Group I, n=60, 24.1%; Group II, n=50, 20.1%).

The technical details of chordal preservation, annulus decalcification and its effect on regional and global ventricular function have been addressed in our previous publications. [13,23,37,38] Size of the bioprosthetic valve ranged from 25 mm to 33 mm [Group I, valve size: 33 mm n=21); 31 mm (n=38); 29 mm (n=94); 27 mm (n=74); 25 mm (n=22)]. The sizes of the implanted

mechanical mitral prosthesis in group II ranged from 24 mm to 31 mm [St. Jude Medical Inc. St. Paul, Minn. mechanical size 31 mm (n=30); 29 mm (n=67); 27 mm (n=56); Medtronic Open Pivot™ AP360° Apex and AP, Medtronic Inc. Mx USA; size 28 mm (n=38), 26 mm (n=52), 24 mm (n=6).

Size of the bioprosthetic aortic valve ranged from 19 mm to 25 mm (size 25 mm, n=44; 23 mm, n=57; 21 mm, n=109; 19 mm, n=39). The sizes of the mechanical St. Jude Medical Inc. were 19 mm, n=17; 21 mm, n=53; 23 mm, n=49; 25 mm, n=39). The ATS medical sizes were 20 mm, n=19; 22 mm, n=50 and 24 mm, n=22.

Patients undergoing redo MAVR for degenerated bioprostheses (n=34) or thrombosed mechanical prostheses (n=44) were subjected to a uniform surgical protocol in all patients undergoing explantation of the degenerated bioprostheses and thrombosed mechanical prostheses standardised by the corresponding author. There were no instances of paravalvular leak on any patients. A mechanical mitral valve [(Medtronic Open PivotTM AP360° Apex and AP, Medtronic Inc., Mx, USA); size 24mm (n=17), 26 mm (n=19); St. Jude Medical Inc. St. Paul, Minn, 27mm (n=21), 29 mm (n=21) was used in patients undergoing explantation for SVD, (Figure 7A-7D). The sizes of the mechanical aortic valve were [St. Jude Medical Mechanical 19mm, n=8; 21 mm, n=24; 23mm, n=28; 25mm, n=18].

Median ischemic time for group I patients was 42 minutes (IQR: 35-70); and for group II was 46 minutes (IQR: 36-70), (SMD= -0.098, p=0.27). Median cardiopulmonary bypass (CPB) time for group I was 59 minutes (IQR: 46-86); and for group II was 59 minutes (IQR: 47-84), (SMD= -0.032, p=0.72) respectively. Ninety-five (36.5%) patients underwent LA reduction for giant LA. No surgery was performed for atrial fibrillation. One hundred and seventeen (23.5%) patients with organic tricuspid valve disease underwent tricuspid valve reconstruction using commissurtomy and Kay's or DeVega's annuloplasty.

Operative mortality and morbidity

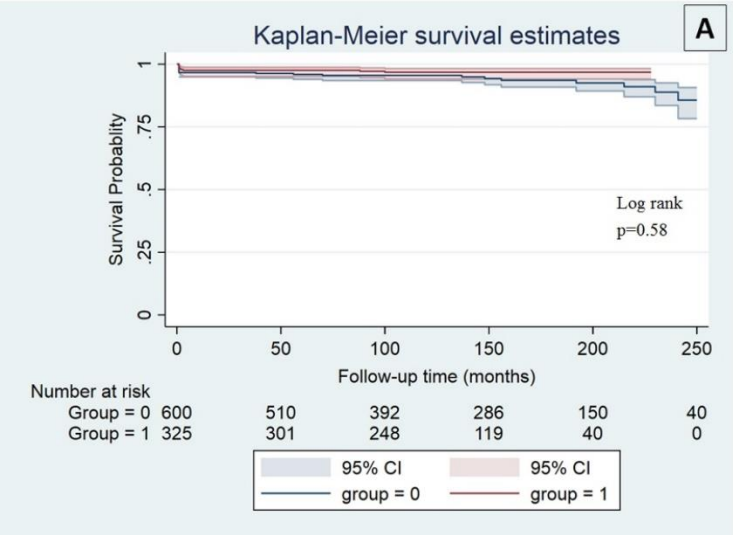
There were 5 (2%) hospital deaths in group I and 8 (3.2%) in group II due to low cardiac output syndrome (LCOS) after reoperation for thrombosed mechanical prosthesis (n=4)/failed mitral valve reconstruction (n=5), intractable ventricular arrhythmias (n=2) and sepsis (n=2) with left ventricular and renal failure. Comparative assessment of early complications between the two groups revealed no differences in incidence of perioperative mortality and morbidities.

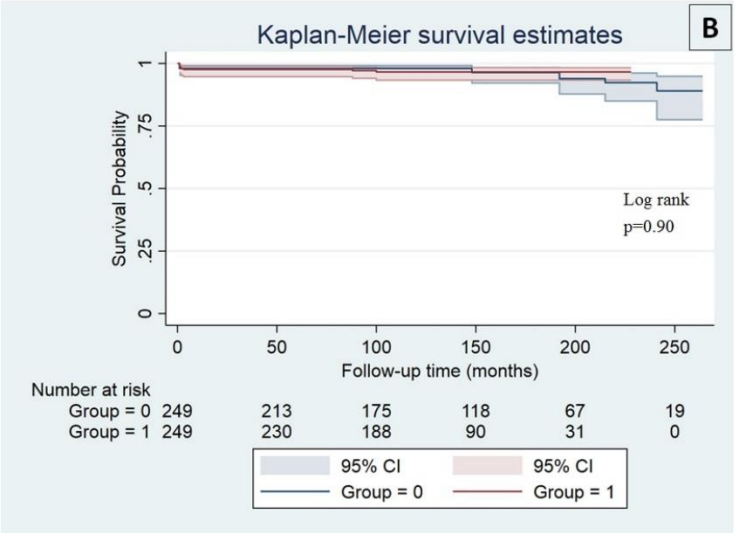
Late outcomes

Late mortality was 1.6% (n=4) in group I and 1.6% (n=4) in group II (p=1). The causes were persistent congestive heart failure (CHF) (n=2), intractable ventricular arrhythmias (n=5), and renal failure (n=1) between 45 days and 215 months following surgery. A combination of persistent CHF, intractable ventricular arrhythmias and renal failure were the causes of death of 12 (15.4%) patients undergoing redo MAVR (Group I; n=3: Group II; n=3). The other causes were anticoagulant-related massive intracerebral haemorrhage (n=4), and sepsis (n=2). On hazard regression analysis, the risk of cumulative mortality was equal in both groups [HR 0.86 (95% CI 0.35, 2.08), p=0.73].

Four patients were lost to follow-up. Follow-up was complete in 473 (99.1%) patients and yielded 5281.8 patient-years data. Four hundred and thirty-one (91.1%) patients were in NYHA class I, while 42 (8.8%) were in NYHA class II. The actuarial survival at a median follow-up of 134 months (IQR: 99.5-178.5) was 96.6%±0.01% (95% CI: 93.31-98.30). There was no difference in actuarial survival between the two groups (log rank, p=0.90, Figures 5A, 5B).

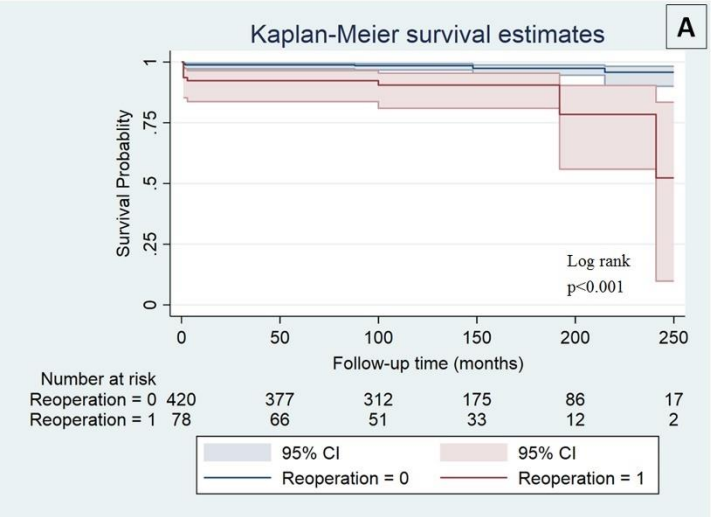
Thromboembolic complications occurred in 46 patients (Group I: n=25; Group II: n=21): transient ischemic attack (n=21), dysarthria (n=14), and hemiplegia (n=11). Two patients in Group I and one patient in group II developed prosthetic valve endocarditis and were managed conservatively. Although cumulative mortality was more in mechanical arm (Group I: 3.2% vs Group II: 4.4%), there was no difference in actuarial survival between two groups (Group I: 92.3%+/0.02% vs Group II: 96.6%±0.01 (log-rank: unmatched p=0.1, matched p=0.90), (Figures 4A, 4B).

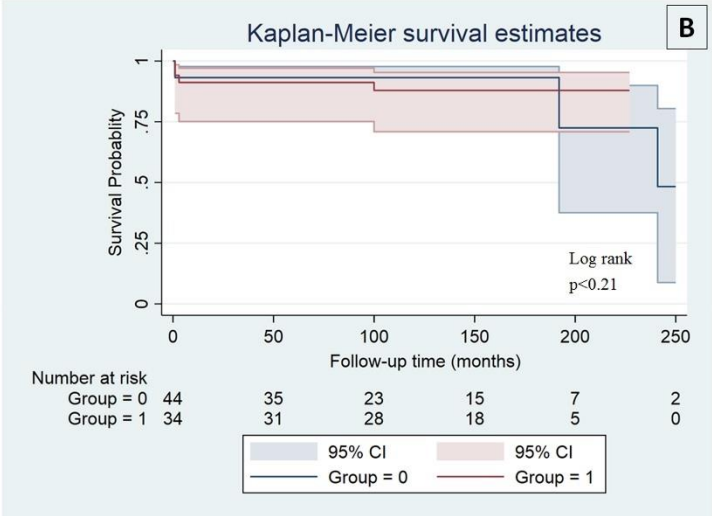




Figures 4A, 4B: Survival probability from Kaplan-Meier curve before (4A) and after (4B) propensity score matching (Log rank: group I vs group II, unmatched p=0.58; matched p=0.90).

Requirement for redo valve replacements was similar between the two propensity matched groups (SMD= -0.11, p=0.21). Patients undergoing reoperation were associated with 5.38 (95% CI 3.09, 9.35) times increased risk of death compared to non-reoperated group (p<0.001) and there was significantly decreased probability of long-term survival (log rank p<0.0001) (Figures 5A, 5B).

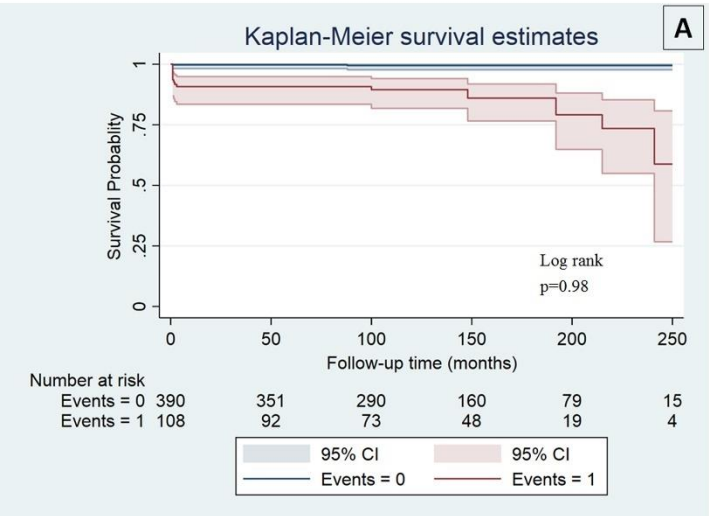


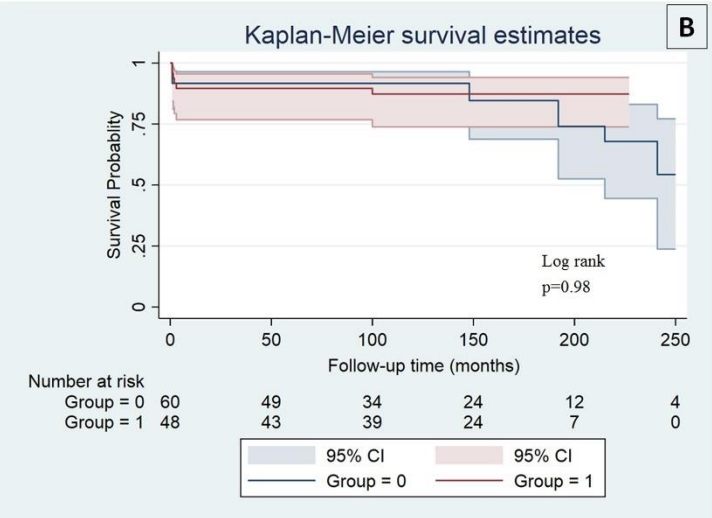


Figures 5A, 5B: Survival probability from Kaplan-Meier curve of patients undergoing reoperation. Figure 5A compares survival probability between reoperation vs no reoperation. Figure 5B depicts survival probability of patients undergoing reoperation between Group I and Group II.

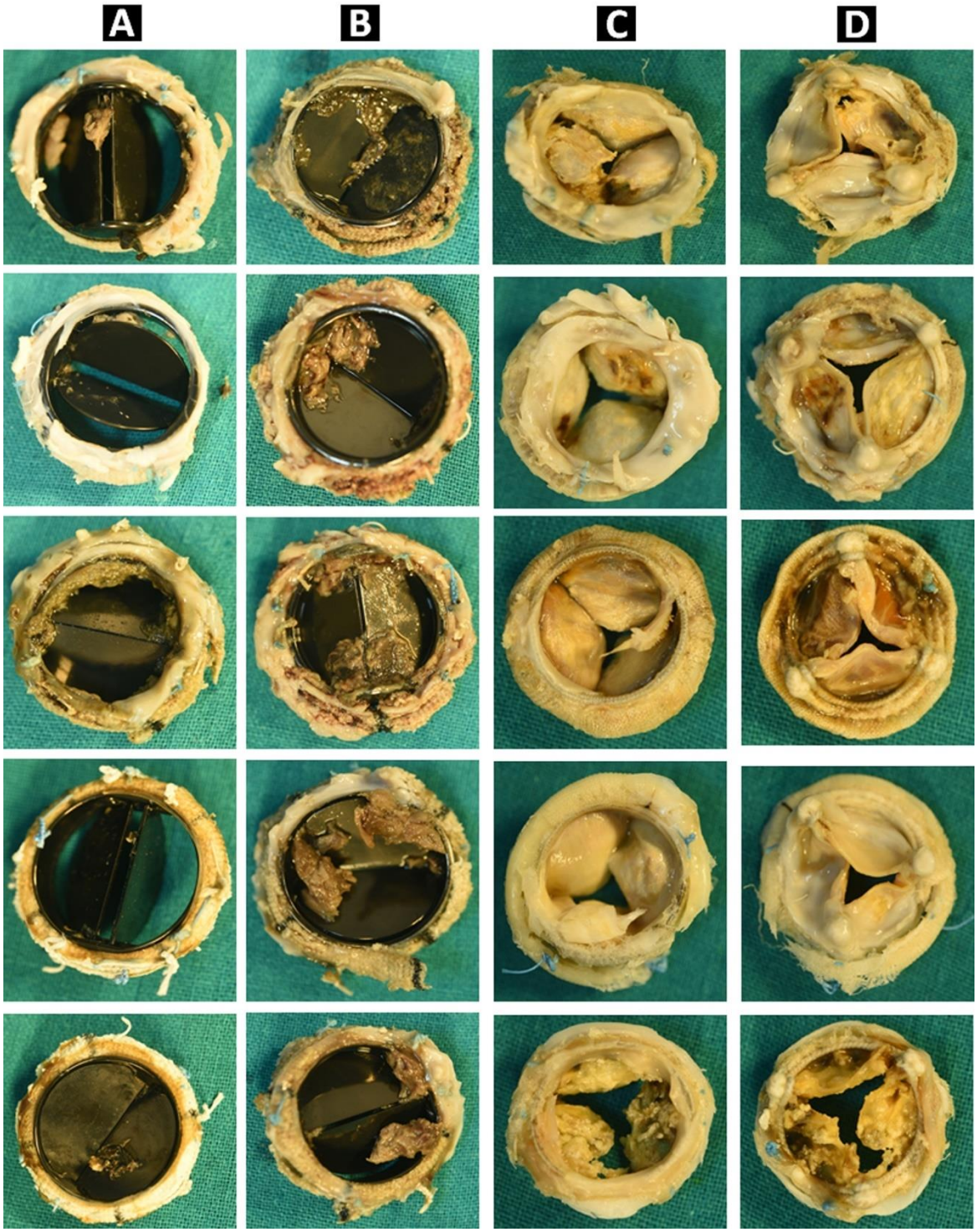
At a median follow up of 134 months (IQR: 79-199), 13.6% (n=34) of group I, and 17.6% (n=44) of group II patients underwent redo MAVR using mechanical prosthesis, and there was no difference in actuarial survival between the two groups (log rank, unmatched p=0.58; matched p=0.90) (Figure 5B). Valve leaflet thickening with mild prosthetic valve stenosis (Epic; mitral n=8, aortic n=3, PERIMOUNT; mitral n=4, aortic n=5) was seen between 88 and 110 months of follow-up and being closely followed-up.

The composites of valve-related cumulative events were similar between the two propensity matched groups [Group I: 19.3% (n=48) vs Group II 24% (n=60), (SMD= -0.117, p=0.19). The actuarial event free survival at a median follow-up of 134 months was 92.3%±0.02% (Group I) vs 96.6%±0.01% (Group II: log rank p=0.90), (Figures 6A, 6B).





Figures 6A, 6B: Survival probability from Kaplan-Meier curve of patients undergoing reoperation. Figure 5A compares survival probability between reoperation vs no reoperation. Figure 5B depicts survival probability of patients undergoing reoperation between Group I and Group II.



Figures 7A-7D: Photographs of explanted St. Jude mechanical valve with thrombotic occlusion of leaflets (A, B) and PERIMOUNT bioprostheses (C, D) showing structural valve deterioration (Cuspal perforation, tear, thickening, calcification, stiffness, wear and abrasions, creep, and stress fracture).

Hemorrhagic complications necessitating hospitalisation occurred in 7 (2.8%) patients in group II. Twenty-five (10.04%) patients of group I and 21 (8.43%) patients of group II experienced thromboembolic complications. The linearized valve-related adverse postoperative cumulative events were 1.37 events/100 patient-years for group I and 1.38 events/100 patient years (p=0.89) for group II. At late follow-up, more patients were in atrial fibrillation in mechanical arm (Group I: 60.0% vs Group II: 72.0%, p=0.17) (Table 2B)

Variables (covariates adjusted)	Hazard ratio (95% confidence interval)	p value
Congestive cardiac failure (on inotropes, ventilation)*	9.84 (4.54, 18.64)	<0.001
Renal failure requiring peritoneal/hemodialysis*	11.64 (6.57, 20.64)	<0.001
Atrial fibrillation*	3.83 (1.63, 8.98)	<0.002
Reoperation for thrombosed mechanical and degenerated bioprostheses*	5.38 (3.09, 9.35)	<0.001
Previous operation*	3.53 (1.93, 6.45)	<0.001
Left ventricular ejection fraction <0.25*	4.25 (2.29, 7.88)	<0.001
Prolonged aortic cross-clamp time*	3.84 (2.19, 6.78)	<0.001
Prolonged cardiopulmonary bypass time*	2.69 (1.84, 8.68)	<0.001

*Variables with increased risk

Table 2: Risk of 0- to 23-years mortality after combined mitral and aortic bioprosthetic and mechanical valve replacement by Hazard regression analysis

The hazard regression model of risk factors for cumulative mortality included preoperative CHF on inotropes and ventilator (HR 9.84, 95% CI: 4.54, 18.64, p<0.001), renal failure requiring peritoneal/hemodialysis (HR 11.64, 95% CI: 6.57, 20.64, p<0.001), atrial fibrillation (HR 3.83, 95% CI: 1.63, 8.98, p<0.002), reoperation for thrombosed mechanical and degenerated bioprostheses (HR 5.38, 95% CI: 3.09, 9.35, p<0.001), previous operation (HR 3.53, 95% CI: 1.93, 6.45, p<0.001), poor left ventricular function (HR 4.25, 95% CI: 2.29, 7.88, p<0.001), prolonged aortic clamp time (HR 3.84, 95% CI: 2.19, 6.78, p<0.001), and prolonged CPB time (HR 2.69, 95% CI: 1.84, 8.68, p<0.001). Propensity score matching did not exhibit any difference in reoperation between two groups (Group I vs Group II: 13.6% vs 17.6%, SMD= -0.110, p=0.21).

Discussion

Comparative data as late (15 years) and very late-term (20 years) performances of bioprostheses and mechanical prostheses in young rheumatics undergoing combined mitral-aortic valve replacements are limited and conflicting. [15-19,24-31,39-41] This is the first propensity matched comparative study on very late-term performance of bioprostheses and mechanical prostheses following combined aortic and mitral valve replacements. The important findings of this retrospective study were:

1. Propensity score matching and multivariable modelling minimised the biases and demonstrated similar long-term survival upto 22 years in both groups of patients.
2. Composites of valve-related mortality, morbidity, defined as per neurologic and functional impairment favored bioprosthesis in selected individuals.
3. Both groups exhibited almost similar valve-related reoperation rates (group I: 13.65% vs group II: 17.6%, SMD-0.11, p = 0.21), and
4. Bioprosthetic arm exhibited lesser cumulative mortality [3.2% (n=8) vs 4.4% (n=11), SMD= -0.18, p=0.01)] and was statistically significant (Table 1).

Unlike other published series, patients in this study were carefully matched with regard to age, NYHA functional status, atrial fibrillation, and other variables as enumerated in table 1. Because combined MAVR was performed more often using mechanical prosthesis than bioprostheses in this study, maximum patients treated with bioprostheses were included and matched with the mechanical prostheses group.

Shared decision-making about the choice of prosthetic valve type is influenced by several factors, as enumerated under. According to American College of Cardiology/American Heart Association 2020 guidelines, a mechanical prosthetic valve may be favored in patients aged less than 50 years under the following circumstances:

- Patient preference (avoid risk of reintervention).
- Complaint patient with either home monitoring or close access to INR monitoring.
- Presence of other indication for long-term anticoagulation (e.g. atrial fibrillation).
- High-risk reintervention (e.g. porcelain aorta, prior radiation therapy).
- Small aortic root size for aortic valve replacement (may preclude valve-in-valve procedure in future).

Implantation of a bioprosthesis in this age group is associated with a lower risk of anticoagulation but there is an increased incidence of structural deterioration with bioprosthesis (15-year risk- 30% for age 40 year, 50% for age 20 year). [1]

A bioprosthetic valve may be favored in patients aged more than 65 years under the following circumstances:

- Patient preference (avoid risk and inconvenience of anticoagulation.
- High risk of long-term anticoagulation.
- Limited access to medical care or inability to regulate vitamin K dependent antagonist.
- Access to surgical centers with low reoperation mortality rate.
- Access to transcatheter valve-in-valve replacement.
- Transcatheter aortic valves have larger effective orifice areas for smaller valve sizes (avoid patient-prosthesis mismatch).[1]

Published data indicate that strong consideration should be given to choosing a tissue over a mechanical prosthesis in patients aged >60 years, but the issue remains largely unsettled in patients aged ≤60 years. Randomised trials comparing biological and mechanical prosthesis in younger rheumatics are scanty. [15-19,24-31,39-41]

Although, these studies have helped define the recommendations for prosthesis selection according to patient's age, they compared valve models implanted in 1970s and 1980s, had a considerable proportion of redo-thoracotomy/sternotomy patients at initial valve implantation, and reported perioperative mortalities at initial operation and at reoperation that were high (>14%) by modern standards, thus potentially biasing against use of bioprosthesis. [7,14,34]

Thirdly, data with sufficient follow-up duration to adequately capture tissue prosthesis, reoperations, and long-term mortality in younger patients is lacking. Fourthly, a rapid development is witnessed in the field of bioprosthesis, with newly introduced devices every year. The production of some of the devices was even stopped before the long-term results were obtainable which indeed is mandatory for every new device.

The rationale for these studies is based on improved durability of bioprostheses, anticipated low risk of reoperation, and avoidance of long-term anticoagulation. Data on long-term survival of patients with bioprostheses, however, are conflicting. [15-19,24-31,39-41]

Valvular heart diseases in developing countries resulting from rheumatic fever is disabling and if untreated leads to congestive heart failure and death. The severity and rapid progression of rheumatic valvular disease in pediatric and younger patients precludes repair in the great majority. Young patients face a difficult choice between a life time of anticoagulation and 1-3% per year bleeding risk with mechanical prosthesis and a significant risk of reoperation due to structural valve deterioration with bioprosthesis.[4,11-14,20-23,37,38]

Whether reoperation is more hazardous than strokes and hemorrhage, long-term valve-related mortality may be the most important criterion for comparison and literature is divided on the recommendation in young rheumatics.[6,42-47]

In our previous propensity matched investigation on 466 consecutive patients undergoing either bioprosthetic MVR (n= 233) or mechanical MVR (n=233), we compared 22 – year composites of valve – related reoperation, obesity, and mortality in young rheumatics aged less than 45 years. At a median follow up of 136 months (IQR: 79-197), our reoperation rate was 17.6% for mechanical prostheses and 13.6% in bioprosthetic arm, while reoperation for structural valve deterioration was associated with 0.27 times lower risk of cumulative mortality than reoperation for thrombosed mechanical processes ($p<0.001$). We concluded that bioprostheses are valid alternative to mechanical bioprostheses in individuals from rural areas, those desirous of pregnancy, patient with bleeding risk, and those with thrombosed mechanical prostheses. Bioprostheses were undifferentiated in terms of composites of valve related- reoperation and mortality. [32]

All biologic valves are at risk of structural valve deterioration. Any patient treated with a bioprosthesis may need reoperation for valve replacement if the individuals life expectancy exceeds that of the valve. In 1999, and 2001 the French investigators reported that the risk of reoperation for SVD of bioprostheses was 3 fold higher in cases involving patients older than 65 years of age ($p=0.02$) who had mitral-aortic valve replacement ($p=0.02$).[48,49]

On the basis of this finding, implantation of 2 bioprostheses would seem contraindicated in patients in whom structural degeneration requiring reoperation in likely to occur after age 65 years. However, alternative use of mechanical valves is associated with a significantly higher risk of potentially lethal haemorrhagic complications. [39,40,50]

In this review, the mean age of both groups of patients was 33.32 ± 7.8 (range 11-70, median 33 years; bioprosthesis), and 33.32 ± 7.95 (range 12-45; median 33 years; mechanical); SMD=0.012; $p=0.19$) respectively. Thus, the survival period of the study population was much longer than the life span of the bioprostheses. Therefore, follow-up of patients treated with bioprostheses was not artificially shortened. Hence, we found that overall actuarial survival was slightly shorter in the bioprosthetic group, although statistically insignificant (group I: $92.3\% \pm 0.02\%$ vs group II: $96.6\% \pm 0.01\%$; Logrank: $p=0.90$; Figures 4A, 4B).

In general, the younger the patients are, the earlier the valve degenerates.[43,46,50] Freedom for SVD-related reoperation rates at 10 and 15 years in patients aged less than 60 years in the published literature has been reported between 71-84% and 62.6%-87.4% respectively.[43,46,50] In our previous investigation on 260 young rheumatics aged less than 45 years undergoing isolated mitral valve replacement, we had demonstrated that at a median follow up of 134 months, our reoperation rate was 8.5% in Epic and 14.6% in PERIMOUNT arm, while reoperation for structural valve deterioration was associated with 3.82 times increased risk of death.[20]

A number of recent articles supported the use of bioprostheses in patients aged less than 60 years with the argument that bioprostheses reduced the postoperative valve-related complications including SVD and mortality. Myken and associates studied Biocor MVR in 1712 patients with a mean follow-up of 6.2 years.[43] The 20-year freedom from actuarial valve related mortality was 92.8% and freedom from SVD was 79.3%. They concluded that bleeding was more hazardous than reoperation.[43] The Biocor MVR durability reported by Pomerant Zeff and associates in 2006 on 546 patients (mean age 48 years) at 15 years was 51.8% for those aged <50 years, 88.7% for those 51-60 years, and 84% for those 61-81 years for reoperative SVD.[47]

Our findings in this review are in accordance with the published investigations of 15-years survival of 53% - 84.4% with mechanical prosthesis and 42% - 58.8% with bioprosthetic combined aortic and mitral valve replacements.[16,17,24-31] The striking variability in the results using the same prosthetic devices is also known to occur from the experience of other centers. Armenti and colleagues cited an actuarial survival of only 76% and 62% at 3 and 5 years, respectively, using St Jude Medical prostheses and their experience was a variance from that of Brown and colleagues whose results were most favourable with this combination.[31,40,53]

Our hospital mortality of 3.2% in the biologic arm and 4.4% in the mechanical arm following propensity matching compares favourably with 2.5% to 12% of other investigators and is not substantially higher than patients with isolated valve replacement in several investigations.[15,19,24-31] Bernal and colleagues from Spain reported a mortality of 10.7% after double valve replacement using the Carbomedics valve. [51] Brown and coworkers from the NHLBI cited an in-hospital mortality of 14%. [40,53] Bortolotti and associates cited hospital mortality of 19% in 221 patients having a dual mechanical prosthesis. [41]

Talwar and associates reported an early mortality of 8.5 % in the DVR group (n=293) in their study comparing aortic valve replacement with mitral valve repair compared with combined MAVR. They did not include patients needing reconstruction of the tricuspid valve. The causes of early mortality where arrhythmia, bleeding and sepsis. [27]

Remaldi and associates reported an operative mortality rate of 7.08% in their 22-year follow-up of 250 patients who underwent mitral-aortic valve replacement using mechanical prostheses. [25] While all our patients following propensity match belonged to NYHA class III and IV, the percentage of patients who belonged to NYHA class III and IV was 66% in their study.

Although literature documents several instances of atrioventricular groove disruption and refractory surgical bleeding following MVR, we did not encounter a single instance of left ventricular rupture in our study. We believe strongly that preservation of the chordopapillary apparatus, implantation of an appropriate sized low profile prosthesis are a sine qua non in its prevention. [15,60,61] We need to remind ourselves of the maxim, “it is not what you do but how you do it”.

In terms of other technical considerations, every attempt was made to preserve the chordopapillary apparatus ensuring implantation of an appropriate sized prosthesis without leaflet entrapment or left ventricular outflow tract obstruction. Total apparatus was preserved using Miki’s techniques whenever possible. In patients with calcified leaflets with annular extension and severe subvalvular fusion, the mitral apparatus was completely excised. The importance of chordal preservation in preventing left ventricular rupture following MVR and preservation of left ventricular function have been detailed in our previous investigation. [37,38] Similar findings have been noted by other investigators. [56-61]

The low in-hospital mortality observed in the study can be attributed to uniform myocardial preservation strategy, preservation of chordopapillary apparatus, implantation of appropriate sized low-profile prostheses, and

performing aortic root enlargement procedures in cases of small aortic root, thus avoiding patient - prosthesis mismatch and atrioventricular groove disruption.[62,63] Timely intraoperative and perioperative institution of intra-aortic balloon counterpulsation in selected individuals undergoing combined mitral-aortic valve replacement with low cardiac output syndrome have further improved our surgical results. The strategies and logic of institution of intraaortic balloon counter pulsation (IABC) in individuals undergoing MAVR have been addressed in our previous investigation.[64]

Some investigators have evaluated late mortality and morbidity of individuals undergoing combined mechanical aortic and bioprosthetic mitral valve replacement.[65-70] There was uniform conclusion that the practice of combining a bioprosthetic and a mechanical prosthesis should be discouraged, as this combination imparts the disadvantage of both valve types and the advantage of neither, especially if the patient requires anticoagulations for reasons other than for a mechanical prosthesis.[40,41,53,71,72]

The major predictor of increased risk in the published investigations including ours continues to be advanced preoperative functional disability, congestive cardiac failure (on inotropes, ventilation) severe pulmonary hypertension, organic tricuspid valve disease, renal failure requiring peritoneal/ hemodialysis, redo valve replacement for degenerated bioprosthesis or thrombosed mechanical prosthesis. The prognostic importance of preoperatively increased pulmonary vascular resistance points to the importance of chronic pressure load on the right ventricle for postoperative outcome. Thus, it is not only genuine tricuspid valve disease but also the chronic overload of the right ventricle with dilation and myocardial failure that burdens the late postoperative outcome.

In this study, massive organic tricuspid incompetence was present in 117 (23.5%) and it was noteworthy that dominant tricuspid stenosis was evident in 49 (9.8%) patients. We followed an aggressive policy on these patients with tricuspid valve disease, performing annuloplasty and commisurotomy with concomitant annuloplasty if indicated. Kay's or Devega's annuloplasty is the method of choice in our experience. Other investigators had also identified the association of tricuspid valve disease as a strong predictor of morbidity and mortality. [73,74]

There was no instance of paravalvular leak in the present review. We believe strongly that interrupted horizontal mattress sutures with Teflon pledgets are a sine qua non in its prevention. In 1986 Sethia and coworkers reported on a 14-year experience with the Bjork-Shiley prosthetic replacement, noting a high incidence of paravalvular leak (2% per year) and suggesting along with other experts that horizontal mattress sutures provide better valve stability and may eliminate this adverse valve-related complication.[75] In 1991, Bortolotti and colleagues noted 7 patients with paravalvar leak for an incidence of 0.67% $\pm$ 0.2% among a group of 221 subjects who underwent double valve replacement with dual mechanical prostheses.[41] Some investigators found a predominance of paravalvular leakage in the mitral position.[76,77]

Our experience with valve thrombosis supports the findings of other series, including single valve replacement; it is a life threatening complication with a 50% mortality rate and is due to inadequate anticoagulation. [23,37,38,45] The inclusion of sudden death in the valve-related deaths remain controversial. Two recent autopsy studies have questioned the valve of Death. Rooney and associates showed in 48 necropsies after sudden death with the Medtronic Hall valve that 90% of deaths were unrelated to prosthesis.[71] Burke found among 37 patients with sudden death that more than half of the deaths were due to cardiac hypertrophy and atherosclerosis, hypothesizing relationship with ventricular arrhythmias.[78]

Notably, we had only 3 cases of prosthetic valve endocarditis who were managed conservatively. All cases of endocarditis occurred in the group of patients with active endocarditis as a surgical indication. This indicates a higher quantity of prosthetic material does not mean a higher risk of infectious complication. Structural deterioration did not occur on any patient with mechanical prostheses.

Literature documents variable instances of major associated cardiovascular events following mechanical and bioprosthetic valve replacements possibly due to widely different patient population, use of different kinds of prosthetic valves, widely different anticoagulation strategies, inclusion of different pathology, non-ligation of LAA, non-reduction of body of LA in cases of giant LA, and inadequate patient compliance. [40,41,48,49,53]

Parallel to the findings in the literature, thromboembolism and bleeding events following mechanical prostheses remain the most dangerous valve-related complication. The inverse relationship between the incidence of thromboembolism and bleeding events following implantation of mechanical prostheses suggests the question of an ideal valve substitute.

Our linearized 2.6% incidence of bleeding is in the range of those reported in the literature. However, Horstkotte and associates in their prospectively, noted a linearized incidence of haemorrhage of 6.1% per patient-year in patients with MAVR.79 According to the guidelines, we included any episode of internal or external bleeding that causes death, stroke, precipitates surgery or hospitalization or requires transfusion. Therefore, in cataloguing all the events that required a hospitalization, we also included benign events treated on our OPD basis.

Armenti and associates studied patients who were implanted with Starr Edwards prosthesis and reported only a 40% freedom from thromboembolism and haemorrhagic complications at 15 years.31 Talwar and associates reported a very high rate (21%) of thromboembolic complications in the MAVR group of their study. They could not point out a specific cause to this phenomenon and termed most of the events as minor. However, 18 of the 62 patients (29.03%) who developed this complications were in atrial fibrillation.[27]

The low incidence of thromboembolic events in this review is presumably related to factors such as inherent difference in coagulable states15,22 and competence of the individual managing the patient's population. A modest degree of education and counselling to the patient has paid off in the follow-up. The importance of meticulous attention to anticoagulant therapy cannot be over-emphasized. In this review, our data pertaining to thromboembolism and anticoagulation related hemorrhage have emphasized and reinforced the importance of our patient population in the interpretation of the results as our series was not typical of the western world. Forty patients with mechanical prosthesis on low-intensity anticoagulant regime carried their pregnancy to term and borne normal children. The oral anticoagulant therapy was substituted with subcutaneous heparin 5,000 units twice daily during the last trimester in individuals with mechanical prosthesis. Warfarin embryopathy and intracerebral haemorrhage in the new-born were not encountered in our experience. The protocol for anticoagulation during pregnancy in two major institutions in India have been addressed in earlier publicatins. [15,22,23,37,38,80] Salazar and colleagues emphasized that women with cardiac valve prostheses should be counselled against pregnancy. [81]

An important argument in favour of bioprosthetic valve is the freedom from chronic anticoagulation. It is pertinent to point out that in our study, a significant number of patients with atrial fibrillation with or without left atrium/left atrial appendage clot, history of thromboembolism, and those undergoing surgical left atrium reduction for giant left atrium were on low-intensity anticoagulation with an INR between 1.5-2.0. With this strategy, we observed the linearized occurrence rates of composites of valve-related cumulative events (bleeding and thromboembolism) of 1.4 events per 100 patient-years, which is comparable to other reports.[7,12-21,23-28,58,70] This low-intensity anticoagulation in selected subset of patients with bioprosthesis offered sufficient protection against thromboembolism on the one hand and bleeding on the other.

In this review, although the overall late survival was statistically insignificant between the bioprosthetic and mechanical prosthetic group, the actuarial rate of nonfatal valve morbidity differed significantly between them. The incidence of reoperation, nonfatal haemorrhagic and thromboembolic events was higher in the mechanical prosthetic group (Table 1).

Literature is divided on the issue of ligation of left atrial appendage and management of giant left atrium during mitral valve surgery. [20,21,82,83] Studies have shown that left atrial appendage plays an important role in genesis of left atrium thrombus in patients with atrial fibrillation and ligation of left atrial appendage during MVR in high-risk population reduces the risk of late thromboembolism and is a recommended procedure in ACC guidelines. [1-4,34] However left atrial appendage ligation may not provide an adequate protection from thromboembolic events in the absence of effective anticoagulation with warfarin.

In this study, 70.8% (n=353) were in atrial fibrillation, 33.5% (n=167) had left atrial size > 65 mm, 23.5% (n=117) had left atrium/left atrial appendage clot, 9.2% (n=46) had preoperative history of thromboembolism, and 30.5% (n=152) had left ventricular ejection fraction < 0.25.

No surgery was performed for atrial fibrillation because ventricular rate was well controlled on pharmacological therapy and there was no intolerance of arrhythmia. Eight patients undergoing redo MVR for SVD had large left atrial clot, atrial fibrillation, low intensity anticoagulation, and unligated left atrial appendage. Left atrial appendage ligation was done in 88.9% (n=443) patients, 38 patients had amputated left atrial appendage during previous surgery and in 17 patients left atrial appendage was not ligated due to small size.

Currently, there is no consensus on management of giant left atrium during mitral valve surgery. Studies have reported surgical mortality between 8% to 23% in patients undergoing surgery for mitral valve and giant left atrium which is unacceptable. [84,85] In our study, 36.5% (n=95) patients underwent left atrium reduction for giant left atrium by plicating the inferior and superior left atrial wall and ligating left atrial appendage. We avoided partial excision on superior wall because it carries greater risk for bleeding and atrioventricular node blockade.

Study Limitations

Although our study is limited by its retrospective nature, propensity score analysis provides a balance of two compared groups and attempt to control for the most of the bias in assignment of valve type.

Randomized controlled trials themselves are limited because randomization requires stratification on many prognostic variables and thus often leads to selection of very specific groups of patients with results that lack generalizability. In addition, randomization is based on few variables that the investigators consider as most significant predictors of outcome.

Thirdly, like other observational cohorts, our results may not be generalizable to all young adults undergoing MAVR in other centers.

Conclusions

This study adds equipoise to the notion of valve choice in young rheumatics aged less than 45 years. Bioprostheses for combined mitral and aortic valve replacements are valid alternative to mechanical prostheses in patients from remote rural areas, those desirous of pregnancy, patients with bleeding risk, and those with thrombosed mechanical prostheses. Bioprostheses were undifferentiated in terms of composites of valve-related reoperation and mortality.

Survival from reoperation in bioprosthetic arm was superior to mechanical arm because of planned elective intervention, mostly when the patients were in functional class I/II. In light of this data, we conclude that choice of prosthesis for mitral and aortic valve replacements should be based on patient's preference, ability to take anticoagulation, and the likelihood of reoperation.

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