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BRIEF RESEARCH REPORT

Clinical experience with the miltonia valve: short-term performance of new bi-leaflet mechanical prosthesis in mitral valve replacement surgery

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Abstract

Purpose This study evaluates the performance of the Miltonia bi-leaflet mechanical prosthesis for mitral valve replacement (MVR).

Methodology Fifty patients were included in this study who underwent MVR using cardiopulmonary bypass (CPB) and mild hypothermia. After surgery, standard postoperative care was provided. Echocardiography was performed preoperatively, postoperatively at discharge, and at a 6-month follow-up to assess hemodynamic performance and detect adverse events.

Results The mean age was 38.88 ± 9.51 years, with a predominance of female patients. The average hospital stay was 9.6 ± 3.8 days. Before surgery, 88% of patients were in New York Heart Association (NYHA) class III, 8% in class IV, and 4% in class II. Post-surgery, 92% improved to class I, 4% to class II ($p < 0.001$). Both mean and peak pressure gradients showed significant improvement post-procedure ($p < 0.001$) and at 6 months ($p < 0.001$) compared to pre-operative status. At the 6-month follow-up, there were no cases of prosthetic valve endocarditis, structural/non-structural valve deterioration, dysfunction, or paravalvular leaks, with a 4% mortality rate. Four patients were diagnosed with prosthetic heart valve thrombosis (PHVT) during follow-up period of 6 months.

Conclusion The Miltonia valve showed excellent hemodynamic performance and significant improvement in NYHA functional class.

Keywords MVR · Miltonia Valve · CPB · Mitral valve · Mechanical valve

Introduction

Currently, valves with a bi-leaflet design are the most widely used for mitral valve replacement (MVR). There has been significant evidence over the past many years that the bi-leaflet mechanical heart valve performs better than previous designs in terms of transvalvular gradients, flow pattern distribution, and perhaps thrombogenic properties [1, 2]. Miltonia mechanical bi-leaflet (Meril Life Sciences Pvt. Ltd., India) was approved for clinical use by the Central

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Drugs Standard Control Organisation (CDSCO), Government of India, in 2018. Its main advantage is the ability to rotate once implanted, utilizing a new sewing ring design.

The aim of this study was to assess the performance of a novel Miltonia bi-leaflet mechanical prosthesis in patients undergoing MVR, also to expand the array of effective options available to surgeons. In addition, we examined the hemodynamic performance of valves in all the patients at a 6-month interval.

Material and methods

Patients

This study was registered on October 18, 2022, in the Clinical Trials Registry-India (CTRI), registration number CTRI/2022/10/046568. Patients were enrolled from October 2022 to July 2023 in this single-center study of the Miltonia mechanical prosthesis. This is an investigatory-initiated, non-regulatory, prospective observational study. The study protocol was approved by Institute ethics committees, and all patients provided written informed consent. A total of 50 patients met the inclusion and exclusion criteria for MVR with a Miltonia mechanical prosthesis.

Inclusion criteria

- Patients who need elective MVR surgeries with or without tricuspid valve repair.
- All adult patients > 18 years.
- Both males and females.

Exclusion criteria

- A lack of informed consent or non-cooperation on the part of the patient.
- Emergency procedures, re-operation.
- Any patient with contraindication to oral anticoagulation.

Post operatively, all the patients were followed up 7 days after discharge, then monthly for 3 months and then every 3 months. The hemodynamic performance of all the patients was assessed at discharge and at 6 months follow-up by estimating the mean and peak gradient across the prosthetic mitral valve.

Statistical analysis

Analysis was conducted using SPSS for Windows (version 22.0; SPSS Inc., Chicago). Descriptive statistics, including mean and standard deviation (SD) for continuous variables and frequencies and percentages for categorical variables, were calculated. McNemar's test was used to compare categorical variables, and a paired *t*-test compared preoperative and postoperative means of quantitative variables. The significance level was set at 0.05. Cochran's *Q* test was used to calculate the sample size.

Device description

The Miltonia bi-leaflet mechanical heart valve features a low-profile design with a pyrolytic carbon orifice ring and mirror-image leaflets. The leaflets coated with pyrolytic carbon and impregnated with tungsten for enhanced radiopacity, open to form an 85° angle.

The sewing ring, made of double velour polyester fabric, is secured with titanium lock rings and a lock wire, and can be rotated in situ. A titanium stiffening ring mounts the sewing cuff to the orifice during surgery, and four markers aid in uniform suture placement.

The valve's open pivot design minimizes shear stress on blood cells, reducing thrombosis risk, and the open hinge mechanism decreases noise, enhancing patient and family quality of life [3].

Surgical technique

A comprehensive medical history was recorded for all patients with blood sample analysis, electrocardiogram, echocardiography, chest x-ray PA (posteroanterior) view, and coronary angiography for patients over 40 years old. Two patients in study exhibited mild coronary plaques not requiring intervention.

All patients were operated with the use of cardiopulmonary bypass (CPB) and mild hypothermia. Myocardial protection was achieved with the antegrade infusion of del-Nido cardioplegia solution and topical cooling with cold saline solution. Most patients had their diseased mitral valve segment excised with partial preservation of the posterior mitral leaflet. In cases of mitral valve regurgitation, complete leaflets (both anterior and posterior) were preserved. Anterior mitral leaflet (AML) segments were fixed to the commissural areas after cutting them. The appropriate size of Miltonia mechanical bi-leaflet valve was implanted in its mitral position during surgery as per the sizing of mitral annulus with interrupted polyester sutures. Concomitant tricuspid valve repair was performed when indicated, using a St. Jude Medical Tailor flexible ring with interrupted polyester sutures. Postoperative care included postoperative administration of low molecular weight heparin (LMWH) and oral anticoagulant therapy, following standard routine care protocols. We started Inj low molecular weight heparin of 1 mg/kg twice daily dose on postoperative day 1 with tablet Nicoumalone with titrated dose adjustment to reach the target international normalized ratio (INR) between 2.5 and 3.5 along

with tablet Aspirin. Once target INR was achieved, LMWH was stopped.

Outcomes

Transthoracic echocardiography was performed pre-procedure, post-procedure at discharge, and at the 6-month follow-up for all enrolled patients. Patients will be monitored for adverse events every 12 months for 5 years.

Performance endpoints measured hemodynamic performance and New York Heart Association (NYHA) functional class improvement.

The safety endpoints included early (≤ 30 days) and late mortality (> 30days) after operation and valve-related morbidity like paravalvular leak (residual leak from valve implantation), prosthetic heart valve thrombosis, prosthetic valve endocarditis, structural (changes intrinsic to the valve, such as fracture, wear, leaflet escape, and suture line disruption of an operated valve) and non-structural valve dysfunction (factors not intrinsic to valve including entrapment by pannus, tissue, or suture), anticoagulation-induced hemorrhage, stroke (cerebrovascular events due thromboembolic episode), and re-operation.

Early mortality was defined as all-cause mortality within 30 days, and late mortality as all deaths occurring after 30 days post-surgery.

Result

This study included 50 patients with either isolated mitral valve disease or mitral valve disease with concomitant tricuspid valve disease. Female patients accounted for 68% (*n*-34) of the cohort, with males comprising 32% (*n*-16). The mean age was 38.8 ± 9.5 years, with the highest number of patients falling within the 31–40 age group. Atrial fibrillation was present in 34 patients preoperatively (Table 1).

Predominantly stenotic mitral valve disease was observed in 35 (70%) of patients, while 8 (16%) had predominant mitral valve regurgitation. Additionally, 7 (14%) had severe tricuspid valve disease alongside mitral valve disease. Rheumatic mitral valve disease was predominant in 47 (94%) of patients, with the remaining cases being degenerative in nature.

All mitral valves were replaced with a Miltonia mechanical valve prosthesis. Tricuspid valve annuloplasty was done in 7 (14%) patients. In our study, we observed a range of valve sizes utilized during MVR. Specifically, 4 (8%) patients received a 25-mm valve, 13 (26%) patients were implanted with a 27-mm valve, and the most common size was the 29-mm valve, administered to 17 (34%) patients. Additionally, 14 (28%) patients underwent mitral valve replacement with a 31-mm valve, and only 2 (4%) patients received the largest size available, a 33-mm valve.

Table 1 Demographic distribution of study subjects (*N* = 50)

Gender	No	Percentage
Male	16	32
Female	34	68
Age (years)		
≤ 30	10	20.0
31–40	22	44.0
41–50	13	26.0
51–60	4	8.0
> 60	1	2.0
	Mean (SD), 38.88 (9.51)	
	Range, 22–65	
Co morbidities	No	Percentage
Smoking	4	(8.0)
Diabetes mellitus	4	(8.0)
Hypertension	6	(12.0)
Hypothyroidism	6	(12.0)
Sickling positive	3	(6.0)
Etiology		
Rheumatic disease	47	(94.0)
Degenerative disease	3	(6.0)
Concomitant procedures		
Tricuspid valve repair	11	(22.0)
LA/LAA clot evacuation	9	(18.0)
Others		
Atrial fibrillation	34	68

SD standard deviation

LA/LAA left atrium/left atrial appendage

Performance endpoints The hemodynamic performance of various valve sizes implanted at the mitral valve position was assessed with the help of transthoracic echocardiography. The peak and mean pressure gradients across the diseased mitral valve preoperatively and the gradients across the prosthetic mitral valve postoperatively are detailed in Tables 2 and 3. It was seen that there was a significant improvement in both the mean and peak pressure gradient across the prosthetic mitral valve ($p < 0.001$) for all valve sizes. Consequently, the valve demonstrated good hemodynamic performance.

The total duration of hospital stay was counted from the day "0"of surgery to the day of discharge which showed a mean of 9.6 ± 3.8 days with maximum (74%) number of patients staying in between 8 and 14 days. Nine patients (18%) were discharged within 7 days. Four patients (8%) stayed for more than 15 days as there was wound infection in two patients and poor control of anticoagulation in the rest.

All patients had significant improvements in their NYHA functional class after surgery with 46 (92%) of patients in NYHA class I and 2 (4%) of patients in NYHA class II ($p < 0.001$) at 6 months follow-up. Preoperatively, majority

Table 2 Comparison of pre-op and post-op peak pressure gradient ($N=50$)

Valve size (N)	Total no. of patients (n)	Pre-procedure peak gradient in severe MS patients Mean (SD)	Patients with severe MS	Peak gradient at time of discharge Mean (SD)	Peak gradient at 6 months Mean (SD)
25 mm	4	18.32 (3.44)	4	10.20 (0.90)	10.00 (1.41)
27 mm	13	18.88 (5.98)	12	8.15 (2.19)	8.15 (1.90)
29 mm	17	18.02 (5.53)	10	9.37 (3.55)	8.91 (2.20)
31 mm	14	17.54 (5.10)	7	8.42 (2.42)	7.86 (1.43)
33 mm	2	16.34 (0.33)	2	8.00 (0.0)	8.00 (1.41)
Overall	50	18.06 (5.17)	35	8.80 (2.71)	8.47 (1.89)
p value	<0.001				

Paired t test, p value <0.001, significant for all valve size from pre-procedure to discharge and also from pre-procedure to 6 months

Table 3 Comparison of pre-op and post-op mean pressure gradient ($N=50$)

Valve size (N)	Total no. of patients (n)	Pre-procedure mean gradient in severe MS patients Mean (SD)	Patients with severe MS	Mean gradient at time of discharge Mean (SD)	Mean gradient at 6 months Mean (SD)
25 mm	4	10.40 (1.45)	4	4.50 (0.57)	4.50 (0.57)
27 mm	13	10.89 (4.57)	12	3.43 (1.11)	3.76 (1.09)
29 mm	17	10.42 (3.30)	10	3.88 (1.46)	4.06 (1.01)
31 mm	14	10.80 (3.86)	7	3.75 (1.33)	3.69 (0.75)
33 mm	2	10.15 (1.20)	2	4.50 (2.12)	4.00 (1.41)
Overall	50	10.66 (3.58)	35	3.80 (1.29)	3.91 (0.94)
p value	<0.001				

Paired t test, p value <0.001, significant for all valve size from pre-procedure to discharge and also from pre-procedure to 6 months

of patients 44 (88%) had NYHA functional class III, 4 (8%) of patients had functional class IV, and only 2 (4%) had functional class II.

Safety endpoints At 6 months follow-up, there were no incidents of re-operation, paravalvular leak, prosthetic valve endocarditis, and structural or non-structural valve deterioration/dysfunction. Two patients suffered from anticoagulation-related hemorrhage. Four patients came back in follow-up with prosthetic heart valve thrombosis (PHVT). There was a mortality of two patients in our study within 6 months follow-up period due to low cardiac output syndrome and one patient among them had stroke (Table 4).

Discussion

Our study examined the outcomes of MVR using Miltonia mechanical valves in a cohort of predominantly young, female patients with mitral valve disease, mostly of rheumatic origin. The results demonstrated significant improvements in hemodynamic performance and functional status following surgery, with the majority of patients achieving NYHA class I at 6 months post-operation. The procedure showed a good safety profile, with no re-operations or significant prosthetic complications reported. However, the occurrence of four cases of prosthetic heart valve thrombosis during follow-up is a concern

Table 4 Distribution of study subjects according to the complications ($N=50$)

Complications	No	Percent
Re-operation	-	-
Paravalvular leak	-	-
Mortality	2	4.0
Anticoagulation-related hemorrhage	2	4.0
Prosthetic valve endocarditis	-	-
Structural valve dysfunction	-	-
Stroke	1	2.0
Prosthetic heart valve thrombosis (PHVT)	4	8.0

that highlights the need for close follow-up and tight control of anti-coagulation in these patients.

There was definitive improvement in the pre-procedural peak and mean pressure gradient after surgery. This improvement of pressure gradients across Miltonia prosthetic heart valve corroborated with the findings of the study of St. Jude Medical and Medtronic Hall valve by Fiore et al. [4]. There was no evidence of Patient Prosthesis Mismatch at the time of discharge and 6 months follow-up. In our 6-month follow-up, there was no evidence of paravalvular leak, prosthetic valve endocarditis, and structural valve dysfunction. An INR of 2.5–3.5 was maintained post operatively in all the patients of our study.

There were two patients with anticoagulation-related hemorrhage (epistaxis) and four patients with prosthetic heart valve thrombosis. Anticoagulation-related bleeding was managed by injection vitamin K and fresh frozen plasma transfusion. The echo finding of PHVT patients was showing movement of only one leaflet which was confirmed with immediate fluoroscopy. These four patients were not taking oral anticoagulations as per advise and presented with low INR (between 1 and 1.4) during admission. The poor compliance of patients with anticoagulation drugs is consistent with findings from other studies [5–8]. The PHVT was managed successfully by thrombolytic drug recombinant tissue plasminogen activator (rtPA), i.e., alteplase. All four patients were successfully thrombolyzed with decrease in gradient across prosthetic valve. The early cause mortality in our study which included death in the same hospital admission ($\leq$30 days) was seen in two patients. The cause of mortality in both the patients was low cardiac output syndrome with one patient among them also having stroke due to air embolism. Uchino et al. also found in their study that the most common cause of in-hospital mortality was low cardiac output syndrome [6].

The mean duration of hospital stay in our patients was 9.62 ± 3.8 days to teach them the need and management of anti-coagulation as most of them belonged to remote rural places. All patients in the study exhibited a significant improvement in their NYHA functional class at the 6-month follow-up, and none of them had a NYHA functional class IV or III, which is consistent with findings from other studies [4, 7, 8].

Limitations

There are a few limitations of this study. It should be noted that Miltonia was a single-arm study without any active comparator group. In addition, the follow-up period was short, and the sample size was small.

Conclusion

With the Miltonia bi-leaflet mechanical valve, hemodynamic performance and NYHA functional class are significantly improved by reducing pressure gradients across the prosthetic mitral valve. Due to the incidence of valve thrombosis observed in few cases, further studies with larger sample sizes and long-term follow-up are needed. For this prosthesis to be declared safe and effective for the long run, multicenter trials are needed.

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Author contributions NKK, PM, GKS and NC performed the surgical procedures. SS was involved in anaesthesia management. SJ collected the data. NKK analysed the data. PM and MW prepared the manuscript. Each author reviewed & approved the manuscript.

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Data availability The corresponding author will provide the datasets upon reasonable request.

Declarations

Ethical declaration The study protocol was approved by Institute ethics committees. Institute ethics committee approval reference no is IEC/2022/1132 dated 01/08/2022. This study was registered on October 18, 2022 in the Clinical Trials Registry-India (CTRI) with registration number CTRI/2022/10/046568.

Conflict of interest It is declared that the authors have no competing interests.

Consent for publication Pre-surgical consent was obtained with consent for publication.

Statement of human and animal rights Not applicable.

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