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PROJECT REPORT

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CERTIFICATE

I, Dr. Ali Shafeeq hereby declare that I have undertaken the work necessary for the project, under the guidance of the Faculty, Department of Cardiology.

Place: Trivandrum
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LIST OF PROJECTS

1. **PERMANENT PACEMAKER IMPLANTATION AFTER AORTIC AND MITRAL VALVE REPLACEMENT: INCIDENCE AND PREDICTORS**

2. **LONG - TERM FOLLOW-UP OF PATIENTS WHO UNDERWENT MITRAL VALVOTOMY WITH METALLIC DEVICE**

PROJECT REPORT I

PERMANENT PACEMAKER IMPLANTATION AFTER AORTIC AND MITRAL VALVE REPLACEMENT: INCIDENCE AND PREDICTORS

Introduction

INTRODUCTION

The risk of developing conduction disturbances after open heart surgery has been reported to be between 10% and 15%.[1,2] These conduction abnormalities do recover in majority of cases. However 0.8% of isolated coronary artery bypass grafting (CABG) and 3-6% of valve surgeries require permanent pacemaker (PPM) implantation following the operations.[3] In the USA, approximately 5% of the 100,000 patients who undergo cardiac valve surgery each year require postoperative PPM implantation before discharge from the hospital.[4]

Aims of the Study

AIMS OF THE STUDY

This study aimed to look into the incidence of PPM implantation following mitral and aortic valve surgery and to evaluate the risk factors for need of PPM implantation.

Review of Literature

REVIEW OF LITERATURE

Conduction disorders following cardiac surgery have been well defined with reported incidence varying from 10% to 15%.These conduction defects may reverse during the hospital stay. However, 1% to 3% will eventually require permanent pacing, and the timing of PPM implantation is not uniformly agreed.

Bareman et al,[1] followed up 93 patients undergoing CABG prospectively to ascertain the natural history and determinants of new postoperative conduction defects. Postoperatively, new bundle-branch or fascicular block developed in 42 (45%) patients and third-degree atrioventricular (AV) block, in 4 (4%). The conduction defect resolved partially or completely by the time of hospital discharge in 54% of patients. In 4 patients with third - degree AV block, AV block resolved on second postoperative day in 1 patient and in the others it persisted beyond second postoperative day. At 2 months of follow-up, all 3 patients with third-degree AV block and had PPM before discharge were no longer in AV block. They concluded that following CABG, the occurrence of new AV conduction defects is related to the number of vessels bypassed, cardiopulmonary bypass pump time, and aortic cross-clamping time.

Chu A et al,[5] studied 913 patients undergoing CABG from 1976 to 1981 and reported that transient (resolving before discharge) and persistent (until discharge) ventricular conduction abnormalities developed in 156 (17%) and 126 (14%) respectively. Complete right bundle branch block (RBBB) was the most frequent type of new ventricular conduction abnormality, followed by left anterior hemiblock and incomplete RBBB found in 60%, 26% and 9% respectively of all patients with transient changes. The corresponding figures in those with persistent conduction defects were 29%, 33% and 26%. Development of new ventricular conduction abnormalities was most strongly related to time of operation ($p<0.0001$) increasing from 2% transient and 7% persistent in 1976 to 36% transient and 22% persistent in 1981. The incidence was higher in older patients. Preoperative ejection fraction and number of diseased vessels were related to development of perioperative ventricular conduction abnormalities but were not independently related after adjustment of other baseline characteristics. Perioperative conduction abnormalities including isolated left bundle branch block (LBBB) did not have worse survival rates at 3 year follow up.

Cook et al,[6] examined the medical records of 800 patients who had undergone CABG in two time periods; 400 patients in the year 1991 and 400 patients in the year 2001. There was a marked decrease in the incidence of new postoperative conduction defects from 1991 (19%) to 2001 (6%). There was

also a change in the most frequently occurring block, from a RBBB in 1991 (10%) to first-degree atrioventricular block (3%) in 2001. Finally, conduction defects in 1991 were more transient. While 19% of 1991 patients showed a conduction defect early postoperatively, only 9% were persistent. In 2001, the incidence of conduction defects at discharge (7%) was equivalent to that in the early postoperative period (6%). Predictors of new conduction defects included year of operation, age, intraaortic balloon counterpulsation, number of vessels bypassed, and crystalloid cardioplegia.

Kumbhani et al,[7] reviewed the epidemiological features, pathogenesis, diagnosis, and management, and the short-term and long-term significance of fascicular conduction abnormalities following CABG, based on the data from 30 studies. Conduction disturbances had an incidence of 3.4% to 55.8% after CABG surgery, the most common being RBBB which was usually transient and benign. They found that the two most important factors predicting conduction disturbances after CABG were myocardial ischemia and type of cardioplegia. There was no difference in long-term survival between patients who developed conduction disturbances after CABG surgery, and those who did not, indicating a benign influence of conduction disturbances on long-term survival, and the lack of the necessity for monitoring or pacing.

Jokinen et al,[8] in a study of 180 patients who underwent elective CABG, determined the long-term prognostic significance of new permanent

conduction defects related to CABG. Sixty-three (35.0%) of the patients developed a new conduction defect (CD+) before hospital discharge. Early (<30 days) and long-term (>30 days) survival rates were 98.9% and 86.1%, respectively. The long-term survival in CD+ patients was significantly lower than in CD- patients (77.8% vs. 90.4%, p = 0.02). However, cardiac survival in CD+ patients and CD- patients did not differ from each other (88.9% and 92.3%, respectively, p=NS). The appearance of preoperative diabetes, intraoperative perfusion time, number of distal anastomoses performed, CABG-derived permanent conduction defects and low preoperative ejection fraction were associated with higher all cause mortality during the long-term follow-up.

Meimoun et al,[9] reported new-onset AV block in 27 out of 115 (23%) patients undergoing mitral valve replacement (MVR). This figure rose to 33% when bundle branch block was included in the post-surgical conduction disturbances. However 44% of these AV block was transient, resolving before discharge. Three (2.6%) of patients had PPM on an average 18 days after surgery. Persistent third degree AV block occurring immediately after surgery was the indication in all patients. Patients were followed up from 6 to 48(mean36) months in this study.

Berdejas et al,[10] in a retrospective analysis of 391 patients who underwent MVR or ring annuloplasty reported new onset AV block in 23.5%

of patients. When bundle branch blocks are included the incidence rises to 38%. During mitral valve surgery, conduction disturbance more likely to develop was AV block (61.3%) rather than bundle branch block (38.7%). Furthermore, all branch blocks were transient and resolved before discharge. Permanent pacemaker was implanted in 17 patients developing complete AV block in the early post operative period. Brodell et al,[11] no difference in second degree or complete AV block when mitral valve repair was compared with MVR. Kim et al,[12] in a retrospective analysis of 155 patients undergoing valve surgery reported 17 (11%) patients having complete AV block in the post surgical period. The data indicated that if complete AV block was present during the first 24 hours after mitral or aortic valve surgery and perists beyond 48 hours, it was unlikely to resolve within the next one or two weeks.

Early studies of conduction disturbances following congenital heart surgery reported incidence of up to 25%.[13] This has been lowered to 1-4% following improved surgical techniques and better anatomical understanding of the surgical techniques.[14] Also early as well as more recent studies report occurrence of late onset conduction disturbances years after congenital heart surgery.[15,16] PPM is warranted for persistent complete heart block (CHB) even if escape rhythm is stable, because of risks of syncope and sudden death are as high 30% during relatively short period.[17,18,19] Population-based follow up study by Smerup et al,[20] reported that most of PPM implantation were in the

immediate postoperative period, while late implantation period was scattered, from postoperative day 20 to 100. Half of the patients who underwent PPM received one between postoperative day 10 and 20. A study by Weindling et al, [21] reported that in 95% of patients post operative conduction disturbances resolved by postoperative day 9.

Complete AV block requiring PPM is a known complication of aortic valve surgery, developing in 5% of patients after percutaneous aortic valvuloplasty[22] or surgical aortic valve replacement (AVR)[23]. Autopsy reports of those who died after surgery had reported direct trauma to the conduction system.[24] LBBB is the most commonly encountered conduction defect after AVR, with incidence of 20-32% [25,26,27] reported in earlier studies and 5.7% in later studies. New-onset LBBB has been reported in 36 % to 40% of patients undergoing percutaneous AVR with CoreValve Revalving System.[28,29] Habicht et al, [30] reported that 13.7% of patients who had normal perioperative electrocardiogram developed late conductions disturbances after AVR. This occurred 3 to 102 months after surgery and only one patient in the study required PPM at 82 months after AVR.

Prognosis of acquired LBBB after AVR has been reported with significantly increased subsequent syncope, AV dissociation and sudden death.[31] Thomas et al,[27] in a series of 173 patients reported 5 patients (11.8%) who developed sudden cardiac death. Most of these events occurred during the

first year of follow up. Fournial et al,[25] reported an incidence of 33% of new conduction disturbances after AVR, LBBB being the most common. Long term follow up of those patients with LBBB after AVR has shown increased incidence of sudden cardiac death among these patients.[13] Dawkins et al,[48] showed in their study that persistent bundle branch block after AVR was the only predictor of adverse events during follow up. The highest incidence was seen in those who developed new LBBB after AVR. Fifty seven percent (57%) of the adverse events occurred in the first 6 months of follow up and 71% occurred one year after surgery. Hence it is advisable to do postoperative PPM implantation in these patients before discharge.

The need for cardiac pacing after surgery arises for two reasons. First, surgical procedures close to the sinoatrial or atrioventricular nodes or the His bundle might result in physical trauma to the conduction system. Secondly, extensive coronary artery disease might compromise myocardial protection during intraoperative cardioplegic arrest, resulting in ischemic effects to the conduction system.

The AV node is located within the right atrium in the apex of the triangle of Koch.[32] It penetrates through the membranous septum and central fibrous body as the bundle of His, emerging in the ventricles on the crest of the ventricular septum, where it gives rise to the fascicles of left bundle branch. Noncoronay cusp of aortic valve, posterior-medial commissure of the

anterior mitral leaflet and the septal leaflet of the tricuspid valve lay close to the AV node. Debridement of the annular tissue at these areas decreases the distance between the AV node and anchoring sutures, thereby increasing the chance for injury to the conduction system. Continuous sutures rather than interrupted sutures have been shown to increase the incidence of postoperative AV conduction abnormalities and PPM.[33] In the study by Maugenest et al,[29] patients who had new –onset bundle branch block had higher mean distance from the proximal end of the frame of the valve prosthesis to the lower edge of noncoronary cusp, than those without new-onset bundle branch block. (10.3±2.7mm vs. 5.5±3.4mm respectively). Ergodan et al,[34] in 465 patients with a mean age 49.9±17.2 years, who underwent AVR reported that, 19 (14.1%) required PPM. Severe annular calcification was documented in 78.9% of them and was found to be a significant risk factor for PPM ($p<0.01$). However, valvular calcification was not found to be associated with requirement for PPM, reflecting the effect of mechanical trauma during PPM implantation. Multivariate analysis showed that annular calcification, bicuspid aortic valve, female gender, presence of RBBB or LBBB, prolonged total perfusion time, and hypertension were risk factors for PPM implantation. Berdajs et al,[10] in a retrospective study to evaluate the causative mechanism underlying postoperative AV block after MVR and ring annuloplasty described histopathological sections of AV node and surrounding structures. They reported that in 13 out of 55 (23%) of the patients, AV node artery

approached the P3 section of the posterior leaflet. Hence they postulated that damage to the AV node artery becomes very probable during the mitral valve ring annuloplasty or prostheses implantation. Utley et al,[35] reported higher incidence of loss of sinus rhythm following mitral valve surgery with superior trans-septal approach. Apart from sinus node dysfunction, atrial tachycardia and flutter are known complications associated with superior trans-septal approach to mitral valve surgery.[36] Data are limited with vertical trans-septal approach, which probably does not cause sinus node dysfunction.[37] Gordon et al, [2] in a prospective study of 10,421 patients identified 8 independent risk factors for PPM implantation, five of which related to the physical trauma to the conduction system (valve operation, repeat operation, ablative arrythmia operation, mitral annulus construction, and active endocarditis), the rest of which related to increased ischemic burden (age 75 years or older, renal failure) or suboptimal intraoperative myocardial protection (use of cold cardioplegia).

There are conflicting reports on the impact of total bypass and cross-clamp time, degree of myocardial cooling[10,38] and method of cardioplegia.[39] These presumably reflect severity of ischemic damage to the conducting system. Dawkins et al[40] reported that none of these factors predicted need for PPM following AVR. Keefe et al,[41] evaluated 102 consecutive patients undergoing isolated AVR. Postoperative CHB was common, occurring in 18

(18%) patients. Six (6%) patients required PPM before discharge, and a further 3 patients (3%) required late PPM (median follow up, 4.2 years). The study could not predict any clinical or operative variables for early development of complete AV block.

Preexisting conduction defects like the presence of prolonged PR interval (>200 ms), and RBBB or LBBB on preoperative electrocardiogram had been reported to be associated with an increased risk of PPM after the operation.[4] Erdogan et al,[34] in their study found the presence of RBBB as a strong predictive factor for PPM after AVR.

Del Rizzo et al,[42] reported in their study that out of 3,448 patients who underwent open heart surgery, 1.3% required PPM. Multivariate logistic regression analysis showed that aortic valve surgery (odds ratio, 8.23; p=0.001), the absence of preoperative sinus rhythm (odds ratio, 5.60; p=0.001); postoperative myocardial infarction (odds ratio, 3.46; p=0.024), and female gender (odds ratio, 2.52; p=0.003) were independent predictors of PPM.

The requirement for PPM after repeat cardiac surgery has been reported to be high. Lewis et al,[43] reported an incidence of 9.7% ,i.e; 54 out of 558 patients who underwent at least one repeat cardiac surgery. Several factors were found to strongly relate to increased need: valve replacement (including AVR), preoperative endocarditis, number of reoperations, age, and degree of

hypothermia during bypass. Increased total aortic cross-clamp and bypass times were also associated with PPM. In the same study hypertension is found to increase the risk of PPM on multivariate analysis. A more severe valvular and annular calcification is associated with hypertension and increased interventricular septal thickness in long-standing hypertension, makes it more difficult for myocardial protection.

Elahi et al,[44] audited the records of 2,392 consecutive adult patients who underwent cardiac valve surgical procedures. Of these, 118 patients required the postoperative implantation of PPM during the same hospitalization. Multivariate logistic regression analysis showed that reoperations (odds ratio [OR], 8.23; $p<0.001$), longer cumulative cross-clamp times (OR, 5.9; $p<0.001$), multiple-valve surgical procedures (OR, 3.46; $p<0.05$), and absence of preoperative sinus rhythm (OR 2.52; $p<0.001$) were independent predictors of the need for PPM after valve surgery.

Best timing for permanent pacing is not fully established after cardiac surgery. Kopalan et al,[4] reported a mean postoperative day of PPM implantation of 8.4±5.8 (median 7) days. Kim et al.,[12] in a series of patients undergoing valve surgery, all those requiring a pacemaker developed AV block within the first post operative day. They suggested waiting for at least 5 days before PPM implantation, If AV block failed to resolve by 48 hours. Berdajs et al,[10] found 4% incidence of CHB in patients undergoing mitral

valve surgery. These patients had PPM implanted at an interval of 4 days after surgery. American Heart Association/American College of Cardiology guidelines recommend PPM for third-degree and advanced second-degree AV block at any anatomic level associated with postoperative AV block that is not expected to resolve after cardiac surgery.[45]

Materials and Methods

MATERIALS AND METHODS

This study was designed as a retrospective analysis of patients who developed conduction disturbances which necessitated PPM implantation between 1998 and 2008. A total of 2,167 patients who underwent isolated AVR (n = 937) and MVR (n = 1230) during this period were analyzed in the study. Patients were identified from the PPM implantation register maintained in the hospital. Patients who had PPM or conduction disturbances requiring PPM per se prior to the surgery, those undergoing redo valve replacement surgeries, or combined MVR and surgical ablation for atrial fibrillation (AF) were excluded from the analysis. Patients with left ventricular ejection fraction <45% were also excluded from the study.

The final analysis included 44 - AVR in 21 and MVR in 23 - patients, and these patients constituted the cases. These cases were compared to age and sex matched controls who had undergone similar procedures during the same period. Pre-, peri- and post-operative variables of the group were compared to assess risk factors for PPM implantation. These variables included, age, sex, type of valvular lesion, medications, coronary heart disease risk factors and preoperative electrocardiographic findings.

The detailed pre-operative evaluation in these cases included a comprehensive echocardiographic examination in all and coronary angiogram in patients above 40 years. All operations were performed under standard cardiopulmonary bypass established between ascending aorta and bicaval venous cannulation. Moderate systemic hypothermia with cold crystalloid antegrade cardioplegia repeated every 30 minutes was maintained for myocardial protection. Continuous monitoring with electrocardiography and central venous and arterial monitoring had been done for all patients, who underwent temporary epicardial pacing following rhythm disturbances after weaning from cardiopulmonary bypass. Electrocardiography was performed daily in all the patients who developed rhythm disturbances post-operatively. All these patients also had a 12-lead electrocardiogram recorded on the day of discharge. The development of conduction disturbances on the electrocardiogram was determined according to the established criteria.

The follow up details were also noted from the hospital records, as recorded during their regular follow up visits to pacemaker clinic. Based on this data, pacemaker dependency on follow up was determined.

STATISTICAL ANALYSIS

Continuous variables are expressed as mean ± SD and compared using the independent *t* test. Categorical variables are compared with Fischer's exact test. A p value <0.05 was considered significant. Multivariate logistic regression analysis was done to find out variables predictive of permanent pacemaker implantation. Statistical analysis was done using SPSS for Windows, Version 16.0.

Results

RESULTS

The analysis intended to identify the incidence and predictors of PPM requirement was done separately for patients who underwent AVR or MVR.

Patients with aortic valve replacement

Out of a total of 937 patients who underwent AVR during this period, 21 (2.24%) required PPM. The baseline characteristics of the cases and controls are shown in Table1.

Five patients had rheumatic aortic valve disease; bicuspid aortic valve was seen in 2 patients, and rupture sinus of Valsalva in one. In the remaining 13 cases PPM was done in patients who had AVR for severe calcific aortic valve disease. Severe aortic stenosis was seen in 11 patients and severe aortic regurgitation in 8. Two had combined aortic regurgitation and aortic stenosis. All patients received VVI pacemakers at the discretion of the physician and patient's affordability. Preoperative resting electrocardiogram showed that all patients who underwent AVR were in sinus rhythm. Eight patients had first degree atrioventricular block. None had AF or AV conduction disturbance more severe than first-degree AV block. There was no difference in the use of digoxin preoperatively between two groups. None in either group was on beta blocker therapy immediately prior to AVR. No difference in left ventricular ejection fraction (LVEF) was also noted between the cases and controls. Out of all parameters analyzed, only the pre-operative PR interval and the frequency of PR interval > 200 ms differed significantly between the groups.

Table 1. Baseline characteristics of the patients who had permanent pacemaker implantation following aortic valve replacement and the control group (n=21)

		AVR-PPM (n=21)	Control (n=21)	*p* value
Clinical Variables				
Age *(years)*		47.1 ± 13	46.9 ± 14.1	NS
Sex				
	Male	15 (71.4%)	15 (71.4%)	NS
Dyslipidaemia		7 (33.3%)	3 (14.3%)	NS
Smoking		0 (0%)	1 (4.8%)	NS
Hypertension		2 (9.5%)	3 (14.3%)	NS
Type2 Diabetes mellitus		0 (0%)	1 (4.8%)	NS
NYHA				
	Functional class II	18 (85.7%)	20 (95.2%)	NS
	Functional class III	3 (14.3%)	1 (4.8%)	NS
Medications				
Digoxin		5 (23.8%)	7 (33.3%)	NS
ECG variables				
Sinus rhythm		21 (100%)	21 (100%)	□
PR interval				
	mean, *msec*	178.9 ± 27.9	161.9 ± 16.6	< 0.05
	≥ 200 msec	7 (36.8%)	1 (4.8%)	< 0.05
LVH with and without strain		21(100%)	21(100%)	-
LAHB		1 (4.8%)	0 (0%)	NS
RBBB		1 (4.8%)	0 (0%)	NS
LBBB		2 (9.5%)	0 (0%)	NS
QRS duration, *msec*		87.6 ± 13.4	85.2 ± 10.8	NS
Echocardiographic variables				
Aortic annulus, *mm*		22 ± 3	21.1 ± 2.3	NS
Aortic valve calcification		14(66.7%)	18(85.7%)	NS
LVEF, *%*		69.2 ± 8.8	71 ± 8.9	NS
PAP mean, *mm Hg*		22.8 ± 5.5	21.6 ± 4.6	NS

AVR = aortic valve replacement; HTN = hypertension, DM = diabetes mellitus; LVH = left ventricular hypertrophy; LAHB = left anterior hemi block; RBBB = right bundle branch block; LBBB = left bundle branch block; LVEF = left ventricular ejection fraction; PAP mean = mean pulmonary artery pressure.

Operative variables of both groups are shown in table 2. Intra-operative findings showed annular calcium in 12 patients in both groups and extension of calcium onto interventricular septum was seen in 10 patients in both groups. The size of prosthesis used was slightly larger in the PPM implantation group 23±1.9mm than the control group, 22.2±2mm (NS). Aortic cross clamp time, cardiopulmonary bypass time, and volume of cardioplegia solution didn't differ significantly between the cases and controls.

Table 2. Operative characteristics of the patients who had permanent pacemaker implantation following aortic valve replacement and the control group

		AVR-PPM (n=21)	Control (n=21)	*p* value
Calcification				
	Annulus	12 (57.1%)	12 (57.1%)	NS
	IVS	10 (47.6%)	10 (47.6%)	NS
Type of cardioplegia				
	KCL	20 (95.2%)	21 (100%)	NS
	St Thomas	1 (4.8%)	0 (0%)	NS
Volume of cardioplegia, *ml*		2033.3 ± 327.2	1940.5 ± 218.9	NS
Bypass time, *min*		129.6 ± 77.2	106.5 ± 29.3	NS
Aortic cross clamp time, *min*		82.8 ± 39.6	73.3 ± 28.8	NS
Minimum temperature, ^0C		28.1 ± 1	27.8 ± 0.6	NS
Size of prosthesis, *mm*		23 ± 1.9	22.2 ± 2	NS

AVR = aortic valve replacement; IVS = interventricular septum; KCL = potassium chloride

The indication for PPM implantation was CHB in 18 (85.7%) and trifascicular block in 3 (14.3%) of patients (Table 3). After AVR, the mean time to PPM implantation was 23.7±59.2 (0-216) months. Sixteen (76%)

patients had PPM implantation during the index admission after a mean duration of 10 (0-28) days from the day of AVR. Four patients had AV block detected while coming off bypass. One patient in the PPM implantation group died during the hospital stay related to postoperative complications, and unrelated to PPM implantation. Mean duration of hospital stay was 16.2±7.5 days in cases while in the control group it was 12.6±2.1 days.

Table 3. Post operative characteristics of the patients who had PPM following AVR and the control group

		AVR-PPM (n=21)	Control (n=21)	*p* value
ECG variables				
	Sinus rhythm	7 (33.3%)	21 (100%)	NS
	Atrial fibrillation	0 (0%)	0 (0%)	□
	1^0 AVB	4 (19%)	0 (0%)	-
	2^0 AVB	4 (19%)	0 (0%)	-
	RBBB	6 (28.6%)	0 (0%)	-
	LBBB	9 (42.9%)	0 (0%)	-
	LAHB	7 (33.3%)	0 (0%)	-
	CHB	18 (85.7%)	0 (0%)	-
	QRS duration, *msec*	141 ± 43.2	89 ± 12.6	<0.01
Indication for PPI				
	Trifascicular block (RBBB+intermittent LBBB)	1 (4.8%)	0 (0%)	NS
	Bifascicular block(RBBB,LAHB and prolonged PR interval)	2(9.5%)	0 (0%)	
	CHB	18 (85.7%)	0 (0%)	< 0.01
Mortality		1 (4.8%)	0 (0%)	NS
Hospital stay, *days*		16.2 ± 7.5	12.6 ± 2.1	< 0.05

AVR = aortic valve replacement; 1^0 AVB = first degree atrio ventricular block; 2^0 AVB = Second degree atrio ventricular block; RBBB = right bundle branch block; LBBB = left bundle branch block; LAHB = left antrior hemi block; CHB = complete heart block; AF = atrial fibrillation

By multivariate analysis only annular calcification and PR interval >200 msec were determinants of PPM implantation following AVR (Table 4). The following variables were not associated with increased risk for PPM implantation following AVR: age, sex, use of digoxin preoperatively, aortic cross clamp time, by pass time, temperature and volume of cardioplegia solution. On follow up, 2 (8.5%) patients had the conduction disturbances reverted. Out of these two, one had trifascicular block. The other had intermittent CHB as indication for PPM implantation, and had only bifascicular block on follow up.

Table 4. Predictors by multivariate analysis

	Beta coefficient	P value
PPI following MVR		
Atrial fibrillation	6.37	0.02
PPI following AVR		
PR interval >200msec	3.91	0.01
Annular calcification	2.95	0.04

PPI = permanent pacemaker implantation; MVR = mitral valve replacement; AVR = aortic valve replacement; LVH = left ventricular hypertrophy

Patients with mitral valve replacement

Out of 1230 patients who underwent MVR during the study period, 23 (1.86%) required PPM. The mean age was 40.7±11.1 years in this group, and 69.6% patients were females. Their baseline characteristics are shown in table 5.

Table 5. Baseline characteristics of the patients who had pacemaker implantation following mitral valve replacement and the control group.

		MVR-PPM(n=23)	Control (n=23)	*p* value
Clinical Variables				
	Age, *years*	40.7 ± 11.1	41.2 ± 11.2	NS
	Sex			
	Male	16 (69.6%)	13 (59.1%)	NS
	Dyslipidaemia	1 (4.3%)	0 (0%)	NS
	Smoking	0 (0%)	1 (4.3%)	NS
	NYHA			
	Functional class II	13 (56.5%)	19 (86.4%)	NS
	Functional class III	9 (39.1%)	4 (17.4%)	NS
	Functional class IV	1 (4.3%)	0 (0%)	NS
Medications				
	Beta blockers	7 (30.4%)	6 (27.3%)	NS
	Digoxin	20 (87%)	17 (77.3%)	NS
ECG variables				
	Sinus rhythm	5 (21.7%)	13 (59.1%)	< 0.01
	Atrial fibrillation	18 (78.3%)	9 (40.9%)	< 0.01
	RBBB	1 (4.3%)	0 (0%)	NS
	CHB	0 (0%)	1 (4.3%)	NS
	RVH	4 (17.4%)	0 (0%)	NS
	QRS duration, *msec*	84.8 ± 8.5	90.9 ± 13.1	NS
Echocardiographic variables				
	Left atrial diameter, *mm*	50.3 ± 9.5	48 ± 6.1	NS
	LVEF, *%*	60.2 ± 5.1	61.7 ± 6.2	NS
	PAH, *mm Hg*	45.5 ± 15.2	53.6 ± 13.1	NS

MVR = mitral valve replacement; RBBB = right bundle branch block; CHB = complete heart block; RVH = right ventricular hypertrophy; LVEF = left ventricular ejection fraction; PAH = mean pulmonary artery hypertension

None of the patients had previous surgery. According to NYHA classification 13 (56.5%) were in FC II, 9 (39.1%) in FC III and 1 (4.3%) was in functional class IV.

None of the patients had hypertension or diabetes mellitus. One patient had dyslipidaemia. Beta blockers were used in 7 (30.4%) and digoxin in 20 (87%) patients who had PPM implantation done. More patients, 18 (78.3%) were in AF in the PPM implantation group, p=<0.01. Right ventricular hypertrophy was seen in 4 (17.4%) of patients, NS. LVEF was almost same in both groups (60.2±5.1 vs. 61.7±6.2%) in PPM implantation and control group, respectively. There was no significant association for PPM implantation with age, sex and presence of pulmonary arterial hypertension.

Table 6. Operative characteristics of the patients who had permanent pacemaker following mitral valve replacement and the control group

	MVR-PPM (n=23)	Control (n=23)	*p* value
Severe subvalvar pathology	22 (95.6%)	13 (61.9%)	< 0.01
Type of cardioplegia			
KCL	19 (82.6%)	22 (95.6%)	< 0.05
St Thomas	4 (17.4%)	0 (0%)	< 0.05
Volume of cardioplegia, *ml*	1328.3 ± 418.6	1218.2 ± 365.7	NS
Bypass time, *min*	103.2 ± 37.2	101.3 ± 30.8	NS
Aortic cross clamp time, *min*	56.7 ± 23.2	54.7 ± 16.1	NS
Minimum temperature, ^0C	28 ± 1.3	28.3 ± 0.9	NS
Size of prosthesis, *mm*	27.2 ± 2.4	27.8 ± 1.7	NS

KCL = potassium choloride

Operative variables of the patients who underwent PPM following MVR and the control group is shown in table 6. Presence of severe subvalvar

pathology as marked in the operative notes was significant, [22 (95.6%) vs. 13 (61.9%), p = <0.01] for prediction of PPM implantation following MVR. The following variables did not show increased risk for PPM: size of prosthesis, bypass time, aortic cross clamp time, volume of cardioplegia and minimum temperature.

All patients had rheumatic mitral valve disease. Thirteen patients had severe calcific mitral stenosis, and four patients had severe mitral regurgitation as the indication for mitral valve replacement.

Table 7. Post operative characteristics of the patients who had permanent pacemaker following mitral valve replacement and the control group.

		MVR-PPM (n=23)	Control (n=23)	*p* value
ECG variables				
	Sinus rhythm	5 (0%)	11 (50%)	< 0.01
	Atrial fibrillation	18(100%)	10 (45.5%)	< 0.01
	Intermittent 2^0 AVB	2 (8.6%)	0 (0%)	-
	RBBB	1 (4.3%)	0 (0%)	-
	LAHB	1 (4.3%)	0 (0%)	-
	QRS duration, *msec*	93.5 ± 18.2	91.8 ± 14.4	NS
Indication for PPI				
	CHB	7 (30.4%)	0 (0%)	< 0.01
	AF + Ventricular pause	13 (56.5%)	0 (0%)	< 0.01
	AF + Slow ventricular rate	3 (13%)	0 (0%)	NS
Mortality		0 (0%)	0 (0%)	□
Hospital stay, *days*		18.5 ± 8.8	12.7 ± 2.3	< 0.01

2□ AVB = second degree atrio ventricular block; RBBB = right bundle branch block; LBBB = left bundle branch block; LAHB = left anterior hemi block; CHB = complete heart block; AF = atrial fibrillation

Post surgical variables of the patient groups is shown in table 7. The indication for PPM following MVR was CHB in 7 (30.4%) patients and 13 (56.5%) had AF with symptomatic pauses and 3 (13%) had AF with slow ventricular rate. In the CHB patients, all had narrow QRS escape rhythm and one patient had intermittent CHB. After MVR, the mean time to PPM implantation was 56.4±68.7 (range 12 days to 288 months) months. Five patients underwent PPM during the index hospitalization, following a mean duration of 17.4 (range 12 to 21) days. Hospital stay was longer for PPM group (18.5±8.8 vs. 12.7±2.3 days). There was no associated morbidity or mortality with PPM implantation. Five patients on follow up had basal rhythm and no pacing on pacemaker interrogation. Four of them had persisting AF and the other had trifascicular block.

By multivariate analysis, only the presence of preoperative AF was determinant of PPM implantation following MVR (Table 4).

Discussion

DISCUSSION

The need for PPM implantation following valve surgery has been reported to be low with incidence of 3 to 6%, and such treatment has been associated with good cardiovascular prognosis. The survival rates after valve surgery has been reported to be 95.4% and 68.9% respectively at 5 and 10 years.[46] We sought to study the frequency, predictors and long term follow up of patients who had undergone PPM following AVR or MVR in our institution between 1998 and 2008.

In our study the incidence of PPM implant was 2.24% and 1.86% following AVR and MVR respectively. In a study by Keefe et al,[41] out of 102 patients who underwent isolated AVR, 6% required PPM implantation before discharge and another 3% had PPM on follow-up. They did not find any operative or clinical predictors for early PPM. Del Rizzo et al, in a study of 3,488 patients who underwent open heart surgery reported that 1.3% required PPM, and absence of sinus rhythm and AVR were predictors for PPM following surgery. However, data related to isolated AVR was not reported in that study. Limogelli et al,[3] reported incidence of 3.2% for PPM in a study of 276 patients who underwent AVR. In this study, the predictors of PPM following AVR were preoperative aortic regurgitation, myocardial infarction,

pulmonary hypertension and postoperative electrolyte imbalance. In contrast to the lower incidence in isolated valve replacement surgeries, the need for PPM following complex cardiac surgery is higher, i.e.; 9.7% with predictors for PPM being AVR, preoperative infective endocarditis, number of reoperations, age and degree of hypothermia, duration of aortic cross-clamp and bypass time. However, our study was restricted to patients undergoing either AVR or MVR. Dawkins et al,[40] in a study of 354 patients who underwent AVR, reported that 8.5% required PPM and predictors for PPM were preoperative conduction system disease and preoperative valve regurgitation. Erdogan et al[34], in a study of 465 patients who underwent AVR reported 19 (4.1%) patients required PPM, and predictors identified were annular calcification, bicuspid aorta, female sex, presence of RBBB or LBBB, prolonged total perfusion time, and hypertension.

In our study, the incidence following AVR was 2.24% and predictors for PPM were presence of annular calcification and PR interval >200msec.Our study did not identify other predictors reported in previous studies in similar studies. This could be because of the relatively lower sample size and the improved surgical techniques with time.

Histological abnormalities of the conduction system is common in aortic valve disease and it has been suggested that factors like age related

changes, mechanical pressure from raised left ventricular pressures, ischemia and primary degenerative disease of the conduction system may play a role.[25,47] Seventy six percent (76%) of patients in this study who underwent AVR had their pacemaker done during the index hospitalization, findings consistent with other studies. The mean hospital stay was 16.2±7.5 and 12.6 ±2.1 days for PPM and control group respectively. The average time for PPM implantation during index hospitalization was 10 days post surgery in our study. Best timing for permanent pacing is not fully established after cardiac surgery. Kopalan et al,[4] reported a mean postoperative day of PPM implantation of 8.4±5.8 days (median 7).Kim et al,[12] in a series of patients undergoing valve surgery, noted that those required PPM eventually had developed AV block within the first post operative day. If AV block did not resolve by 48 hours, they recommended waiting for at least 5 days before PPM implantation. Berdajs et al,[10] found 4% incidence of complete AV block in patients undergoing mitral valve surgery. Patients had pacemaker implanted at an interval of 4 days after surgery. Our study shows longer waiting period before decision for PPM is taken. This is not surprising as there are no clear guidelines on this issue.

Our study showed incidence of 1.9% for PPM following MVR. In a study by Meimoun et al,[9] out of 115 patients , 3 (2.6%) had PPM for

persistent CHB at an average 18 days following surgery. In the study by Berdejas et al,[10] 17 out of 391(4%) patients required PPM following MVR or mitral valve repair. It was done with mean interval of 4 days. Our study shows that all requiring PPM during index hospitalization had CHB in the immediate post-operative period. The average time period to PPM implantation in the MVR group was 223 (range 16 to 960) days post MVR in our study. Of note, all had narrow QRS escape probably suggesting physical damage to AV node artery as suggested by Berdejas et al, [10] However, this cannot be conclusively addressed without electrophysiological testing. This study also showed that 16 out of 23(70%) had PPM done for AF with symptomatic pause or slow ventricular response. Out of these 23 patients, only 5(21%) had pacemaker implanted during the index hospitalization, with mean of 15 days following MVR. This shows that considerable number of patients had undergone PPM implantation for variables not associated with surgery.

By multivariate analysis we found that presence of preoperative AF only predicted risk for PPM implantation in the MVR group. Study by Merin O et al,[48] also showed that MVR was not predictive of postoperative pacemaker implantation, further explaining the lower incidence of PPM implant in MVR group.

The development of conduction defects after cardiac surgery may also be associated with degree of myocardial cooling, method of cardioplegia[16], aortic cross clamp time and bypass time. This study did not show any risk associated with this on postoperative pacemaker implantation. This may be in part due to the improved techniques in myocardial preservation during cardiopulmonary bypass.

Limitations of the Study

LIMITATIONS OF THE STUDY

This study had certain limitations. First, the analysis was done retrospectively, and the data was collected from the medical records during admission, preoperative surgical notes and pacemaker follow up clinic notes. Second, the sample size was smaller which was related to the lower frequency of this complication in isolated valve surgeries. Third, the patients who were not willing to have PPM implanted or had post-operative conduction disturbances not necessitating PPM were not analyzed in this study. Last, some patients might have undergone PPM implantation in another centre and would not have been enrolled in this study. These facts would limit extrapolating the interpretations to a larger group prospectively.

Conclusion

CONCLUSION

The study showed a lower frequency of significant conduction disturbances necessitating PPM, with a slightly higher incidence in patients following AVR as compared to those who had MVR. Majority of postoperative pacemaker implantation following AVR was indicated due to AV conduction disturbances, had PPM implanted during index hospitalization, and the indication and the need for pacing persisted even at long term follow up. In contrast, following MVR, indication for pacing during index hospitalization was low, as most of them had pacing done for AF with symptomatic pauses on follow up. Presence of annular calcium and PR interval>200msec predicted PPM implant following AVR suggesting likely direct mechanical injury to the adjacent conduction system during AVR. On the other hand, these factors didn't predict PPM implant in patients with MVR, suggesting lesser role for collateral injury to conduction system during valve replacement.

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PROJECT REPORT II

LONG -TERM FOLLOW-UP OF PATIENTS WHO UNDERWENT MITRAL VALVOTOMY WITH METALLIC DEVICE

Introduction

INTRODUCTION

Inoue et al,[1] introduced percutaneous balloon mitral valvotomy (PBMV) in 1984. Since then, it has become the established procedure for treatment of severe mitral stenosis.

PBMV has become alternative procedure to surgical valvotomy with studies showing comparable results in the immediate and long-term outcomes.[2-6]

Cribier et al, [7] in 1997, introduced metallic device whose principle is similar to the Tubb's dilator used for surgical valvulotomy. There are numerous studies reporting favorable immediate, and short-term results.[7-10] However, there are few long-term follow-up studies of patients who underwent metallic valvotomy.[11-14]

Aims of the Study

AIMS AND OBJECTIVES

This study aimed to report on, long-term clinical and echocardiographic follow up of patients who underwent mitral valvotomy with metallic device. And also to analyze data to predict factors that has influence on long-term out come.

Review of Literature

REVIEW OF LITERATURE

According to World Heart Federation estimate, there are 12 million people currently affected by rheumatic fever and rheumatic heart disease worldwide. Rheumatic heart disease is a manifestation of rheumatic carditis, which occurs in 60% to 90% of cases of rheumatic fever. Prevalence of rheumatic heart disease in India is reported to be 4.54/1000 population.[15]

Mitral stenosis due to rheumatic fever results from pathological process of leaflet thickening and calcification, commissural fusion, chordal fusion, or a combination of these processes.[16] With reduction in (MVA) by the rheumatic process, blood can flow from the left atrium to the left ventricle only if propelled by a pressure gradient. This diastolic transmitral gradient results in elevation of left atrial pressure which gets transmitted to the pulmonary venous circulation and results in symptoms of dyspnea which is the fundamental manifestation of mitral stenosis.[17]

The natural history of untreated mitral stenosis has been well defined from studies in the 1950s and 1960s.[18] Overall, the 10-year survival of untreated patients presenting with mitral stenosis is 50%-60%, depending on symptoms at presentation.[19] Once significant symptoms appears, there is

dismal 0% - 15%, 10 year survival rate.[20] Mean survival drops to less than 3 years with presence of severe pulmonary arterial hypertension.[21]

In the late 1940s, Harken and Bailey described closed mitral valvulotomy (CMV).[22] By 1960s and 1970s, with the development of cardiopulmonary bypass; open surgical valvulotomy replaced the closed procedure in most of the countries. In 1984, Inoue et al, [1] introduced the idea of PBMV and it became the standard technique for successful and safe treatment in many centers. Al-Zaibag et al, [23] introduced double balloon technique as an alternative to Inoue balloon technique. However, this technique fell in favor because it was technically more demanding, requiring longer procedure time. This may result in inadvertent complications like death, left ventricular perforation and stroke. In fact, single Inoue balloon yields equivalent efficacy when compared to double-balloon technique with lower procedural risks.[24] Cribier et al, [7] in 1997 introduced metallic device whose principle is similar to the Tubb's dilator used for surgical valvotomy. The main goal was to provide a device that can be used several times without any loss of performance after proper sterilization, thus decreasing the procedural costs.

The mechanism of successful PBMV is the opening of fused commissures as shown by pathological studies.[25] Metallic valvotomy also performs in a similar manner by separating the commissures without any injury to the leaflets or chordae. In comparison to CMV, PBMV has shown

better success rates and comparable restenosis rates.[3-5] Immeadiate and short-term follow-up of percutaneous metallic mitral valvotomy (PMMV) also has shown comparable results to that of PBMV.[7-11]

The metallic valvotome,[7] (Medicorp Inc, Nancy, France) consists of four parts. The metallic dilator, the catheter, the metallic guide wire and the activating pliers. The metallic dilator made of stainless steel, is like a cylinder 5cm long and 5mm wide with slightly tapered tip. Its distal half has two hemi cylindrical bars 20mm in length that can be opened out in parallel, up to a maximum of 40mm, with a lever-arm system. The dilator is screwed to distal end of the catheter which is 13Fr and 170cm long. Its proximal end is connected to the activating pliers and also has a connector for recording distal pressures. The metallic guide wire is made of stainless steel, with a length of 270cm and a diameter of 0.035in. A metallic bead 2mm in diameter is soldered at the junction of the stiff core and the 10cm-long-floppy distal end. The metallic dilator is advanced across the mitral valve, over the metallic guidewire which is placed in the left ventricle. The metallic bead is positioned in contact with the distal end of the dilator and the guidewire is solidly locked into the metallic dilator with a threaded fastener located on the activating pliers. Squeezing the arms of the pliers causes a backward traction of the guidewire and the metallic bead that is transmitted to the distal end of the dilator, thus forcing the distal bars to spread out. Release of the pressure closes

the dilator. The activating plier consists of, (1) a caliper that allows opening of bars to be altered to 30, 35, 37 and 40 degrees with the help of a cursor, (2) a safety lock that prevents complete closure of the dilator after the release of the pressure exerted on the pliers, and (3) a threaded fastener, which is designed to block the metallic guidewire into the metallic device at the time of opening.

In adults with BSA >1.5m^2 and without severe calcifications, the dilator is usually open to 40mm at first. In other patients, the bars are separated to 37mm to start with (or35mm in children), with a stepwise increase in opening according to the results.

After dilatation, the metallic dilator can be unscrewed from the catheter and can be sterilized by autoclave for reuse. Only the catheter is meant for single use.

The achievement of final MVA >1.5cm^2 without moderate or severe mitral regurgitation (MR) is considered as the end point of immediate success. Several studies have shown that MVA usually doubles (from 1.0 to 2.0cm^2), with a 50% to 60% decrease in transmitral gradient following PBMV. In the NHLBI Balloon Valvuloplasty Registry, 738 patients with mean age, 54±15 years, had PBMV. When single- and double-balloon procedures were compared, the final MVA was larger (1.7±0.7 vs. 2.0±0.8cm^2, $p<0.001$), increase in mitral regurgitation was similar (4% vs. 12%, $p=0.08$), and

interatrial shunts occurred more frequently (2% vs. 12%, p = 0.04) after double-balloon procedures.[26] In the VID study, MVA postvalvulotomy, increased significantly with larger MVA achieved by the metallic valvotome and the double-balloon (2.1±0.49 vs. 2.0±0.23cm^2)respectively; while MVA achieved by Inoue balloon was smaller(1.87±0.39cm^2, p=0.01).[12] These results are consistent with the immediate results of the initial experience in 153 patients, by Cribier et al.[8] The procedure was successful in 92% of cases and resulted in a significant increase in MVA, from 0.95±0.2 to 2.16±0.4 cm^2. No increase in MR was noted in 80% of cases. Bilateral splitting of the commissures was observed in 87% of cases. Complications were 2 cases of severe mitral regurgitation (1 requiring surgery), 1 pericardial tamponade, and 1 transient cerebrovascular embolic event. Harikrishnan et al,[14] in a study of 230 patients who had PMMV reported success rate of 92.7 % with MVA increasing from 0.85 ± 0.12 to 1.95 ± 0.31cm^2 p=0.001. However, Bhat et al,[10] in a randomized comparison of 100 patients reported that immediate results with PMMV were similar or marginally better than Inoue balloon mitral valvulotomy (IBMV), post procedure MVA was 1.86±0.34cm^2 vs.1.69cm^2, respectively. Guerios et al, [11] in a randomized comparison of IBMV (n=27) and PMMV (n=23) reported the final mean MVA was bigger in the PMMV group (2.17±0.13 vs. 2.00±0.36cm^2; p=0.04), but after 6-month and 3-year follow up, this difference was no longer significant. (2.06±0.27 vs. 1.98±0.38cm^2, p=0.22; and 1.86±0.32 vs.1.87±0.34cm^2, p=0.89) respectively.

Mitral valve anatomy as assessed by 2D echocardiography is a strong predictor of the immediate results of PBMV. Fawzy et al, [27] in long term follow up of 518 patients, (mean age, 31±11 years) who underwent successful PBMV reported significantly larger MVA in those with Wilkins score <8.0 than those with the score>8.0, both immediately after PBMV (2.0±0.3 vs. 1.82±0.3cm^2, p<0.001) and also at follow-up (1.8±0.33 vs. 1.5±0.33cm^2 p<0.0001) respectively. In the NHLBI Balloon Valvuloplasty Registry, the leaflet mobility score was related to the immediate post-PBMV MVA: 2.2± 0.8 cm^2 for grade 1, 1.9± 0.7cm^2 for grade 2, 1.7 ± 0.7cm^2 for grade 3, and 1.9±0.9cm^2 for grade 4, p < 0.001. Results of the MVA after PBMV showed a similar relationship for each echocardiographic variable. The total morphology score showed a weak relationship to MVA immediately after PBMV (r=0.24), which was persistent at 6 months after PBMV (r=-0.25). [28]

Most of the adverse complications related to PMMV occur during interatrial septal puncture, manipulation of metallic guidewire in the left ventricle and valvulotomy of mitral valve by the device. Major complications arise from passage of Brockenbrough needle into adjacent ascending aorta and postatrial pericardial space. PBMV can be done with a mortality of <1% as the experience with the procedure increased.[29] Harikrishnan et al,[14] in their study of patients who had PMMV, reported mortality of only 0.41% and

cardiac tamponade in 2 patients, both due to LV tear. IBMV is reported to result in haemopericardium in 0% to 2.0%.[30]

Severe mitral regurgitation has emerged as the most frequent and serious complication after PBMV and its frequency has been reported to be stable over time, irrespective of the method used.[31] The mechanism of increase or new appearance of mitral regurgitation is reported to be due to excessive tearing of commissures, or incomplete closure of a calcified leaflet, localized rupture of subvalvar apparatus and shortened chordae after splitting of commissures. Kim et al, [32] in their study of 380 patients (mean age 44±11 years), reported that the most frequent mechanism was commissural MR, which occurred in 27 out of 47 (57%) patients, whereas noncommissural MR occurred in 20 (43%) patients, and in 12 (26%) patients with subvalvular damage resulting in chordae rupture and flail motion and in 8 (17%) patients with leaflet laceration. The 8-year event-free survival rate was significantly lower in patients with significant MR than in those without (47±8% vs. 83±3%, $p<0.001$) respectively and was significantly higher in patients with commissural versus noncommissural MR (63±11% vs. 29±11%, $p<0.001$) respectively. They reported that noncommissural MR, atrial fibrillation (AF) and higher mean transmitral gradient immediately after PBMV, predicted the likelihood of mitral valve replacement (MVR).

It is argued that the higher size (18Fr) of the septal dilator used in PMMV will result in larger interatrial septal defect and increased incidence of persistent left to right shunts. The incidence left to right shunts after PBMV has been reported to be 10% to 25% in the literature.[33, 34] However Cequier et al,[35] reported 62%, higher incidence due to their method of detection by venovenous indicator dilution technique. At 6 month follow-up they reported that though the left to right shunt persists, it is small with ratios of pulmonary to systemic flow less than 1.5.Harikrishnan et al, [14] reported in their study of PMMV, that 3% of patients had persistent of left to right shunt immediately after the procedure and three years follow-up only two had persistent small shunt.

The best results of PBMV are observed in young patients who have rheumatic mitral stenosis with favorable anatomic characteristics. After PBMV at least 90% of patients were alive without intervention on the mitral valve and with few or no symptoms upto 5 to 7 years after the procedure.[36, 37]

Iung et al, [38] reported long-term follow-up results of PBMV in 1024 patients, whose mean age was 49±14 years;10-year actuarial rates of survival with no cardiovascular-related death, no subsequent procedure on the mitral valve, and good functional results were 56±4% in the entire population and 61±5% after good immediate results.

Fawzy et al, [39] in their long term follow up of 520 patients (mean age 31±11 years) reported, event-free survival (free from death, redo MBV, mitral valve replacement, NYHA class III or IV) at 10, 15, and 17 years as 82±2%, 45±5%, and 31±6% respectively, and was significantly higher for patients with MES ≤ 8 (90 ± 2%, 60 ± 5%, and 51±8%, respectively; p< 0.001). They reported Wilkins score ≤ 8 (p< 0.001), age (p<0.001), and post-procedure MVA (p=0.016) as predictors of event-free survival.

Palacios et al, [40] reported survival rates in those with Wlikins score ≤ 8.0 or > 8, as 82% and 56%, respectively, when only patients with successful PBMV were included in the analysis. The mean age of the study population was 55±15 years and followed up was for mean, 4.2±3.7 years. They identified post-PBMV mitral regurgitation ≥ 3+, Wilkins score >8, age, prior CMV, NYHA class IV, pre-PBMV mitral regurgitation ≥ 2+, and higher post-PBMV pulmonary artery pressure, as independent predictors of combined events at long-term follow-up.

Some patients experience functional deterioration many years after the procedure, which is likely related to mitral restenosis. In the study by Fawzy et al, [39] restenosis occurred in 133 (25.6%) patients, and was less frequent (16.7%) in patients with a low mitral echo score (Wilkins score ≤ 8). Actuarial freedom from restenosis at 10, 15, and 17 years was 73±2%, 43±4%, and 23±6%, respectively, and was significantly higher in patients with Wilkins

score ≤8 (84±2%, 52±6%, and 36±9%, p<0.001)respectively. They reported Wilkins score >8 (p<0.0001) and post-procedure MVA (p=0.044) as predictors of restenosis.

Fawzy et al, [41] analyzed 559 consecutive patients who had successful PBMV for regression of pulmonary arterial hypertension. Patients were allocated to three groups on the basis of their pulmonary artery systolic pressure (PASP) at cardiac catheterization immediately before PBMV: group A (n=345) had PASP <50 mmHg; group B (n=183) had PASP 50-79 mmHg; and group C (n=31) had PASP ≥80 mmHg. The mean PASP was 38.5±6.8 mmHg in group A (mild PH), 59.0±7.7mmHg in group B (moderately severe PH), and 97.8 ± 17.0 mmHg in group C (severe PH). At follow up, Doppler-monitored PASP fell to normal, and was similar in groups A, B and C (29±8, 31±9, and 29±5mmHg, respectively; p=NS). Severe pulmonary hypertension normalized over 6-12 months in patients with successful PBMV and follow-up MVA >2.0$cm^{2.}$

The immediate decrease in the pulmonary artery pressure is due to the elimination of the passive component of pulmonary hypertension. A progressive decline in reactive pulmonary arteriolar vasoconstriction might further decrease pulmonary resistance over a period of one week to several months.[42] An irreversible component, caused by pulmonary arteriolar medial

hypertrophy, might cause persistent or recurrent pulmonary arterial hypertension.[43]

Significant tricuspid valve regurgitation (TR) is a common finding in patients with severe mitral stenosis and in the majority of cases, it is functional resulting from right ventricular and tricuspid annular dilation caused by long standing pulmonary hypertension. Hannoush et al, [44] demonstrated regression of significant TR after successful PBMV in relatively young patients (mean age 25±10-years) with severe rheumatic mitral stenosis and concomitant significant pulmonary hypertension (70±22mmHg). Sagie et al, [45] reported no regression of TR in relatively older patients (mean age 57± 15 years) with severe mitral stenosis and mild pulmonary hypertension (46±15mmHg). The probable reason for this diverse finding is that those with non-severe pulmonary hypertension had worse right ventricular function or more likely to have organic TR.

Significant reduction of left atrial (LA) size following PBMV has been shown by several investigators.[46, 47] Stefadouros et al, [48] studied 205 patients (mean age 31±11years). LA size at baseline and at mean follow-up of 31±21 months after successful PBMV (post procedure MVA 1.5cm^2, MR $\leq$ 2) was analyzed. LA anteroposterior dimension decreased in 87% of the patients (from 48.7±7mm to 42±6.6mm; $p<0.001$) whereas in 13% it remained unchanged or even increased. Similarly LA volume was decreased in 93.5% of

patients ($92\pm29cm^3$ - $61\pm24cm^3$,$p < 0.001$) whereas in the remaining 6.5% of patients it remained unchanged or even increased. LA anteroposterior dimension returned to normal in 29.2% of patients in sinus rhythm and in none of the patients with AF.

The only long-term though relatively small (30 patients in each group), randomized study comparing surgical closed, open, or percutaneous valvotomy, has been reported by Ben-Farhat et al,[36] in young population with pliable, noncalcified valves. The 7-years results were better for open and percutaneous procedures than for CMV, as assessed by a higher event free survival (93%, 90%, and 50%,), better follow-up MVA ($1.8cm^2$, $1.8cm^2$, and 1.3 cm^2) and lower restenosis rate (6%, 6%, and 37%)respectively. In long - term surgical series, Hickey et al, [49] reported event-free rate from MVR of 78% at 10 years and 47% at 20 years, on 103 patients who had undergone CMV (mean age 38 years). Rihal et al, [50] reported event-free rate from MVR of 57% at 10 years and 24% at 20 years, on 267 patients (mean age 43 years) who underwent CMV.

Materials and Methods

MATERIALS AND METHODS

Those who underwent PMMV during the period from June 1998 and December 2000 were included in the study. There were a total of 248 patients. On the basis of immediate results the procedure was successful in 230 patients (92.7%).Out of this group of patients, 153 were available for long- term follow-up.

METHODS

Two dimensional (2D Echo), Doppler and color flow imaging were done by transthoracic echocardiography (TTE) prior to the procedure, to asses severity of mitral stenosis, valve morphology and MR. The MVA was calculated as the average of mitral valve area obtained from continuous wave Doppler study using the pressure half time method and also by planimetry using the short axis 2D Echo view. Pulmonary artery systolic pressure (PASP) was estimated by continuous wave Doppler echocardiography using the modified Bernoulli equation (4× [peak tricuspid regurgitant velocity] 2) with 10mmHg added for the estimated right atrial pressure. Morphological characteristics of the mitral valve apparatus, which included leaflet mobility, thickness and calcification and subvalvar disease, were graded using a 4–point scoring system (1-4) devised by Wilkins et al.,[51] The total echo score, with a

maximum of 16, was obtained by adding the score for each of the four individual mitral components. The TTE study was performed in all patients immediately after the procedure, 24 hours after the procedure and on follow up visits.

Trans esophageal Echocardiography (TEE) was performed 1-2 days prior to the procedure, to exclude presence of left atrial clot and to assess MR. Those patients less than 20 years old did not undergo TEE unless they had dense left atrial spontaneous echocardiographic contrast or atrial fibrillation (AF).

Those patients who had greater than mild MR, left atrial thrombus and extensive commissural calcification were excluded from the study.

Informed consent was obtained from all patients prior to the procedure. All procedures were done under surgical standby for closed and open surgical procedures. The procedure was done under local anesthesia and right femoral vein was the entry site in all the patients. All patients were given prophylactic antibiotics and after septal dilatation all patients were heparinised. PMMV was performed using the antegrade transseptal technique. Septal puncture was done by Brockenbrough technique.

Standard hemodynamic measurements of right and left heart included mean transmitral gradient and MVA calculated from the Gorlins formulae. All hemodynamic measurements were obtained before and immediately after the procedure. Left ventricular angiography in the 30 degree right anterior oblique view was performed before the procedure in all patients with more than mild MR. Severity of MR on angiography was graded 1 to 4 as described by Sellers et al.[52] Transatrial shunting was assessed after the procedure with oximetry run and on follow-up with color flow examination. Commissural splitting was measured in the short-axis parasternal view for anterior and posterior commissures and was scored on the basis of score by Fernandez-Oritz et al,[53](0=no split, 1-partial or complete splitting of one commissure, 1.5=partial splitting of one and complete splitting of the other commissure, 2=complete splitting of both commissures).

Successful procedure was defined as immediate postprocedure MVA $\geq$ to 1.5cm^2 and no MR>2/4 according to Sellers classification. Restenosis was defined as loss of greater than 50% of the original increase in MVA or follow-up MVA <1.5cm^2.

FOLLOW UP

Patients records were retrospectively examined for clinical and echocardiography data at time of mitral valvuloplasty and at last follow-up.

According to our Department policy patients are routinely evaluated at 1 month, 6 months and then yearly. At one month follow-up, only clinical examination was done and then during subsequent visits, patients had detailed clinical examination and echocardiographic evaluation. Patients who never came up for follow-up and those who did not have follow-up in the preceding one year, were contacted by post mail and asked to report for review. Those who could not report were asked to consult local Cardiologist and send the echocardiographic and clinical report.

STATISTICAL ANALSIS

Results were expressed as mean ± SD or percentage. Group analysis was performed with analysis of variance, and the chi square or t test as appropriate. Step wise Cox multivariable regression analysis was used to identify variables for mitral restenosis. Statistical analysis was done using SPSS for Windows, Version 10.0.

Results

RESULTS

Records of 248 patients who underwent the procedure were examined for baseline characteristics. The procedure was successful in 230 patients (92.7%). A total of 157 patients were available for the follow up. Table 1 shows the baseline characteristics of the study population.

Table 1. Baseline Characteristics of the Patients (n=157)

Clinical Variables		
Age, *years*		32.3 ± 10.1
Sex		
	Male	44 (28%)
	Female	113 (72%)
Height, *cm*		155.3 ± 8.1
Weight, *kg*		48.2 ± 8.7
Body Surface Area, m^2		1.4 ± 0.1
NYHA		
	Class II	107 (68.2%)
	Class III	50 (31.8%)
Rhythm		
	Sinus Rhythm	142 (90.4%)
	Atrial Fibrillation	15 (9.6%)
Previous Valvulotomy		39 (24.8%)
Echocardiographic Variables		
Left Atrial Diameter, *mm*		43.9 ± 5.5
2D MVA, cm^2		0.83 ± 0.15
Doppler MVA, cm^2		0.87 ± 0.17
TMG, *mmHg*		14.5 ± 5.5
PASP, *mmHg*		52.1 ± 22.9
Bilateral Commissural Fusion		154 (98.1%)
MR Grade(1-4)		0.69 ± 0.77
Wilkin's Score		
	Mean	8.4 ± 1.4
	≤ 8.0	86 (54.8%)
	> 8.0	71 (45.2%)

MVA = mitral valve area; TMG = transmitral gradient; PASP = pulmonary artery systolic pressure; MR = mitral regurgitation

The mean age of the population is 32.3±10.1 years and there were 113 (72%) females. 107 patients were in the NYHA class II. Electrocardiography showed AF in 15(9.6%) patients. The mean Wilkins score was 8.4±1.4.The 2D Echo MVA was 0.83±0.15cm^2.

Table 2. Post Mitral Valvulotomy Variables

Echocardiographic Variables		
	2D MVA, *cm²*	2.0 ± 0.3
	Doppler MVA, *cm²*	1.9 ± 0.3
	TMG, *mmHg*	3.9 ± 2.0
	PASP, *mmHg*	37.5 ± 15.1
	Open Commissures	1.6 ± 0.5
	MR Grade(1-4)	1.87 ± 0.93
Procedural Complications		
	TIA	1 (0.6%)
	LV apical tear	1 (0.6%)
	ASD	7 (4.4%)

MVA = mitral valve area; TMG = transmitral gradient;
PASP = pulmonary artery systolic pressure; MR = mitral regurgitation;
TIA = transient ischaemic attack; LV = left venticular;
ASD = atrial septal defect

Post procedure echocardiographic variables and the complications associated with it is shown in table 2. Following mitral valvotomy there was significant decrease in the transmitral gradient from 14.5±5.5mmHg to 3.9±2.0mmHg, ($p<0.01$). 2D Echo MVA increased from baseline of 0.83±0.15cm^2 to 2.04±0.34cm^2, ($p<0.01$).There was also significant decrease in the pulmonary artery systolic pressures from 52.1±22.9mmHg to 37.5±15.1mmHg, ($p<0.01$).The average number of split commissures were

1.6±0.5 and 86 (54.8%) patients had both commissures split. One patient had a TIA. Iatrogenic atrial septal defect (ASD) was demonstrated in 7 patients (4.4%) by oximetry run after the procedure.

Seven patients had to cross over to the Inoue balloon technique. In four patients it was not possible to cross the mitral valve with balloon floatation catheter and in one with the metallic device. 3 out of these 5 patients underwent IBMV, among them one developed anterior mitral leaflet tear and severe MR and underwent emergency MVR; another had good result, and the other had unsuccessful procedure and was referred for MVR. Another two patients crossed over due to inadequate valve area obtained by the metallic device. Both underwent IBMV, one had good result, and the other was a failure and hence referred for MVR. Two patients developed cardiac tamponade due to LV tear, one died (mortality rate=0.41%) and the other survived following open repair and open mitral valvulotomy.

Emergency MVR was done in four patients who developed severe MR after dilatation due to leaflet tear. Five patients had moderate MR due to excessive splitting of commissures.

FOLLOW UP EVALUATION

Patients who had successful procedure were followed-up. Table 3 shows clinical and echocardiographic variables of these patients.

Table 3. Follow-up Characteristics of the Patient (n=157)

Clinical Variables		
	Follow-up Duration, *years*	9.1 ± 1.2
	NYHA	
	Class I	100 (63.7%)
	Class II	48 (30.6%)
	Class III	9 (5.7%)
	Rhythm	
	Sinus Rhythm	127 (80.9%)
	Atrial Fibrillation	30 (19.1%)
Echocardiographic Variables		
	Left Atrial Diameter, *mm*	42.36 ± 6.14
	2D MVA, cm^2	1.57 ± 0.4
	Doppler MVA, cm^2	1.54 ± 0.4
	TMG, *mmHg*	6.7 ± 4.6
	PASP, *mmHg*	29.5 ± 12.8
	MR Grade(1-4)	1.05 ± 1.03
	Mitral re-stenosis	68 (43.3%)
	ASD	5 (3.18%)

MVA = mitral valve area; TMG = transmitral gradient; PASP = pulmonary artery systolic pressure; MR = mitral regurgitation; ASD=atrial septal defect.

The mean follow-up period was 9.1±1.2 years. Mean MVA decreased to 1.57±0.4cm^2 on follow-up. The mean transmitral gradient assessed by Doppler echocardiogram was 6.7±4.6mmHg. LA diameter at follow-up evaluation was 42.36±6.14mm. 100 (63.7%) patients were in NYHA class I. 48 patients (30.5%) were in NYHA class II. 9 developed NYHA class III symptoms, one due to AF with fast ventricular rate and the remaining (5%)

had mitral restenosis. The significant decrease in PASP, post procedure, was sustained at follow-up. The mean PASP at follow-up was 29.5±12.8mmHg. Five (3.1%) patients had ASD by color echocardiography with 4.1mm as mean size of the defect .There were no right heart volume overload in any of these patients.

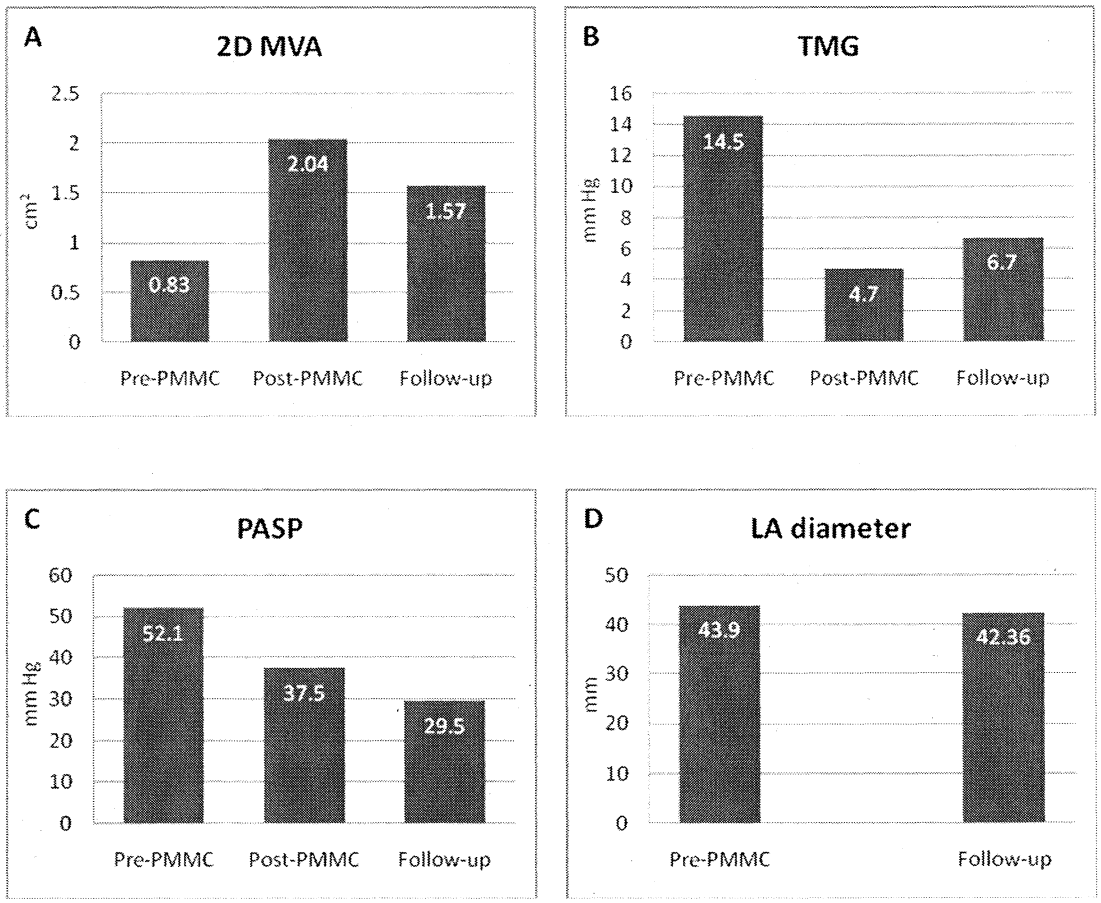

Fig. 1. Hemodynamic and echocardiographic changes before and after PMMC and after and at Follow-up in 157 patients. A: 2D mitral valve area. B: transmitral gradient. C: Pulmonary artery systolic pressure. D: Left atrial diameter.

Mean values of mitral valve area, transmitral valve gradient, pulmonary artery systolic pressure and LAD diameter compared at prior to the procedure, 24 hours after the procedure and at follow-up is shown in figure 1.

Table 4. Complications at Follow-up

MVR	6 (3.8%)
PBMV	6 (3.8%)
DVR	1 (0.6%)
Death	2 (1.3%)
Cerebrovascular Accident	4 (2.5%)
Congestive Cardiac Failure	1 (0.6%)
Infective Endocarditis	1 (0.6%)

MVR = mitral valve replacement; PBMV = percutaneous balloon mitral valvotomy; DVR = double valve replacement

Complications reported on follow-up of the study population is shown in Table4.Thirteen (8%) patients had mitral reintervention on follow-up, six had MVR, 6 patients underwent PBMV and one had undergone DVR, for associated aortic valve disease. In the MVR group, two were done due to calcific mitral re-stenosis and four due to progression of MR. There were only two deaths, both related to complications of stroke.

Table 5. Predictors by multivariate analysis

	Beta coefficient	P value
Reintervention		
Wilkin's Score (≤ 8R)	1.20	0.02
2D MVA	-1.48	0.08
Mitral restenosis		
Wilkin's Score (≤ 8R)	0.97	0.01
Post Procedure 2D MVA	-2.97	0.00

MVR = mitral valve replacement

Predictors for mitral restenosis and reintervention is shown in table 5. The results showed Wilkins score >8.0 and post procedure MVA as predictors of restenosis and reintervention on follow-up.

Discussion

DISCUSSION

Cribier et al, [7] in 1997 introduced a metallic device, which works by stretching and subsequent separation of the commissures, once it is open across the mitral valve. The advantage of using this device is its low cost as it can be reused several times after sterilization without losing its efficacy.[8, 13]

Randomized trials have shown that PBMV and open mitral valvotomy to be superior to CMV. [5, 6] The only long-term randomized study comparing surgical, open and percutaneous mitral valvulotomy has been reported by Farhat et al.[6] At 7 years of follow up percutaneous and open procedures were better than closed commissurotomy as assessed by lower restenosis rate (6% vs. 6% vs. 37%) and larger follow up MVA (1.8 vs. 1.8 vs. 1.3cm^2) and higher event free survival (93% vs. 90% vs. 50%) respectively.

Several short term studies have reported good immediate success rate following metallic commissurotome. Harikrishnan et al, [14] reported immediate success rate of 92.7%. Cribier et al, [8,54] reported 92% and 93% in a series of 153 and 500 patients, respectively. These success rates are similar to that which has been reported by Arora et al, [55] that is, 93.6%, in a series of 600 patients.

Harikrishnan et al, [14] showed that MVA significantly increased following PMMV, from 0.85±0.14cm^2 to 1.95±1.33cm^2. Bhat et al, [10] showed in a comparative study PMMV gave better postprocedure MVA area results than IBMV (1.86cm^2 vs. 1.69cm^2) respectively. Moustafa A et al, [12] in another comparative study showed that PMMVgave the best results (2.1±0.49cm^2 versus 2.0±0.23cm^2 versus 1.87± 0.39cm^2) for PMMV, double balloon, Inoue balloon technique, respectively. The patients in this follow-up study also showed comparable result with immediate gain in MVA being 2.04±0.34cm^2.

Harikrishnan et al, [14] in short term follow up of the same group of patients reported that only 3% of the patients had ASD immediately after the procedure and only 2 had restrictive ASD on their follow up. This study shows 5 patients had restrictive ASD on follow-up. Fawzy et al, [39] reported that ASD had closed in their patients at follow-up of 6 to 12 months. Cequier et al, [35] in their study of long term follow-up of left to right atrial shunting after PBMV found out that it is very frequent after this procedure and persists at 6 months, though haemodynamically not significant. Independent predictors of ASD in their patients were smaller increases in MVA after PBMV (p=0.01), absence of previous surgical commissurotomy (p=0.02), mitral valve calcification (p=0.02), and smaller left atria (p=0.06). Plausible cause for persistent ASD in this study may be due to metallic device creating larger defect during atrial septal puncture and also ASD manifesting as the mitral restenosis worsens.

Fawzy et al,[41] in their follow-up for 13 years, of PBMV in 559 patients found out that PASP following the procedure regressed to normal levels at follow up of 6-12 months; 29±8mmHg for those with PASP <50mmHg at baseline, 31±-9mmHg for those with baseline PASP 50-79mmHg and 29±5mmHg for those with baseline PASP over 80mmHg. This study also shows comparable results to the above study with PASP of 29.5±12.8mmHg at follow-up.

Short -term 8 months follow- up, by Bhat et al, [10] in a comparative study showed that PMMV patients had slightly better MVA than IBMV (1.80cm^2 vs. 1.74cm^2) though this was not significant. Harikrishnan et al., [14] reported in their study that in a mean follow up of 3.34±0.66 years that MVA decreased to 1.67±0.37cm^2, a decrease of 16% from the pre procedure. Guerios et al, [11] in a comparison study between PMMV and IBMV reported 3 year follow up of MVA to be 1.86 ±1.32 vs. 1.87±0.32cm^2,p=0.89)respectively. This was from a mean final MVA of 2.17±0.13cm^2 vs. 2.00±0.36cm^2, p=0.04.

Restenosis following balloon mitral valvotomy has been reported to be 3% to 70% at 3 years.[56,57] This study shows that 5% of patients on follow-up has mitral restenosis .Hernandez et al, [58] reported mitral restenosis of 39% at 7 years of follow-up in a population with mean age of 59years after IBMV. However Ben Farhat et al, [59] reported mitral restenosis of 34% at 10 years in a

younger population (mean age= 33±13 years), after PBMV. Fawzy et al, [39] in a long-term follow up PBMV series reported 21% of restenosis. And also as shown by Harikrishnan et al, [14] and Bhat et al, [10] at short term follow-up of PMMV, there was significant decrease in the MVA. This had been explained by a stretching effect of the commissurotome on the annulus and recoil effect few months later.

Predictors of restenosis from this study are post procedure MVA, p=0.028 and Wilkins score, p<0.001. Fawzy et al, [39] showed mitral restenosis occurred less frequently(11%) in those who had Wilkins score <8.0.Predictors of restenosis in their study were Wilkins score >8.0 (p=0.01) and post-procedure MVA(p=0.000).Ben-Farhat et al, [59] in their series of 654 patients showed that freedom from restenosis at 10 years was associated with low Wilkins score(77% for score ≤8.0,45% for score of 9-11, 50% score for ≥12.0),larger MVA before PBMV (p=0.03) and large MVA (p=0.001),and lower mitral valve gradient (p=0.04) after PBMV. The best results after PBMV are seen in young patients with pliable non calcific valves and moderate impairment of the subvalvar apparatus. [60]

Thirteen patients had reintervention; most of them in later part of the follow up period. Only one patient had DVR were done for progression of preexisting aortic valve stenosis . The predictors of event free survival in this study were Wilkins score and post procedure MVA. Fawzy et al, [39] reported

event-free survival to be significantly higher for patients with favorable mitral valve anatomy (88% at 10-years, 66% at 15-years).In their study they found favorable valve anatomy, age and post procedural MVA to be predictors of event free survival. Results for the series of 128 patient s by Pavlides et al, [61] showed Wilkins score (p=0.02) and post procedure mitral valve area (p=0.001) to be independent predictors of event free survival. Palacios et al, [40] in their study of 879 patients found out MR $\geq$ 3+,echo score >8,age,prior surgical commissurotomy, NYHA class IV, pre PBMVMR $\geq$ 2+ and higher post pulmonary artery pressure as independent predictors of combined events at long-term follow-up. This study shows event free survival of 98.7% and 94.3% at 7 and 9 years respectively.

Limitations of the Study

LIMITATIONS OF THE STUDY

It is a retrospective analysis of recorded data in a patient group who had undergone percutaneous mitral valvotomy using a metallic device.

One third of the patients who underwent the initial procedure were not available for follow-up.

There may have been unrecorded events like reintervention and mitral restenosis in the patients who have not followed-up. Hence the occurrence of these events may be underestimated.

Conclusion

CONCLUSION

This long-term follow-up study shows that mitral valvotomy with metallic device has good outcome in terms of mitral restenosis and event-free survival. Though the initial gain in the MVA is higher for metallic valvotomy, it has not translated into higher MVA on long-term follow-up. And there may be higher incidence of persistence of restrictive ASD after mitral valvotomy with metallic device.

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