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Mitral Valve Replacement in Severe Pulmonary Artery Hypertension — a Single Center Single Surgeon Experience.

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ABSTRACT

Background: Pulmonary artery hypertension (PAH) is a major risk factor in patients presenting in our hospital for mitral valve replacement (MVR) surgery. In this prospective study, we have focused on hemodynamic changes and post-operative results of MVR in patients with severe PAH. **Methods:** 136 consecutive patients who underwent mitral valve replacement for severe rheumatic mitral valve disease with severe PAH (pulmonary artery pressure (PAP) > 50 mmHg) were studied prospectively for immediate postoperative hemodynamics and outcomes from December 2013 to January 2016. The mean age of the patients was 34.3 years. 74 (54.41%) patients had mitral stenosis, 30 (22.05%) had mitral regurgitation and 32 (23.52%) had mixed lesions. Patients were randomly given two groups based on preoperative pulmonary artery pressures. In 120 patients (88.23%, group I) PAP was sub-systemic or systemic, with a mean of 59.6 mmHg. Sixteen patients (11.76%, group II) had supra-systemic PAP with a mean of 84.2 mmHg **Results:** After mitral valve replacement, the PAP and pulmonary vascular resistance (PVR) decreased significantly in group I to near normal levels. However, in group II, despite reduction in the PAP and PVR, significant residual PAH remained. Operative mortality was 1.6% in group I and 12.5% in group II. **Conclusion:** In patients with mitral valve disease undergoing mitral valve replacement, PAH is a significant risk factor. In cases with sub-systemic or systemic PAH, results are very good but significant PAH persists even after MVR is cases of supra-systemic PAH causing continuation of symptoms.

Keywords: Mitral Valve Replacement, Pulmonary Artery Hypertension

INTRODUCTION

Rheumatic heart disease is an auto-immune disease caused because of molecular mimicry. Antibodies produced against cell wall of streptococcus also act against myocardium and joints. In the acute condition, there is pancarditis involving inflammation of the myocardium, endocardium, and epicardium. In chronic stage, there is valvular fibrosis, resulting in stenosis and/or insufficiency. It is very common in the developing countries, and its incidence in India and south-east Asia is high and is the leading cause of valvular heart disease.

A significant number of people here live in overcrowded colonies with lack of proper hygiene, have poor nutritional intake and medical health care is also out of reach. Rheumatic fever commonly involves the age group 5 years to 25 years. The highest incidence is observed in children aged 5-15 years and in developing countries where medical health care is not easily approachable and the patient compliance is also less.[1]

Hence, patients with mitral valve disease present in early phase of life for surgery, usually in the second to third decade of life. A large number of patients especially from rural areas present at a very late stage of the disease when the pulmonary artery pressure (PAP) is very high, at times nearing the systemic pressure. In the initial stages, only pulmonary veins are involved, but later pulmonary arterial hypertension (PAH) supervenes.

The presence of pulmonary arterial hypertension (PAH) has been considered a risk factor for poor outcome in patients undergoing mitral valve replacement (MVR), with operative mortality ranging from 15% to 31%.[2,3] This prospective study was done to assess the postoperative hemodynamics changes and outcomes after MVR in the presence of severe PAH.

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MATERIALS AND METHODS

This prospective study was conducted at SMS hospital, Jaipur (Rajasthan) which is a major referral centre for patients from north and west India. The

study period was from December 2013 to January 2016. There were 544 isolated MVR operations performed during this period for severe rheumatic mitral valve disease. On preoperative echocardiography, patients who were found to have severe PAH based on estimated right ventricular systolic pressures > 50 mmHg were enrolled in the study. Two groups were made: group I was patients with systemic or sub-systemic PA pressures; group II patients had supra-systemic PA pressures. The two groups were matched for age, sex, height, weight, body surface area, New York Heart Association (NYHA) functional class and the presence of preoperative atrial fibrillation. Both group patients were given similar medical management.

All preoperative assessments were carried out by 2-dimensional transthoracic echocardiography. Transesophageal echocardiography was done in some patients to assess LA/LAA clots. Patients more than 40 years of age underwent isolated coronary angiography to rule out coronary artery disease. After due informed consent, all patients underwent MVR with mechanical valve.

Cardiac output (CO) was measured by the thermodilution technique using 10 mL of 0.9% icy cold saline and a hemodynamic monitor having inbuilt capacity to measure hemodynamic parameters. Mean and systolic pulmonary artery pressure, pulmonary capillary wedge pressure (PCWP), pulmonary vascular resistance (PVR) and cardiac index (CI) were calculated. Baseline (control) hemodynamic and arterial blood gas (ABG) measurements were obtained before the induction of anesthesia and repeated after induction, immediately after MVR when the patient had been weaned from cardiopulmonary bypass (CPB) and the hemodynamics had been stabilized, 6 hours and 24 hours and 48 hours after the operation.

Technique of MVR

Patients underwent operation via median sternotomy and aortocaval cannulation. Cardiopulmonary bypass was performed with a membrane oxygenator and a non-pulsatile roller pump. Mild hypothermia (nasopharynx temperature, 28–32 °C) was used, and 2.4-L/min/m2 flow rates were maintained during bypass. Myocardial protection was supported with topical ice slush and intermittent antegrade blood cardioplegia, Mitral valve was approached through the left atrium as it. Whenever possible, subvalvular apparatus was preserved. The valve used was St. Jude Medical® Mechanical Heart Valve (SJM; St. Jude Medical Inc.; Minneapolis, Minn) in all the patients. Valves were secured with pledgeted horizontal mattress sutures using 2-0 Ethibond (Ethicon, Inc., a Johnson & Johnson company; Somerville, NJ). Before the aortic cross-clamp was removed, patients received terminal warm cardioplegic solution. No patient required reinstitution of cardio-pulmonary bypass.

All patients were given narcotic analgesics and vasodilator infusion in the form of nitroglycerine apart from the inotropes (dopamine, adrenaline and dobutamine), which were discontinued when the hemodynamics had stabilized and they could be extubated. No patient required intra-aortic balloon pump.

Statistical Analysis

All values are mentioned as mean ± standard deviation (SD) and range. Unpaired Student's t test and chi-square test were used for comparison of data of the two groups, where applicable. For statistical analysis, the statistical-software SPSS version 18.0 for windows (SPSS Inc., Chicago, IL) was used. A p value < 0.05 was considered statistically significant.

RESULTS

Table 1: Baseline characteristics of the two groups.

		Group I (n=120)	Group II (n=16)	P value
Mean age (years)(range)		32.87 (15-47)	35.58 (26-47)	0.25
Sex ratio (male : female)		1:1.14 (56:64)	1:1.28 (7:9)	0.72
NYHA class	III	68	6	0.124
	IV	34	10	
Lesion in mitral valve	Dominant stenosis	56 (46.66%)	8 (50.00%)	0.28
	Dominant regurgitation	26 (21.66%)	3 (18.75%)	
	Mixed lesion	38 (31.66%)	5 (31.25%)	
Atrial fibrillation		76 (63.33%)	12 (75%)	0.655
Tricuspid regurgitation	Moderate	22 (18.33%)	0	
	Severe	98 (81.66%)	16 (100%)	0.18
Mean duration of symptoms (range)		2.8 years(5 months to 8 years)	3.6 years(3 year – 12 year)	0.285

On preoperative echocardiography, 136 (25%) patients were found to have severe PAH based on estimated right ventricular systolic pressures > 50 mmHg. Group I had 120 patients (88.23%) whereas 16 patients (11.76%) were in group II. These patients were between 15 and 47 years of age, with a mean age of 34.3 years. The duration of symptoms ranged from 5 months to 12 years and was comparable in both the groups. In group I, the dominant valvular lesion was mitral stenosis (MS) in 56 (46.66%) patients, mitral regurgitation (MR) 26 patients (21.66%), and mixed lesions in 38 (31.66%) patients. In group II, 8 patients (50.00%) had severe mitral stenosis, 3 patients (18.75%) had mitral regurgitation and 5 patients had mixed lesions (31.25%). Tricuspid regurgitation (TR) was severe in 81.66% of patients in group I and in 100% of

patients in group II (p = 0.18). The baseline characteristics of these patients are shown in [Table 1]. The mitral valve was approached through the left atrium in all the patients. Complete or partial preservation of subvalvular apparatus was possible in majority of patients (94.85% i.e. 516 out of 544 patients). De Vega tricuspid annuloplasty was performed in 18 patients in group I and in 5 patients in group II (p = 0.22). The mean CPB time was 70 ± 20 minutes in group I and 110 ± 25 minutes in group II (p < 0.001) and the aortic cross clamp time was 49 ± 18 minutes in group I and 57 ± 28 minutes in group II (p = 0.076). These operative data are depicted in [Table 2].

Table 2: Comparison of operative and post-operative data in the two groups.

		Group I (n=120)	Group II (n=16)	P value
Cardio pulmonary bypass time (min.)		70 ± 20	110 ± 25	<0.001
Aortic cross clamp time (min.)		49 ± 18	57 ± 28	0.076
De vega's tricuspid annuloplasty		18	5	0.22
Ventilation time (hrs.)		22.7 ± 10.7	33.4 ± 18.5	0.03
Adrenaline	Used (n, %)	111 (92.5%)	16 (100%)	0.45
	Duration (days)	2.4 ± 1.6	3.8 ± 2.4	0.49
Dobutamine	Used (n, %)	96 (80.0%)	16 (100%)	0.54
	Duration (days)	4.2 ± 1.8	6.2 ± 2.4	0.61
Dopamine	Used (n, %)	54 (45%)	8 (50.00%)	0.26
	Duration (days)	2.9 ± 1.6	3.2 ± 1.8	0.68
Nitroglycerine	Used (n, %)	110 (91.66%)	16 (100%)	0.13
	Duration (days)	2.5 ± 1.5	2.8 ± 1.6	0.23
ICU stay (days)		2 ± 1	4 ± 3	0.032
Hospital stay (days)		7 ± 3	13 ± 8	0.085
Mortality		2 (1.6%)	2 (12.5%)	0.48

The preoperative and postoperative changes in hemodynamics of the two groups are presented in [Table 3]. Group II patients had a higher baseline mean PA pressure, systolic PA pressures, PCWP and PVR but lower cardiac index than group I patients (p < 0.05). In group I, the mean PAP fell by 35.59% from a mean preoperative level of 55 ± 7 to 37 ± 6 mmHg, 6 hours following MVR (p < 0.001) and it continued to decrease over the next 24 hours (p < 0.001). Systolic PA pressures fell from 81 mmHg preoperatively to 49 mmHg after 6 hours and to 36 mmHg 24 hours after the surgery (p < 0.001). PCWP decreased by 60% from 37 to 16 mmHg within 6 hours of surgery. Similarly, the pulmonary vascular resistance (PVR) decreased by 51% from a mean preoperative value of 524 to 256 dyne·s·cm−5 six hours after MVR (p < 0.001). Mean cardiac index increased from 1.89 to 2.68 L·min−1·m−2 (p < 0.001) in the same duration [Table 3]

In group II, the mean PAP decreased by 27.28% from a mean preoperative level of 86 ± 11 to 58 ± 9 mm Hg within six hours following MVR (p < 0.001); it decreased over the next 24 hours but this decrease was not statistically significant. Systolic PA pressures decreased by 34.01% from 109 ± 16 to 72 ± 11 mmHg in 6 hours after MVR but further decrease was only 3.65% in next 18 hours. PCWP decreased to a mean of 28 from 44 ± 12 mmHg in initial 6 hours of surgery and further decreased to 19 mmHg at 24 hours postoperatively (p < 0.05). The PVR decreased by 25% from a mean preoperative value of 780 ± 129 to 585 ± 74 dyne·s·cm−5 six hours after MVR (p < 0.001). Pulmonary vascular resistance continued to decrease significantly even after that [Table 3]. This group of patients showed persistent low cardiac output even after MVR. Mean cardiac index increased marginally from 1.4 to 1.64 L·min−1·m−2 .This increase was however statistically significant (p = 0.001).

Table 3: Preoperative, intraoperative and postoperative hemodynamics of patients

	Base line		Post-intubation		6 hours postoperatively		24 hours postoperatively		48 hours postoperatively	
	Group I	Group II	Group I	Group II	Group I	Group II	Group I	Group II	Group I	Group II
MPAP (mmHg)	55 ± 7	89 ± 11	46 ± 7	78 ± 12	37 ± 6*	58 ± 9*	29 ± 5*	53 ± 8	22 ± 6	43 ± 10
Systolic PAP (mmHg)	81 ± 13	109 ± 16	70 ± 11	98 ± 14	49 ± 7*	72 ± 11*	36 ± 8*	66 ± 10	31 ± 9	61 ± 8
PCWP (mmHg)	37 ± 10	44 ± 12	29 ± 10	35 ± 9	16 ± 5*	28 ± 4*	15 ± 4	19 ± 3*	14 ± 4	17 ± 5
CI (lt/min/m2)	1.89 ± 0.3	1.4 ± 0.2	2.1 ± 0.2	1.49 ± 0.3	2.68 ± 0.6*	1.64 ± 0.4*	2.98 ± 0.7*	1.84 ± 0.3*	2.87 ± 0.5	1.98 ± 0.6
PVR (dynes·sec·cm−5/m2)	524 ± 176	780 ± 129	506 ± 164	754 ± 125	256 ± 118*	585 ± 74*	234 ± 98*	548 ± 68*	198 ± 92	528 ± 58

PAP = pulmonary arterial pressure, PVR = pulmonary vascular resistance, PCWP = pulmonary capillary wedge pressure, CI = cardiac index; *Shows statistically significant change in hemodynamics (p < 0.05).

Patients in group II needed to be mechanically ventilated postoperatively for a longer duration (34.4 ± 20.6 hours vs 22.6 ± 12.7 hours) (p = 0.04). Inotropic support in the form of epinephrine, dobutamine and vasodilators like nitroglycerine was also required for a longer duration in group II patients but it was not statistically significant. Post-operative Echo during the ICU stay revealed RVSP

≥ 50 mmHg + RAP (severe PAH) in 75 (62.5%) patients of group I and severe PAH in 9 (56.25%) patients of group II. The duration of ICU stay was longer in group II compared to group I (p = 0.032), but the duration of hospital stay was comparable (p = 0.078). Two patients from group I (1.6%) and two patients from group II (12.5%) died in the immediate post-operative period constituting an overall mortality rate of 2.9% [Table 2]. Although this difference is large, it did not reach statistical significance because of small sample size of group II. Both deaths in group II were caused by persistent low cardiac output due to right ventricular dysfunction. The two patients in group I died because of low cardiac out- put syndrome and sepsis. There was no operative mortality for routine MVR without significant PAH (n = 408) at our institute during this period.

Complications recorded in the surviving patients during hospital stay were bleeding leading to re-exploration in four patients, hepatitis in two patient and acute renal failure in four patients and at follow-up, thromboembolic episodes in two patients.

At follow-up, patients were assessed for symptomatic improvement and by echocardiography at 1 month and 12 months post-operatively. Follow up was 100% complete in the 132 surviving patients. At one month follow- up, 104 patients (86.67%) were in NYHA class II in group I and 11 (90%) patients of the survivors were in NYHA class II in group II which was also statistically not significant. Echocardiography showed severe PAH in 42 patients (77.7%) in group I versus 10 patients of group II (100%). At 12 months follow-up, among the 64 survivors, there were 3 deaths, two of which were in group I and the other in group II. Patients were assessed for severe PAH, by echocardiography, which was prevalent in 38 patients (73.0%) in group I and in 9 patients (100%) in group II.

DISCUSSION & CONCLUSION

The surgery of rheumatic valvulopathies is an essential part of the hospital services of cardiac surgery of the developing countries. The valvular lesions are unfortunately already highly evolved, mutilating, leaving little chance for conservative surgery, the patients are of ore and already at a stage of PAH much evolved.

Severe pulmonary hypertension results from simple back pressure resulting from elevated left atrial pressure, and increased pulmonary vascular resistance.[4] The latter may have both a dynamic element, which is immediately reduced by lowering left atrial pressure, and an organic element from pulmonary vascular disease, which may or may not slowly regress after operation.[5] Thus, even severe pulmonary artery hypertension will very likely regress toward normal after MVR. This reduction often occurs soon after valve replacement, and thus seems related largely to the sudden drop in left atrial pressure and to a reversal of the severe spastic pulmonary vasoconstriction that accompanies left atrial hypertension in some patients.

Pulmonary artery hypertension is a common complication of mitral valve disease. This is more frequently seen in the Indian population where unlike the western population the etiology is commonly rheumatic and presented at a younger age.[1]

The significant reduction in mPAP post-induction in our study could be explained by relieving the vasoactive component of PH followed by relief of the obstructive component by MVR. On comparing both groups regarding their MAP at various stages of our study, we detected a significant difference post induction, being higher in the severe PH group. This could be related to the reduction of pulmonary vasoconstriction (the latter being more in severe PH), which increases the venous return to the left atrium, increasing the cardiac output, leading to increased SBP and MAP.[6]

The outcomes of our study indicate that even though hemodynamics of severe PAH after MVR in group I patients significantly improved but this improvement is less in patients who have supra-systemic PA pressures (Group II in our study). Also, the mortality rate of MVR is significantly higher in group II of our study. In group II patients, the decrease in MPAP, systolic PA pressures, PCWP and PVR is less significant compared to those patients who have severe PAH.

Thus, when these patients present, they often have advanced disease and severe PAH due to lack of medical care. The higher mortality seen in group II could be attributed to a more severe form of the illness due to earlier onset and more longstanding disease. This has been believed to lead to refractory right ventricular failure in the post-operative period.[5,7] Even adequate post-operative management in the form of use of vasodilators, high FiO2 and elective post-operative ventilation fail to reduce the high mortality in supra-systemic PAH to acceptable levels.

Nevertheless, all recent literature shows a regression or even normalization of the sPAP in 90% of the patients, in particular the young subjects, with improvement of the quality of life. Thus, we will say "yes", it is necessary to operate patients in moderate or severe PAH because the benefit is incontestable and the results are convincing.[8,9,10]

However, it will be necessary to say that these rheumatic heart diseases are the translation of the failure of the prevention of acute rheumatic fever and that it is essential to review the antirheumatic prevention protocols and evaluate them in daily practice. Finally, it should not be forgotten that we cannot eradicate the acute rheumatic fever without improving the socio-economic level of the populations, and it is better to prevent this disease

than to manage its complication valvular heart disease which has a heavy socio-economic burden on the society.

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