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Original Article

In Hospital Outcome of Mitral Valve Replacement with Severe Pulmonary Hypertension

Rubaiya Reza Tumpa, Al-Masum Ziaul Haque, Md. Kamrul Hasan

Department of Cardiac Surgery, NICVD, Dhaka

Key words:
Mitral valve, Mitral Regurgitation, Pulmonary Hypertension, Valve replacement.

Abstract

Background: *In patients undergoing surgery for mitral valve replacement (MVR) for valvular heart disease, pulmonary artery hypertension (PAH) has been considered a major risk factor. In this prospective study, we have studied the early hemodynamic changes and post-operative outcomes of MVR among patients with mild to severe PAH in Bangladesh perspective.*

Methods: *Total 60 patients who underwent mitral valve replacement for predominantly mitral regurgitation (MR) and mixed lesion with mitral stenosis (MS) having pulmonary arterial hypertension ranging from mild to severe pulmonary artery pressure (PAP) were studied prospectively for immediate postoperative haemodynamic and outcome. The mean age of the patients was 36.23±9.18 years. Total 13 (21.66%) patients had mitral regurgitation and 47 (78.33%) had mixed lesion with mitral stenosis. Patients were divided into two groups based on preoperative pulmonary artery pressures. Group A patients with mild to moderate pulmonary hypertension (PASP 40-59 mm of Hg) and Group B patients with severe pulmonary hypertension (PASPe" 60 mm of Hg).*

Results: *After mitral valve replacement, pulmonary arterial systolic pressure (PASP) decreased significantly in Group A to near normal levels (PASP41.25±7.25). In Group B also the PASP decreased insignificantly (PASP 61.85±9.12) but significant residual PAH remained. Operative mortality was nil (0%) in Group A and 6.7% in Group B.*

Conclusions: *Mitral valve replacement is safe and effective at the presence of PAH as long as the PASP is below or equal to 60 mm of Hg. With PASP >60 mm of Hg, MVR carries a high risk of mortality and the patients continues to have severe PAH in the postoperative period.*

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Introduction:

Mitral regurgitation (MR) is the second most common form of valvular disease requiring surgery. It has the prevalence of 2% in the general population and is even more in the elderly.[1] Improvements in the diagnosis, quantification and operative techniques for mitral valve (MV) either in the form of repair or replacement allow the restoration of normal life expectancy after surgery.[2] The timing and type of surgery depends upon a number of factors, one of the most important being whether the MR is primary or secondary. Organic (or primary) MR arises as a result of pathology affecting one or more components of the mitral valve apparatus, other causes of primary mitral regurgitation include rheumatic disease, with rare causes being drug-induced mitral valve disease, healed infective endocarditis, and mitral regurgitation associated with systemic disease. Whereas functional (or secondary) MR is a consequence of annular dilatation and geometrical distortion of the sub-valvular apparatus secondary to left ventricular (LV) remodeling and dyssynchrony, most usually associated with cardiomyopathy or coronary artery disease.[3]

Unlike the western world in which rheumatic disease is becoming rare in the past few decades, the disease remains endemic in the developing

Address of Correspondence: Dr. Rubaiya Reza Tumpa, Department of Cardiac Surgery, NICVD, Sher-e-Bangla Nagar, Dhaka, Bangladesh. E-mail: rubaiyarezatumpa@gmail.com

world as the most common cause of MS and MR.[4] Almost 1/3rd of rheumatic patients suffers from pure MS, while the remainder suffers from combined MS and MR.[5] Both conditions lead to pulmonary hypertension (PH) in advanced stages, which is associated with poor prognosis.

A diagnosis of severe mitral regurgitation is made if 50% of the total stroke volume is diverted to regurgitant flow.[6] Long-standing volume overload can result in progressive left ventricular enlargement and stretching of the myocytes beyond their normal contractile length. This stretching will lead to a decreased contractile state from reduced myofibre content and interstitial fibrosis with an increase in left atrial and left ventricular diastolic pressures, producing symptoms of dyspnoea.[7] As stated by Kirklin and Barratt-Boyes,[8] whenever severe pulmonary hypertension is present pre-operatively, it is usually the combined result of simple back pressure, resulting from elevated left atrial pressure and increased pulmonary vascular resistance (PVR). Pulmonary vascular resistance is the resistance against blood flow from the pulmonary artery to the left atrium. Right heart catheterization is the gold standard investigation for determining pulmonary haemodynamics including vascular resistance, but its routine use is limited by its invasive nature and incurring cost.[9]

Pulmonary hypertension is common among patients referred for mitral valve surgery for MR. Although it is generally acknowledged that the presence of PH has a negative impact on operative outcomes, available data are remarkably scant and generally from small series.[10] However, the effect of pulmonary venous hypertension on pulmonary circulation is highly variable ranging from no effect to severe pulmonary vascular resistance.[11] Long standing pulmonary hypertension increases after-load on the right ventricle (RV) leading to hypertrophy and eventually Cor-pulmonale.

Normal pulmonary artery systolic pressure at rest is 18-25 mm Hg, with a mean pulmonary pressure ranging from 12 to 16 mm Hg. This low pressure is due to the large cross-sectional area of pulmonary circulation, which results in low resistance. An increase in pulmonary vascular resistance or pulmonary blood flow results in pulmonary hypertension.[12] Because of the impact of pulmonary hypertension on outcome, guidelines (American College of Cardiology/ American Heart Association and European Society of Cardiology, 2017) for mitral valve (MV) surgery in asymptomatic MR include significant PH defined as a systolic pulmonary artery pressure (PASP) > 50 mm Hg at rest or > 60 mm Hg with exercise (Class IIA indication). Preoperative PASP > 30 mm Hg and normal left ventricular ejection fraction (LVEF) are associated with significant reduction in postoperative LVEF in patients with degenerative MR, sPAP > 50 mm Hg is associated with lower postoperative LVEF and worse symptoms after MV surgery; and in studies assessing the perioperative risks in MV surgery, a sPAP > 65 mm Hg has the highest sensitivity and specificity for risk of perioperative death.[13] Ghoreishi[14] reported operative mortality of 12% in 148 patients with severe PH undergoing MV surgery for mitral regurgitation.

Study Methods:

This prospective study was conducted in Department of Cardiac Surgery of National Institute of Cardiovascular Diseases (NICVD) a renowned tertiary center in Bangladesh. The study period was from July 2018 to June 2019. There were 60 isolated MVR operations performed during this period for rheumatic mitral valve disease. we see the in hospital out-come so Patients were followed up after surgery till discharge from hospital.

Patients were divided into two groups based on preoperative echocardiography (Hitachi, aloka color Doppler transthoracic echocardiography machine). Group A were patients (n=30) with mild to moderate pulmonary hypertension (PASP: 40-59 mm of Hg) and Group B were patients (n=30) with severe pulmonary hypertension (PASP ≥≥60 mm Hg). The groups were comparable with respect to age, sex, height, weight, body surface area, New York Heart Association (NYHA) functional class and presence of preoperative atrial fibrillation. Patients in both groups were on a similar treatment regimen that consisted of loop diuretics, digoxin, beta blocker, angiotensin- converting enzyme inhibitor and calcium channel blockers. Cardiac catheterization was not undertaken in any of these patients as per institutional protocol. After due

informed consent, all patients underwent MVR with St Jude bileaflet mechanical valve.

On arrival in the operating room, continuous electrocardiographic monitoring was started and invasive arterial blood pressure recording established. Baseline (control) haemodynamic and arterial blood gas (ABG) measurement were obtained before the induction of anesthesia. Aortic Cross Clamp time and Extra Corporeal Circulation time (in minutes) was recorded. Any per-operative event was recorded. In all cases hemodynamic optimization was attempted by volume management, pacing support and catecholamine administration when necessary. Post-operative events such as total ICU stay, inotrope support, any event of arrhythmia, thromboembolic manifestation, any sign of failure was noted.

The statistical analysis was done by using the Statistical Package for Social Sciences version 23.0 for Windows (SPSS Inc, USA). Chi-Square test was used to analyze the categorical variables, shown with cross tabulation. Student t-test was used for continuous variables. p value of <0.05 was taken as significant.

Results:

Table I shows baseline characteristics of the patients, there were total 60 patients and it was observed that mean age was 36.23±9.18 years in Group A patients, and mean age in Group B was 37.8±10.9 years.

Among total 60 patients 37 (61.66%) were male and 23 (38.33%) were female, male and female ratio was 1.6: 1.

NYHA class distribution among two groups in Group A, 53.3% patient had Class I (n=16), 36.7% Class II (n=11) and 10% patient had Class III (n=3) failure. In Group B, 16.7% had Class I (n=5), 33.3% Class II (n=10), 23.3% Class III (n=7) and 26.66% had Class IV (n=8) failure. The results were statistically significant (p= 0.018).

Pre-operative echocardiography features, at the time of study entry, are plotted below. Based on the PASP level study population was divided into two groups. Total 13 patients had pure Mitral Regurgitation and rest 47 patients had mixed lesion of both MS and MR. Among all 29 patients had severe Mitral Regurgitation.

Per operative variable like total operative time, cross clamp time and time in weaning from CPB were quite similar and there was no statistically significant difference between the two groups.

There was statistically significant difference in post-operative outcomes between the two groups regarding prolong mechanical ventilation, prolong ICU stay, incidence of arrhythmia, prolong inotrope support and pulmonary complications are plotted below-

Table-I

Demographic characteristics between two groups (N=60).

Demographic characteristics	Group A (n=30) No. (%)	Group B (n=30) No. (%)	p-value
Age (in years)			
<30	6(20.0)	5(16.7)	
31-40	16(53.3)	14(46.7)	
41-50	8(26.7)	11(36.7)	
Mean ± SD	36.23±9.18	37.8±10.9	0.551^{ns}
BMI (kg/m^2)			
Normal (18.5-24.9)	14(46.7)	16(53.3)	
Overweight (25.0-29.9)	12(40.0)	9(30.0)	
Obese (>30.0)	4(13.3)	5(16.7)	
Mean ± SD	24.98±3.69	25.68±3.87	0.479^{ns}

Data were expressed as frequency and percentage and mean ± SD

Unpaired student t-test was performed for quantitative variables and Chi-square test was performed for qualitative variable between two groups

s= significant (p<0.05) ns = not significant (p>0.05)

Among study population, post-operative Echo finding done at 10th post-operative day shows, Group B patients had significant decrease in pulmonary pressure than Group A patients but the result is not statistically significant. On the other hand, there was reduction in post-operative left ventricular ejection fraction in both groups which were statistically significant.

The figure 1 below shows the pre- and post-operative reduction of Pulmonary Artery Systolic Pressure (PASP) in both groups plotted in using Bar diagrams.

Table-II

Distribution of the study by preoperative variables (n=60).

Preoperative variables (Mean values)	Group-A (n=30)	Group-B (n=30)	p value
PASP	47.43±6.82	74.33±10.70	<0.001[s]
RV dysfunction (TAPSE) (mm)	19.35±3.17	16.22±2.64	0.001[s]
LVEF (%)	56.17±6.10	53.53±6.65	0.115 [ns]
LVIDd (mm)	46.7±4.78	52.41±5.69	0.001[s]
LVIDs (mm)	28.64±3.16	22.21±3.13	<0.001[s]
LA size (mm)	52.87±5.36	62.27±21.05	0.021 [s]
Echo-morphology of mitral valve			
Mitral valve area	0.88±0.58	1.17±1.04	0.183[ns]
Dominant regurgitation	6(20.0%)	7(23.3%)	0.754[ns]
Mixed lesion (Both MR and MS)	24(80.0%)	23(76.7%)	0.754[ns]

Table-III

Per operative variables between two groups (n=60).

Variables	Group-A(n=30)	Group-B(n=30)	p value
Total operative time (min)	315.7±22.85	328.2±32.7	0.092[ns]
Cross clamp time (XCT) (min)	81.50±21.94	74.23±33.11	0.321[ns]
Extra corporeal circulation time (ECCT) (min)	123.1±36.9	107.5±37.1	0.108 [ns]
Valve size	28.87±2.46	28.27±1.78	0.284 [ns]
Arrhythmia	3(10.0%)	5(16.7%)	0.451 [ns]
Prolong time in weaning from CPB	0(0.0%)	2(6.7%)	0.150[ns]

Table-IV

Comparison of postoperative complication between two groups (n=60).

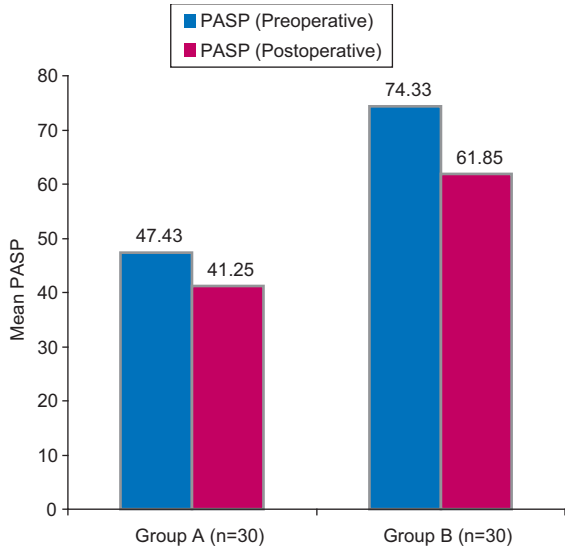
Postoperative complications	Group-A (n=30)No. (%)	Group-B (n=30)No. (%)	p value
Prolong mechanical ventilation time (>24 hrs.)	0(0.0)	4(13.3)	0.040[s]
Prolong ICU stay (>120 hrs.)	3(10.0)	10(33.3)	0.029[s]
Prolong inotrope support (>48 hrs.)	5(16.7)	15(50.0)	0.006[s]
Incidence of arrhythmia	2(6.7)	9(30.0)	0.021[s]
Low output syndrome	3(10.0)	10(33.3)	0.029[s]
Neurological complications (stroke)	1(3.3)	2(6.7)	0.556[ns]
Pulmonary complications	2(6.7)	5(16.7)	0.231[ns]
Wound infection	3(10.0)	5(16.7)	0.451 [ns]
Prolong Hospital stay (>14 days)	0(0.0)	6(20.0)	0.010[s]
Death	0(0.0)	2(6.7)	0.150[ns]

Table-V

Comparison of postoperative Echo findings on 10th POD between two groups (n=60).

Postoperative Echo findings on 10th POD	Group-A (n=30) Mean ± SD	Group-B (n=30) Mean ± SD	p value
Pulmonary pressure changes (PASP)	41.25±7.25	61.85±9.12	0.245 ns
Gradient across mitral valve	28.63±3.54	29.12±6.61	0.721 ns
Size of LA	44.13±21.05	47.52±11.78	0.445 ns
RV dysfunction (TAPSE) (mm)	18.13±3.02	14.82±1.78	<0.001 s
LVEF (%)	60.63±4.93	57.52±5.7	0.027 s

Data were expressed as frequency and percentage and mean±SD
Unpaired student t-test was performed for quantitative variables



Discussion:

The present prospective study focused on the influence of pulmonary hypertension in patients with organic MR. In our population the etiology is commonly rheumatic unlike the western population and presented at a younger age.[15] Baseline characteristics shows that the age distribution of the study population were in between 18-50 years. Among them 47 male and 23 were female. Mean age group were between 30-40 years. Average duration of symptoms was 4 years. Among them 56% (n= 34) had NYHA functional status Class II or more. NYHA functional status was improved by one class or more in 56 (93.33%) patients. Among 60 patients only 3 patients had hypertension and 6 patients had type 2 diabetes.

LA size (mm) in Group A was 52.87±5.36 and in Group B was 62.27±21.05 which was statistically significant (p=0.021). Left atrial enlargement is frequent in chronic organic MR,[16] is progressive.[17] In organic MR, higher LA enlargement is associated with paradoxically higher pulmonary pressure and with marked hormonal (B-natriuretic peptide) activation[18] and reduced functional capacity. In chronic MR, LA enlargement predicts future AF[19] and limited observations suggest that it is associated with subsequent occurrence of heart failure.[20] The present study confirms and most importantly extends these observation as we found post-operative AF (atrial fibrillation) in 2 patients of Group A and in 9 patients of Group B which was statistically significant (p= 0.021).

Operatively both groups did not have significant difference concerning total bypass time, cross clamp time, total operative duration, which is similar to the study done by Mohammad[21] and his colleagues and also in India by Kumar and his colleagues.[22] In all cases MVR was done with St Jude Bileaflet Mechanical valve. Since 1979, St Jude Medical double – leaflet valve is used preferentially, which is associated with better haemodynamic and is therefore considered the gold Standard.[23] post-operative valve gradient is the difference in pressure on each side of the prosthetic mechanical valve. Normal Doppler values of prosthetic valves in Mitral position for St Jude bileaflet mechanical valve is 5±2 mm Hg (Mean gradient). Selection of suitable type of mitral prosthetic valve is crucial to avoid acute left heart failure. Preservation of subvalvular apparatus is beneficial to maintain normal left ventricular geometry, stabilize and even improve left ventricular systolic and diastolic functions.

Incidence of post-operative low cardiac output syndrome can be reducing as well.[22] In this study there was statistically significant incidence of low output syndrome in Group B (33.3%) than Group A (10%) with a p value of 0.029. However, prolong duration of inotrope support was needed for Group B patients which was statistically significant.

Pulmonary arterial pressure decreases significantly after mitral valve replacement with relief of mitral stenosis or regurgitation. However, many factors including pain, anxiety and anoxia are still present which can increase pulmonary arterial pressure after cardiac surgery. Therefore, moderate sedation and analgesia are beneficial to patients.[24] post-operative mechanical ventilation is the first step to avoid occurrence of hypoxia. When the tissue becomes hypoxic, pulmonary arteriole starts to constrict and pulmonary arterial pressure increases. In our study 4 patients of Group B needed prolong mechanical ventilation, which was significant (p= 0.040). This similar finding was also found in the study done by Kumar.[21]

Ventilator associated pneumonia (VAP) is one of the most serious but common complication of patients with mechanical ventilator.[24] In our study, 2 patients in Group A and 5 patients in Group B developed pulmonary complication, though it was statistically insignificant.

Surgical site infection (SSI) is a devastating complication for any surgery. In our study total 8 patients had superficial type of surgical site infection. Among them 5 patients were cured with regular dressing and appropriate antibiotic according wound culture and sensitivity. Only 3 patients needed secondary closure. This finding was also statistically insignificant (p= 0.45).

Regarding hospital mortality, two patients from Group B died in the immediate post-operative period constituting an overall mortality rate of 3.33%. This was not statistically significant because of small sample size. Both dead patients were female, body weight below 50 kg, with giant LA size (one had 58 mm LA and another had 63 mm size LA), both of them had reduced TAPSE before operation (15 mm of Hg and 17 mm of Hg respectively) with grade II + MR and both had severe pulmonary hypertension (PASP 60 mm and 70 mm of Hg respectively. One patient had pre-operative atrial fibrillation (AF). Cause of death in both cases was persistent low cardiac output due to right ventricular dysfunction.

On comparing both groups in our study regarding their follow up echocardiography on 10th POD, we detected statistically significant difference regarding cardiac dimensions (LVEDD, LVESD), PASP and pressure across the valve between both groups. This finding is consisted with the finding found by Mohammad.[21]

Conclusion:

From this study we can come conclude that post-operative outcomes are worse following MVR in patients with mitral valve disease with severe pulmonary hypertension. Pulmonary artery pressure remains significantly high on 10th postoperative day following MVR in patients with severe preoperative pulmonary hypertension. MVR should be done before pulmonary artery pressure becomes severe in patients with mitral valve disease.

Study Limitations: Our study has a few limitations which we could not address: -

- Small sample size and short follow up interval.
- Most of our patients were young and having less associated co morbidities. Therefore, the results of this study may not be applicable to the elderly populations.

Conflict of Interest - None.

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