Early Outcome of Mitral Valve Replacement in Patient Having Mitral Stenosis with Moderate Pulmonary Hypertension

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Abstract:
Background: Mitral valve replacement (MVR) plays a central role in the management of patients with mitral stenosis with moderate to severe pulmonary hypertension. Pulmonary hypertension has an impact on short term outcome of MVR. It can influence left ventricular function (low output syndrome), incidence of arrhythmia, ARDS leading to respiratory failure and right ventricular failure which may be irreversible.

Methods: The immediate postoperative hemodynamics in 40 patients with moderate to severe pulmonary arterial hypertension who underwent mitral valve replacement (BLMV) between July 2010 and June 2012 were studied prospectively. Patients were divided into two groups: Group A (n=20): Patient having MS with moderate pulmonary hypertension (PASP: 40-59 mm-Hg) and Group B (n=20): Patient having MS with severe pulmonary hypertension (PASP > 60 mm-Hg). Total two follow up were done- 1st follow up after 10 days and 2nd follow up after 1 month of MVR. Each patient was assessed by medical history, clinical examination & color doppler echocardiogram.

Results: It was shown that surgery can be beneficial for the patients if MVR is done in the state of mild PAH irrespective of age but beyond this level of PAH, the patients may still remain with mild pulmonary hypertension which may trigger the cascade of pulmonary vascular Disease may be the cause of unsatisfactory outcome. So, early surgical outcome of mitral stenosis with moderate pulmonary hypertension is better than mitral stenosis with severe pulmonary hypertension.

Conclusion: We conclude that MVR in patients having MS with moderate PAH is a safe and effective measures for preventing pulmonary hypertension related complications.

(Cardiovasc j 2021; 13(2): 177-182)

Key Words: Mitral Valve Replacement, Mitral stenosis, Pulmonary Arterial hypertension, chronic rheumatic heart disease.

Introduction:
Mitral valvular disease is a common surgical problem in developing countries. Large number of young people are involved which is seen usually in poor socio-economic groups. Mitral valve (40 to 50 percent of cases) most frequently involved in rheumatic heart disease.1 Although rheumatic valve disease was the predominant cause of mitral stenosis in the west, its prevalence has decreased in recent decade. This is in sharp contrast to the developing world, where chronic rheumatic heart disease is endemic and remain the most common cause of both mitral stenosis and regurgitation.2 A recent community based study in Bangladesh reported prevalence of RF to be 1.2 per 1000 and RHD prevalence 1.3 per 1000.3 Another study in Bangladesh reported rheumatic heart disease constitutes 26 to 34 percent of the hospitalized patients with cardiovascular disease in Bangladesh.4 Mitral valve is most commonly affected in rheumatic heart disease followed by aortic in percentage of 90% and 31% respectively in Bangladesh.4 Mitral valve replacement is associated with an operative mortality of 4-

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There is also valve related complications including structural valve deterioration, thromboembolic and haemorrhagic events, endocarditis, perivalvular leaks and haemolysis. Also valve replacement means that the patient has to take life-long anticoagulant therapy with regular hospital visits to check for coagulation status. Mitral valvular disease results in elevated left atrial and pulmonary venous pressures. Pulmonary oedema ensues when pulmonary venous pressure is greater than plasma oncotic pressure. Pulmonary artery hypertension may be caused by compensatory vasoconstriction and intimal hypertrophy of the pulmonary arterioles, together with direct transmission of the elevated pulmonary venous pressure. Recent studies have high lightened the possible influence of chemokines and cytokines on several types of pulmonary arterial hypertension in rheumatic heart disease. Following MVR an immediate reduction in PASP hypertensive than plasma oncotic pressure. Pulmonary artery hypertension may be caused by compensatory vasoconstriction and intimal hypertrophy of the pulmonary arterioles, together with direct transmission of the elevated pulmonary venous pressure. Recent studies have high lightened the possible influence of chemokines and cytokines on several types of pulmonary arterial hypertension in rheumatic heart disease.

Following mitral valve surgery, severe pulmonary hypertension has been an important risk factor for patient outcome. Pulmonary hypertension may be encountered in the intensive care unit in patients with critical illness such as acute respiratory distress syndrome, left ventricular dysfunction, and pulmonary embolism, as well as after cardiothoracic surgery. The intensive care unit management of patients can prove extremely challenging, particularly when they become hemodynamically unstable. Patients with decompensated pulmonary hypertension, including those with pulmonary hypertension with cardiothoracic surgery, require therapy for right ventricular failure. It has recently been established that right ventricular (RV) function can be impaired in valvular heart disease associated with pulmonary hypertension. RV function has been shown to be a major determinant of clinical outcome. Multivariate analysis showed only acute presentation and right ventricular hypertrophy as predictors of perioperative death or major complications respectively. Two-dimensional (2D) echocardiography is helpful for assessment of the mitral valve morphology with characterization of severity and extent of the pathological process. Doppler echocardiography in perioperative period is a useful non-invasive monitor for measuring pulmonary hypertension and other cardio-pulmonary haemodynamic parameters. Following mitral valve replacement marked post-operative improvements occur and those with highest pulmonary hypertension (PAH) are often benefited most. Rapidly diminishing pulmonary vascular resistance (PVR) following valve replacement has been documented by several authors. Decline in pulmonary vascular resistance underlies the symptomatic relief after valve replacement.

Methods:
The study was carried out on patients with predominant mitral stenosis with moderate to severe pulmonary hypertension undergoing mechanical heart valve replacement in NICVD by July, 2010 to June, 2012. All consecutive patients fulfilling the enrollment criteria, admitted to NICVD were included. 40 patients (20 in each group) were included according to the advice of ethical committee. Patients were divided into two groups: Group A (n=20): Patient having MS with moderate pulmonary hypertension (PASP: 40-59 mm-Hg) and Group B (n=20): Patient having MS with severe pulmonary hypertension (PASP > 60mm-Hg). Patient having mitral valve stenosis with moderate to severe pulmonary hypertension diagnosted by preoperative echocardiography were included and exclusion criteria were mitral regurgitation of grade two or more, significant structural aortic, pulmonary or tricuspid valvular disease, associated with coronary artery disease, preexisting lung disease—Like asthma, pulmonary tuberculosis and history of pulmonary lobectomy, significant co morbidities—Chronic liver disease(CLD), Chronic kidney disease(CKD),neoplasm etc. and mitral re-stenosis following CMC. Follow up done at 10 days and 1 month after surgery. Each patient was assessed by medical history, clinical examination & echocardiogram in post-operative period. Data was processed using software SPSS (Statistical Package for Social Sciences) version 16.0. Comparisons were made between echocardiographic values of two groups. For all analytical tests, the level of
significance was set at 0.05 and \( p < 0.05 \) was considered significant. The protocol was approved by ethical committee of NICVD. A preformed data sheet were prepared by which data was collected meticulously. Every participant gave written informed consent and enjoyed an equal right even if they withdraw them from any stage of study regarding treatment.

**Results:**

**Age distribution:**

Age distribution of the patients between two groups were almost similar with mean ages of Group-A and Group-B being 38.15±12.21 and 35±11.21 years respectively. Most of patients belongs to 20-40 years 11(55%) vs. 14(60%) 40-60 years are 30% vs. 20% above 60 years are 5% in both groups and below 20 years were 10% vs. 5%. Sex distribution between two groups which was similar with a slight male preponderance in either group 55% vs. 60% (11 vs 12) and female being 45% vs. 40% (9 vs. 8) all are statistically not significant. Significant improvement of PASP, PADP, mPAP and RVSP were detected in group-A patient one month after surgery than that of group-B patients.

<table>
<thead>
<tr>
<th>Table-I</th>
<th>Postoperative normalization of PASP.</th>
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<tbody>
<tr>
<td>Group</td>
<td>Pre-Operative high</td>
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<tr>
<td></td>
<td>PASP (&gt;33 mm-Hg)</td>
</tr>
<tr>
<td>Group-A(n=20)</td>
<td>20(100%)</td>
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<tr>
<td>Group-B(n=20)</td>
<td>20(100%)</td>
</tr>
<tr>
<td>p value</td>
<td>NA</td>
</tr>
</tbody>
</table>

# Data were analyzed using Chi-square (c²)/ Fisher’s exact test. Figures in the parentheses denote corresponding percentage. (n= number of patients, S= Significant, Not Applicable).

<table>
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<tr>
<th>Table-II</th>
<th>Postoperative normalization of PADP.</th>
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<tr>
<td>Group</td>
<td>Pre-operative high</td>
</tr>
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<td></td>
<td>PADP (&gt;15mm-Hg)</td>
</tr>
<tr>
<td>Group-A(n=20)</td>
<td>20(100%)</td>
</tr>
<tr>
<td>Group-B(n=20)</td>
<td>20(100%)</td>
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<tr>
<td>p value</td>
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</tbody>
</table>

# Data were analyzed using Chi-square (c²) test. Figures in the parentheses denote corresponding percentage.

<table>
<thead>
<tr>
<th>Table-III</th>
<th>Postoperative normalization of mPAP.</th>
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<tbody>
<tr>
<td>Group</td>
<td>Pre-Operative high</td>
</tr>
<tr>
<td></td>
<td>mPAP (&gt;25mm-Hg)</td>
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<tr>
<td>Group-A(n=20)</td>
<td>20(100%)</td>
</tr>
<tr>
<td>Group-B(n=20)</td>
<td>20(100%)</td>
</tr>
<tr>
<td>p value</td>
<td>NA</td>
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</tbody>
</table>

# Data were analyzed using Chi-square (c²) test. Figures in the parentheses denote corresponding percentage. (n= number of patients, S= Significant, NA=Not Applicable).
Discussion:
Pulmonary arterial hypertension has long been considered a risk factor for poor outcome in patients undergoing MVR, with operative mortality. Najafi and colleagues, found the degree of PAH correlated strongly with perioperative mortality, ranging from 16% in patients with mild PAH to 23% in severe PAH and 61% when PAP was at systemic levels. Despite the high operative mortality in most series of MVR in patients with severe PAH, a striking improvement in survival was noted. The improved outcome was attributed to better myocardial preservation, preservation of the subvalvular apparatus, and improved postoperative care.

Numerous studies have examined haemodynamic changes in this subset of patients at different intervals after mitral valve procedures. Most have demonstrated an immediate reduction in ASP and PVR, signifying a sudden drop in left atrial pressure and reversal of the severe spastic pulmonary vasoconstriction that accompanies left atrial hypertension in some patients and there is slow regression of elevated PASP and PVR several months postoperatively. These reports point toward the involvement of multiple factors in the development of PAH in mitral valve disease.

In our study also carries similar features, where the mean PASP and PADP fell significantly immediately following MVR in moderate pulmonary hypertension and 16(80%) patients shown normal PASP in group-A where it was only 5(25%) in group-B. These features also observed in PADP and mPAP where both PADP and mPAP normalized in 19(95%) patients in group-A which was 55 percent in group-B. But this decline continued over a period of time in patients with severe PAH (group B) where mean PASP declined from (68.55±8.38) mm-Hg to (59.8±9.86) mm-Hg, PADP from (30.35±4.17) to (25.40±4.24) mm-Hg in 2nd follow up and that of mPAP from (52.30±6.19) mm-Hg to (33.40±9.31) mm-Hg. Our group B patients showed the unique characteristics of advanced disease, which is seen only in developing countries. Earlier study of Kaul et al., “Mitral valve replacement in the presence of severe pulmonary hypertension.” found persistent rise of PASP (110±18.9) to 47.5±12.4) mm-Hg after MVR, which also support our study. Another study of Vincens et al., “Long-term outcome of cardiac surgery in patients with mitral stenosis and severe pulmonary hypertension”. Found persistent rise of PASP (from 81±18 to 50±18 mm-Hg) and PADP (from 36±7 to 25±7 mm-Hg) and that of mPAP (from 74.16±18.5 to 30.8±5.5mm-Hg) which again support our study. Reactive pulmonary arterial vasoconstriction, which may be responsible for part of the disproportionate elevation of PASP & PADP.16

It has recently been established that RV function can be impaired in valvular heart disease. RV function has been shown to be a major determinant of clinical outcome. Vincens and colleagues identified clinical right heart failure as a predictor of operative mortality, and both right ventricular systolic pressure (RVSP) and right ventricular hypertrophy as predictors of poor outcome. In our study all the group-B patient had elevated RVSP (55±5.41) mm-Hg reduced only to (48.40±8.42) mm-Hg after one month follow up and 18(90%) patients in group-A shown normalization of RVSP in comparison to 7(35%) patients in group-B, which supports the previous study.

Further study of Walls et al., (2008) “Persistent Pulmonary Hypertension after Mitral Valve Surgery: Does Surgical Procedure Affect Outcome?” Found persistied rise of RVSP after MVR (52±12 mm-Hg to 42±6 mm-Hg) which is similar to our study. These findings probably reflect more severe or long-
standing pulmonary hypertension & may increase the risk of right ventricular failure after surgery. This prompted us to operate on these patients on the basis that relief of obstruction at the valvular level might reduce the reactive component of pulmonary vascular disease, and this might alleviate some of the debilitating symptoms.19

There was no significant change in EF of patients undergoing mitral valve replacement in both groups of moderate to severe pulmonary hypertension. Pre-operative EF was (59.70±6.36) % in Group-A and (58.35±5.49) % in Group-B. Mild increase of EF after MVR observed in both groups where EF were (61.40 ±5.01) % and (59.40±4.3) % respectively. Rakesh et al., (2008) observed in their study, “Determinants of early decline in ejection fraction after surgical correction of mitral regurgitation”, significant decreases in left ventricular ejection fraction (mean, -8.8) and left ventricular end-diastolic dimension (mean, -7.5). The magnitude of the early decline in ejection fraction was similar in patients who had mitral valve repair and replacement. Further study of Walls et al., “Persistent Pulmonary Hypertension after Mitral Valve surgery: Does Surgical Procedure Affect Outcome? Found slight increase of LVEF (54.1% to 54.5%) after MVR with mechanical valve, which is similar to our study. The decrease in postoperative ejection fraction was independently associated with a lower preoperative ejection fraction, the presence of atrial fibrillation, advanced New York Heart Association functional class, greater left ventricular end-diastolic and end-systolic dimensions, and larger left atrial size.14,20

Mean mitral valve gradient (MVG) was (24.35±4.28) mm-Hg in Group-A and (27.0±8.55) mm-Hg in Group-B which were decreased to (12.35±6.35) mm-Hg and (10.60±1.85) mm-Hg respectively. Persistent elevation of MVG supports Tewari and Basu by their study of “Left ventricular outflow tract obstruction after mitral valve replacement.” showed elevated MVG observed after MVR due to small LV cavity, redundant mitral valve leaflets, anteriorly placed chordal apparatus, and a thickened septum, which support our study.21

There was no difference in per-operative cross-clamp (XCT) time and bypass (CPB) i.e., total operation time in both groups. In group-A mean cross-clamp time & CPB time were 75.65± 16.08 minutes & 122.45±22.42 minutes respectively and in group-B them were75.10±13.78 minutes & 122.35±22.11 minutes respectively. Mubeen et al., (2008) mentioned in their study “Mitral Valve Replacement in Severe Pulmonary Arterial Hypertension.” The mean CPB time was 67.6 min (range, 32–137 min) and the mean aortic cross clamping time was 32.8 min (range, 17–85 min). Our study also similar to this study in range. These were possible due to proper pre-operative assessment & management of pulmonary hypertension related risk factors and proper anesthetic and CPB related management.22

Mean age of the patient in my study was (38±12) years which was not significant (p=0.410) and most population belongs to 20-40 years of age group (62.5%). Mubeen, et al. reported a study of mitral valve replacement in severe pulmonary arterial hypertension, shown mean age was 36±3.6 years, which is similar to our study and people of this group are more vulnerable to chronic rheumatic heart disease in our country.22

There was male preponderance in the study which was not significant (p=1.00). Male, female ratio was 1.35:1. Almost similar ratio were reported by Mustafa et al. in 1984 from Chest Disease Hospital Kuwait and Palmar et al. in 1963 from the joint Cardio-Respiratory Service of the Royal Victoria Hospital and Montreal children’s Hospital.23,24

Majority of the patients (72.5%) were in normal weight for height. Both groups were almost identical in respect to BMI (p=0.446). So, there was minimum chance of malnutrition or overweight related peri-operative non-cardiac causes of mortality or morbidity that can alter results of the study.

We acknowledge that the lack of follow-up of pulmonary vascular dynamics by catheterization constitutes a limitation of this study and were related primarily to economic factors. The small number of patients limits the statistical significance of the study. Despite these limitations, to the best of our knowledge, this study is the only series of patients with high PAP undergoing MVR in the modern era in our country.

**Conclusion:**

We conclude that MVR in patients having MS with moderate PAH is a safe and effective measures
for preventing pulmonary hypertension related complications. Which is if done during the state of mild to moderate pulmonary hypertension and before the onset of severe pulmonary hypertension the full reversibility of pulmonary vasculature can still be achieved. Careful long-term follow-up and conduction of a double-blind clinical trial are required to examine the early as well as late effects.

Conflict of Interest - None.

References:
21. Tewari, P., Basu, R., 2007. Left Ventricular Outflow Tract Obstruction After Mitral Valve Replacement. Available at: <http://www.ptewari123@yahoo.co.in; ptewari@sppgi.ac.in>.