Pak Heart J

EFFECTS OF PULMONARY HYPERTENSION ON EARLY OUTCOMES AFTER MITRAL VALVE REPLACEMENT

Iftikhar Paras[1], Hammad Azam[2], Allah Buksh Khaki[3], Mirza Ahmad Raza Baig[4], Shaukat Ali Rao[5]

[1,3,4] Cardiac Surgery Department Chaudhary Pervaiz Elahi Institute of Cardiology Multan, Pakistan
[2,5] Department of Cardiac Surgery, Sheikh Zayed Hospital Rahim Yar Khan, Pakistan

Address for Correspondence:

Dr. Iftikhar Paras,

Cardiac Surgery Department Chaudhary Pervaiz Elahi Institute of Cardiology Multan, Pakistan

E-Mail: hammad.surgery@gmail.co

Date Received: January 05, 2015
Date Revised: January 28, 2015
Date Accepted:February 17, 2015

Contribution
All the authors contributed significantly to the research that resulted in the submitted manuscript.

All authors declare no conflict of interest.

This article may be cited as: Parasl, Azam H, Khaki AB, Baig MAR, Rao SA. Effects of pulmonary hypertension on early outcomes after mitral valve replacement. Pak Heart J 2015;48(2): 96 - 100.

ABSTRACT

Objectives: The objective of this study was to determine the safety of Mitral valve replacement surgery in the presence of severe pulmonary hypertension.

Methodology: This was a randomized control trial in Chudhary Pervaiz Elahi Institute of Cardiology. Patients of Mitral stenosis undergoing Elective Mitral valve Replacement were included in this study. In Group I, there were patients with moderate pulmonary hypertension (30-60 mm of Hg) and in Group II patients with severe pulmonary hypertension (>60 mm of Hg) were included.

Results: Patients included in the study were 30, with 15 in each group. There was no significant difference in age, gender, and other risk factors i.e. smoking, diabetes, and obesity in both groups. However pre-operative CVP was significantly high in Group II patients ($p = 0.05$). CPB times, need of inotropes and nitrates, and number of patients with prolonged ventilation time were significantly high in Group II ($p > 0.0001$, 0.02, 0.003 and 0.02 respectively). There was significant decrease in Pulmonary Artery Pressures after surgery in Group I and II ($p > 0.0001$, > 0.0001 respectively). Regression analysis showed strong correlation between pulmonary artery pressures before surgery and after surgery ($ß = 0.708$).

Conclusions: Mitral valve replacement should be offered even in the presence of severe pulmonary hypertension, however these patients need extra post-operative care due to increased morbidity.

Key Words: Mitral Valve Replacement, Pulmonary Hypertension.

INTRODUCTION

Mitral Stenosis is a life threatening cardiac disease usually secondary to Rheumatic fever in developing countries. Mitral valve dysfunction results in pulmonary hypertension. Initially Left atrial pressure rises then pulmonary venous hypertension develops. Raised blood pressure in pulmonary vasculature leads to the development of pulmonary arterial hypertension. That results in Tricuspid valve incompetence and right ventricle dysfunction. Increased pulmonary vascular resistance and pulmonary hypertension contribute to clinical symptoms of mitral valve disease.[1] Different studies have shown variations in pulmonary blood pressure after Mitral valve replacement in the presence of severe pulmonary hypertension. In this study, in Operating Room (OR) pulmonary blood arterial pressure (PAP) was noted pre-operatively and immediately after MVR surgery and hemodynamic changes in the early post-operative period were observed and there clinical influence on early outcome was noted.

METHODOLOGY

This was a Randomized Control Trial conducted in cardiac surgery department, Chaudhary Pervaiz Elahi Institute of Cardiology, Multan, Pakistan. The study was conducted from 1st February 2012 to 30th January 2014. Patients undergoing Elective Mitral valve Replacement were included in this study. Patients with Mitral stenosis having moderate to severe pulmonary hypertension with indication of surgical intervention were included, while patients having age <12 years (Pediatric patients), those having severe TR, involvement of other valves or some other cardiac diseases and undergoing emergency surgery were excluded from the study.

Patients were divided into two groups depending on their pre-operative Pulmonary Artery Pressures (PAP) based on fresh echocardiographic assessment. There were fifteen patients in each group. In Group I (G=I) there were patients with moderate pulmonary hypertension (PAP 30-60 mmHg) and in Group II (G=II) patients were with severe pulmonary hypertension (PAP >60 mmHg). In OR, invasive measurement of mean pulmonary blood pressure was noted just after sternotomy and pericardiotomy and before closure of chest after surgery. For that purpose we used a purse string suture of 5/0 prolene on pulmonary artery from which direct measurement of mean PAP was done with invasive monitor with the help ordinary 5 cc needle and non collapsible syringe pump line after de-airing. Two readings were noted for each patient of both groups.

Surgical procedures were carried out through median sternotomy and standard Cardiopulmonary bypass. Systemic cooling was achieved by lowering patient body temperature to 32 °C, tropical ice slush for local cooling of the heart. Aortic cross clamp was applied and cold blood cardioplegia was used to arrest and protect the myocardium. Left atrium was opened through classical approach. Mitral valve was excised preserving PML at least according to valve disease status. All the valves were replaced with Prosthetic Bi-leaflet Mechanical valves (St.Judes) using technique of semi-continuous method using 2/0 prolene sutures. Left Atrium was closed with 3/0 prolene suture was replacement of valve. In post-operative course ventilation time, inotropic support weaning time, need for nitrates and ICU stay were noted.

Pre-operative, per-operative and post operative data was analyzed by using SPSS (Version 17). Numerical variables were compared using t-test for independent variables and Paired-Samples t-test for dependent variables. Chi-square test and Fischer's Exact test were applied to compare categorical variables. Simple linear regression was applied to see the effect of pre-operative pulmonary pressures on post-operative pulmonary artery pressures and to develop a regression model. P-value of <0.05 was considered significant.

RESULTS

Patients undergoing Elective mitral valve replacement included in the study were 30. Mean age of patients were 29.33 ± 4.89 in Group I and 30.60 ± 4.62 in Group II. There were 8 (53.3%) females in Group I while 10 (66.6%) were males in Group II. There were no significant differences in pre-operative risk factors i.e. smoking, diabetes, obesity and NYHA Class in patients of Group I and Group II (Table 1).

Per-operative data analysis showed significantly increased CPB times in Patients of Group II as compared to Group I (p >0.0001) while aortic cross clamp times were almost same in both groups (p = 0.10). Per-operative central venous pressure was high in Group II patients 9.93 ± 4.78

Table 1: Comparison of Demographic and Pre-operative Variables

Variable		Group I (n=15)	Group II (n=15)	P-value
Age (years) (mean+S.D)		29.33 ± 4.89	30.60 ± 4.62	0.47
Gender	Male n (%)	7 (46.7%)	10 (66.7%)	0.26
	Female n (%)	8 (53.3%)	5 (33.3%)	
Diabetes n (%)		3 (20.0%)	1 (6.6%)	0.59
Smoking n (%)		2 (13.3%)	3 (20%)	1.00
Obesity n (%)		1(6.6%)	1 (6.6%)	1.00
NYHA class	III	6 (40%)	9 (60%)	0.27
	IV	9 (60%)	6 (40%)	

Table 2: Comparison of Per-operative and Post-operative Characteristics

Variable	Group I (n=15)	Group II (n=15)	P-value
CVP	7.40 ± 1.35	9.93 ± 4.78	0.05
X-Clamp ± time (mins.)	38.66 ± 4.83	41.60 ± 4.707	0.103
CPB ± time (mins.)	59.20. ± 3.12	71.0 ± 3.22	>0.0001
Need for High Inotropic support*	3 (20%)	8 (53.3%)	0.02
ICU stay time (days)	4.20±3.18	5.53±1.20	0.18
Needs for High Nitrates **	0 (0.00%)	7 (46.7%)	0.003
Prolonged Ventilation time > 6 hours (%)	3 (20%)	8 (53.3%)	0.02

CVP= Pre-operative Central Venous Pressure,
X-Clamp = Cross Clamp, ± CPB = Cardiopulmonary Bypass,
*High inotropic support= adrenaline > 0.041 ug/kg/min,
**High Nitrate dose = 0.1-10 (ug/kg/min)

vs. 7.40 ± 1.35 mmHg in Group I (p = 0.05). Higher number of patients in Group II required high inotropic support and high levels of nitrates in immediate post-operative periods (p = 0.02 and 0.003 respectively), as shown in table 2.

There was significant decrease in pulmonary artery pressures (PAP) immediately after mitral valve replacement in patients of Group I and Group II. But this decrease in pressures was more marked in Group II patients. The PAP was decreased to about 30 mmHg in Group II patients, whereas in Group I the average decrease in pressure was about 15 mmHg after surgery (Table 3). Two patients having pre-operative PAP > 80 mmHg were having no significant immediate fall in PAP after MVR.

Simple linear regression was applied to see the effects of Pre-operative Pulmonary Artery Pressures (PAPb) on Post-operative Pulmonary artery pressures (PAPa). The regression analysis showed a strong correlation between them. The regression equation achieved was PAPa = -6.78+0.708 (PAPb).

The equation means that there will be a decrease of 7.08 mmHg in PAPa after every 10 mmHg rise in PAPb. So there is a regression of about 70% in PAP after surgery.

DISCUSSION

Pulmonary artery hypertension is a serious and important complication of mitral valve diseases. Increase in PAP which is associated with enhanced PVR, is a reflection of left atrial hypertension. Elevated PVR is as a result of combined effects of pulmonary vasoconstriction, and morphologic alterations in pulmonary vasculature.[2] Severe pulmonary

Table 3: Within Groups Comparison of Pulmonary Artery Pressures

Pulmonary Artery Pressures	Before Surgery	After Surgery	P-value
Group I	45.13±7.79	30.66±3.55	>0.0001
Group II	68.93±12.26	36.53±22.66	>0.0001

hypertension results in higher rates of mortality (10-15 %) during the peri-operative period and also in the long term in patients scheduled for mitral valve replacement.[3] The main aim of our study was to see the status of pulmonary hypertension immediately after MVR in OR when patient is weaned off from CPB. Basically we tried to see the safety of Mitral valve surgery in the presence of severe pulmonary hypertension and the behavior of patient in early post-operative period. In our both study groups, any incident of mortality was not encountered in the early postoperative period However, morbidity in terms of higher CPB, cross clamp time, need for inotropic support and ICU stay was found to be higher in the group (Group 2) with severe pulmonary hypertension.

As far as pathophysiology of pulmonary hypertension is concerned, it is because of severe vasoconstriction due to a potent vasoconstrictor Endothelin-1. Its levels are three times elevated in patients of Mitral stenosis than in normal individuals.[4] Sustained untreated pulmonary hypertension indirectly results RV dysfunction. In resistance cases of prolonged pulmonary hypertension there are micro-vascular changes that occur.[5] Preoperative echocardiographic assessment is primary test to give impression about disease course. In the studies of Barberi et al and Le Tourneau et al, patients having PAP more than 50 mmHg were having significant mortality.[6,7] Some consider PAP pressure>110 mm of Hg as a contraindication for surgical intervention.[8] However ACC/AHA 2006 guidelines for the management of valvular heart disease recommend MVR for the patients with severe pulmonary hypertension.[9] RV dysfunction is a serious condition which is considered as a factor responsible for increased mortality after MVR.[10] As a part of RV dysfunction there is tricuspid valve insufficiency which further deteriorates surgical outcomes.

Following mitral valve surgery, left atrial loading can be adequately decompressed. This decompression is significantly influential in the regression of pulmonary hypertension. Various investigators have demonstrated significant decreases in PAP, and PVR long after surgical repair. In a study by Tempe et al, rapid and similar decreases in mean PAP values during the postoperative period in patients with mild-moderate and severe pulmonary hypertension were observed, however in the patient group with mild-moderate degrees of hypertension this decline

was more apparent, and the cardiac index increased more sharply.[11] However he demonstrated similar effects on mortality, and morbidity. In this study, a rapid drop in PAP values was observed in Group II categorized according to extent of increases in PAP values. Still any significant intergroup difference as for mortality could not be found, while higher rates of morbidity were detected in the increased PAP Group II.

Foltz et al, indicated that pulmonary hypertension develops in the early postoperative period by way of at least three mechanisms.[12] The first one is passive transmission due to increase in the left atrial pressure. The second one is reactive pulmonary arteriolar vasoconstriction, and the last one is the development of morphologic alterations. The authors indicated that the first mechanism was rapidly reversible after MVR. They demonstrated that regression in other mechanisms occurred within a few months after MVR They explained this regression in terms of PVR index. In this study, the patients were followed up for a short term (2 months). It is known that there is additional decrease in PAP during exercise in the following 6-12 months after mitral valve surgery.[13]

In our study, there was significant fall (>50% regression) in PAP immediately after mitral valve replacement. In two patients from Group II there was no significant fall in mean PAP and these patients were having >80 mm of Hg mean PAP. Post-operative prosthesis-patient mismatch is considered a factor responsible for residual pulmonary hypertension.[3] In past there was use of first generation prosthetic valves(Starr Edwards) and second generation (Bjork Shelley) with variable post operative gradient and residual pulmonary hypertension. In our study we used Saint Judes bileaflet mechanical prosthesis of adequate sizes with no significant post operative gradient as it has proven favorable outcome after valvular Surgery.[14] In Group II patients there was a gross difference seen in OR as well as in ICU after surgery. During surgery total CPB time was prolonged in Group II patients along with the higher dose of inotropic support needed in OR. After surgery in ICU the patients of Group II were having prolonged ventilation time (>6 hours), prolonged need for inotropic support and nitrates.

The management of severe pulmonary hypertension should be started right from pre-operatively. Before operation use of nitrates like Sildinafil is now considered to have beneficial role in post-operative pulmonary hypertension regression.[15] During surgery use of vasodilator iloprost in inhalation form is shown to increase chances of separation of patent from CPB in the presence of severe pulmonary hypertension.[16] Adequate ventilation time and use of inotropic drugs especially dobutamine and nitrates have been shown supportive role in smooth recovery of patients with severe pulmonary hypertension. However sometimes it takes many months to years to recover from this condition. In modern third world cardiac surgical setups now mortality of MVR in the presence of severe pulmonary hypertension is around 2.3%.[17]

CONCLUSION

Mitral valve replacement should be offered even in the presence of severe pulmonary hypertension; however these patients need extra post-operative care due to increased morbidity.

REFERENCES

1. Braunwald E: Valvular Heart Disease. In: Braunwald E,editor Heart Disease. 4th ed. Phaladelphia: Saunders;1992. pp 796-97.
2. Walston A, Peter RH, Morris JJ, Kong Y, Behar VS. Clinical implications of pulmonary hypertension in mitral stenosis. The American journal of cardiology. 1973;32(5):650-5.
3. Li M, Dumesnil JG, Mathieu P, Pibarot P. Impact of valve prosthesis-patient mismatch on pulmonary arterial pressure after mitral valve replacement. Journal of the American College of Cardiology. 2005;45(7):1034-40.
4. Le Tourneau T, Richardson M, Juthier F, Modine T, Fayad G, Polge A-S, et al. Echocardiography predictors and prognostic value of pulmonary artery systolic pressure in chronic organic mitral regurgitation. Heart. 2010;96(16):1311-7.
5. Snopek G, Pogorzelska H, Rywik TM, Browarek A, Janas J, Korewicki J. Usefulness of endothelin-1 concentration in capillary blood in patients with mitral stenosis as a predictor of regression of pulmonary hypertension after mitral valve replacement or valvuloplasty. The American journal of cardiology. 2002;90(2):188-9.
6. Mubeen M, Singh AK, Agarwal SK, Pillai J, Kapoor S, Srivastava AK. Mitral valve replacement in severe pulmonary arterial hypertension. Asian Cardiovascular and Thoracic Annals. 2008;16(1):37-42.
7. Barbieri A, Bursi F, Grigioni F, Tribouilloy C, Avierinos JF, Michelena HI, et al. Prognostic and therapeutic implications of pulmonary hypertension complicating degenerative mitral regurgitation due to flail leaflet: a multicenter long-term international study. European heart journal. 2011;32(6):751-9.
8. Barclay RS, Reid JM, Stevenson JG, Welsh TM, McSwan N. Long-term follow-up of mitral valve replacement with Starr-Edwards prosthesis. British heart journal. 1972;34(2):129.
9. Bonow RO, Carabello BA, Chatterjee K, de Leon AC,

Faxon DP, Freed MD, et al. 2008 focused update incorporated into the ACC/AHA 2006 guidelines for the management of patients with valvular heart disease: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (Writing Committee to revise the 1998 guidelines for the management of patients with valvular heart disease) Endorsed by the Society of Cardiovascular Anesthesiologists, Society for Cardiovascular Angiography and Interventions, and Society of Thoracic Surgeons. Journal of the American College of Cardiology. 2008;52(13):e1-e142.

10. Datt V, Tempe D, Geelani M, Tomar A, Virmani S, Goel M, et al. Atrial septostomy for acute right ventricular failure following mitral valve replacement-a case report. Annals of cardiac anaesthesia. 2004;7(1):62.
11. Tempe DK, Hasija S, Datt V, Tomar A, Virmani S, Banerjee A, et al. Evaluation and comparison of early hemodynamic changes after elective mitral valve replacement in patients with severe and mild pulmonary arterial hypertension. Journal of cardiothoracic and vascular anesthesia. 2009;23(3):298-305.
12. Foltz B, Hessel 2nd E, Ivey T. The early course of pulmonary artery hypertension in patients undergoing mitral valve replacement with cardioplegic arrest. The Journal of thoracic and cardiovascular surgery. 1984;88(2):238-47.
13. Zielin ski T, Pogorzelska H, Rajecka A, Biedermavn A, Sliwin ski M, Korewicki J. Pulmonary hemodynamics at rest and effort, 6 and 12 months after mitral valve replacement: a slow regression of effort pulmonary hypertension. International journal of cardiology. 1993;42(1):57-62.
14. Ikonomidis JS, Kratz JM, Crumbley AJ, Stroud MR, Bradley SM, Sade RM, et al. Twenty-year experience with the St Jude Medical mechanical valve prosthesis. The Journal of thoracic and cardiovascular surgery. 2003;126(6):2022-31.
15. Bomma C, Ventura HO, Daniel G, Patel H. Adjunctive sildenafil for the treatment of pulmonary hypertension after mitral valve replacement. Congestive Heart Failure. 2006;12(6):347-8.
16. Rex S, Schaelte G, Metzelder S, Flier S, De Waal E, Autschbach R, et al. Inhaled iloprost to control pulmonary artery hypertension in patients undergoing mitral valve surgery: a prospective, randomized?controlled trial. Acta Anaesthesiologica Scandinavica. 2008;52(1):65-72.
17. Vincens JJ, Temizer D, Post JR, Edmunds LH, Herrmann HC. Long-term outcome of cardiac surgery in patients with mitral stenosis and severe pulmonary hypertension. Circulation. 1995;92(9):137-42.