ORIGINAL ARTICLE

Determinants of Decrease in Pulmonary Hypertension Following Percutaneous Transvenous Mitral Commissurotomy

Ahmad Noor, Tahir Saghir and Khan Shah-e-Zaman

ABSTRACT

Objective: To identify the determinants of decrease in pulmonary hypertension after percutaneous balloon mitral commissurotomy.

Study Design: Quasi experimental study.

Place and Duration of Study: National Institute of Cardiovascular Diseases, Karachi, from March to October 2007.

Methodology: Adult patients with severe mitral stenosis and pliable valve having no significant mitral regurgitation, aortic valve disease, or left atrial thrombus were selected for Percutaneous Transvenous Mitral Commissurotomy (PTMC) by double balloon method. All patients underwent echocardiography of left and right heart catheterization before and after PTMC. Univariate and multivariate analysis was done to assess the relation of age, gender, left atrial size, right ventricular size, gradient across mitral valve, valve area, valve area per meter,^{2} body surface area, and presence of Tricuspid Regurgitation (TR) on the decrease in pulmonary arterial pressure.

Results: Of the 100 cases included in the final analysis, 60% were female, 84% were in sinus rhythm and had a mean age of 27 years. There was a 48% decrease in mean left atrial and 29% decrease in right ventricular systolic pressure immediately postprocedure. The mitral valve area increased from 0.883 ± 0.1261 cm^2, pre-ballooning to 1.7864±0.28445 cm^2 post-PTMC, a percent change of 102.41%. In multivariate analysis, mean left atrial pressure (p=0.00: CI=0.317-0.007), younger age (p=0.010: CI=-0.667 to -0.095) and right ventricular size (p=0.038: CI: 0.25-0.871) were independent predictors of decrease in systolic pulmonary arterial pressure post-PTMC.

Conclusion: Younger age, mean and left atrial pressure and right ventricular size were independent predictors of decrease in pulmonary systolic pressure immediately post-PTMC.

Key words: *Pulmonary hypertension. Percutaneous balloon mitral commissurotomy. Determinants.*

INTRODUCTION

Pure Mitral Stenosis (MS) develops in approximately 40% of all patients with rheumatic heart disease.[1] Mitral stenosis is still very common in this country as there is a high incidence of rheumatic fever.[1] After an episode of rheumatic fever, the latency period is 10-20 years or more before the onset of symptoms.[2] Pulmonary Hypertension (PH) frequently complicates mitral stenosis. Pulmonary Arterial Hypertension (PAH) is defined as a sustained elevation of systolic pulmonary arterial pressure to more than 25 mmHg at rest or to more than 30 mmHg with exercise, with a mean pulmonary-capillary wedge pressure and left ventricular end-diastolic pressure of less than 15 mmHg.[3] At a stage when patient with mitral stenosis need intervention, 50% of the patients have moderate pulmonary hypertension while 25% of the patients have severe PAH.[4] Pulmonary hypertension significantly influences symptomatology and long-term prognosis.[2] Mitral valve replacement, surgical or percutaneous balloon mitral commissurotomy often result in regression of pulmonary hypertension. Percutaneous Balloon Mitral Commissurotomy (PTMC), first described in 1984, has had good short and intermediate-term results.[5] Its effectiveness and long-term results have now been well-documented.[6,7] Pulmonary artery pressures also decrease following PTMC.[8,9] The improvement in pulmonary hypertension after PTMC is explained by the improvement in the mitral valve area and subsequent decompression of left atrium and pulmonary venous beds. PTMC is commonly performed by antegrade access to the mitral valve through transseptal puncture by one of the four techniques (Inuoe, double balloon, metallic commissurotome, single balloon and multitrack system) as described by Vahanian *et al.*[10,11] Because of its lower cost the double balloon techniques are mostly used in our institution.[12]

The determinants of change and extent of reversibility in pulmonary hypertension among patients undergoing balloon valvuloplasty has not been studied extensively, though some authors have suggested predictive models about overall outcome of the patients following PTMC.[5,13] This study was done to determine the immediate effect of PTMC on pulmonary pressure. Such knowledge will help to identify patients of higher likelihood of benefiting from PTMC.

Department of Cardiology, National Institute of Cardiovascular Diseases, Karachi.

Correspondence: *Dr. Ahmad Noor, Faizur Rehman Hospital, Metroville, SITE, Karachi.*
E-mail: noorahmad74@yahoo.com

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The objective of this study was to identify the determinants of decrease in pulmonary hypertension after PTMC.

METHODOLOGY

The study was conducted from March to October 2007. Patients with severe rheumatic mitral-valve stenosis were assessed in the clinics of the National Institute of Cardiovascular Diseases, Karachi, and selected for PTMC. History was obtained from all patients, who also underwent physical examination, two-dimensional echocardiography and Doppler study. Informed consent was obtained for the procedure. Patients not in sinus rhythm underwent a transesophageal echocardiography before undergoing the procedure to rule out left atrial thrombus.

All adult patients undergoing PTMC with pure mitral stenosis and pulmonary hypertension diagnosed on pre-procedure echocardiography were included in the study. Patients under 14 years of age, with significant aortic valve disease, greater than mild mitral regurgitation, failed PTMC or left atrial clot were excluded. Cardiac catheterization was performed before and after the procedure. Pulmonary artery, right and left ventricular and left atrial pressures were recorded in all patients. After a single atrial transseptal puncture, an 8-French Mullins sheath was advanced to the left atrium. A balloon floatation catheter was used to cross the mitral valve, after which one 0.035 inch (0.9 mm) extra stiff guidewire was placed in the apex of the left ventricle or advanced to the ascending aorta. A septostomy dilator was used to dilate the septum after which two valvuloplasty balloons, 5.5 cm long were inflated simultaneously across the mitral valve (ranging from 14 mm to 20 mm). The therapeutic end point was nearly complete elimination of the mitral valve gradient without a substantial increase in mitral regurgitation. All patients underwent M-mode, two dimensional and Doppler echocardiography pre-procedure and then one day after the procedure. Mitral pressure gradient, mitral valve area and right ventricular systolic pressure were measured. All patients underwent right heart catheterization with measurement of hemodynamic variables before and after valvuloplasty. A successful immediate result was defined as a mitral valve area of 1.5 cm or a 50% increase after PTMC without 3/4 mitral regurgitation.[5] Patients were discharged from the hospital after echocardiography was performed one day after the procedure, if there was no immediate complication.

Data was collected on a pre-tested questionnaire. A verbal consent was taken from all patients before filling their information.

Data was entered and analyzed by computer software SPSS version 13.0. Frequency and percentages were computed for categorical variables like gender, ethnicity, NYHA class, and presence of Tricuspid Regurgitation (TR). Mean and standard deviation were estimated for continuous variables like age, valve area, valve area per meter^2, mean pulmonary artery pressure, left atrial size, right ventricular size, gradient across mitral valve. Paired t-test were used to compare mean difference between pre- and postobservation for valve area, mean pulmonary artery pressure, LA size, right ventricular size, gradient across mitral valve and mean and systolic pulmonary artery pressures with 0.05 level of significance.

Possible factors affecting the outcome variable were studied pre- and post-PTMC in univariate and multivariate analysis.

RESULTS

PTMC was attempted in 108 patients suffering from symptomatic severe rheumatic mitral stenosis during the study period. The procedure was successful in 100 patients; those constituted the study group and were included for further analysis. Two cases were referred for urgent surgery after balloon induced severe Mitral Regurgitation (MR). Among 2 cases, the procedure was abandoned because of fluoroscopic evidence of significant calcification of the mitral valve. Four cases did not achieve significant hemodynamic results and they were referred for evaluation regarding mitral valve replacement or closed commissurotomy.

Most of the patients were young, age ranging from 15 to 50 years. Fifty percent of the patients were younger than 25 and 83% were younger than 35 years (27.72±7.78 years). Majority (60%) were females and in NYHA class III (58%), 19% in NYHA IV and 23% in NYHA II. Eighty six percent of the patients were in sinus rhythm at the time of assessment. There were 3 pregnant women with severe MS undergoing PTMC in the 8th month of the pregnancy.

The mitral valve area, measured by echocardiography, increased from mean 0.883±0.1261 cm^2 pre-ballooning to 1.78±64 0.28445 cm^2, a percent change of 102.31%.

The mean pre-ballooning systolic pulmonary artery pressure was 67.12 ± 19.73 mmHg. There was a 48% decrease in mean left atrial pressure immediately post-procedure. Right ventricular systolic pressure and pulmonary artery systolic pressure decreased by 29%. Table I shows the hemodynamic results of PTMC.

In univariate analysis for decrease in systolic pressure of pulmonary artery, age, gender, right ventricular size, presence of TR, body surface area, mitral valve area, mitral valve area per unit body surface area, left atrial size and mean left atrial pressure were studied. Among these, right ventricular size, pre-cath mean left atrial pressure and Tricuspid Regurgitation (TR) were significantly associated with decrease in systolic pulmonary artery pressure (Table II).

In multivariate analysis for independent predictors of decrease in pulmonary pressures, younger age, right ventricular size, and pre-cath left atrial size were independently associated with decrease in pulmonary pressures (Table III).

Among the 100 cases included in the final analysis, there was no sepsis, no thromboembolic episode. One patient had vasovagal syncope; 2 had transient atrial fibrillation post-procedure; 46% did not get any mitral regurgitation; 29% patients had mild mitral regurgitation, while 25% had moderate mitral regurgitation.

Table I: Showing the hemodynamic results of PTMC.

Catheterization echocardiography	Main hemodynamic results variables	Before PTMC mean ±SD	After PTMC mean ±SD	p-value
Catheterization data	Left atrial pressure (mmHg)	33.25±7.09	17.88±6.38	< 0.01*
	Right ventricular systolic pressure (mmHg)	68.75±18.67	48.82±12.96	< 0.01*
	Pulmonary artery systolic pressure (mmHg)	68.88±19.23	48.50±13.49	< 0.01*
	Mean pulmonary artery pressure (mmHg)	45.99±12.31	31.83±8.16	< 0.01*
	Mean left artioventricular gradient	21.97±7.60	4.97±4.14	< 0.01*
Echocardiographic data	Valve area cm^2	0.88±0.13	1.79±0.28	< 0.01*
	Valve area/m^2 BSA	0.61±0.10	1.25±0.31	< 0.01*
	Pulmonary arterial systolic pressure (mmHg)	60.12±17.9	33.4±11.9	< 0.01*
	Peak pressure gradient across mitral valve (mmHg)	20.7±6.6	6.4+2.3	< 0.01*
	Mean pressure gradient across mitral valve (mmHg)	18.42±7.2	11.85±3.6	< 0.01•

Table II: Showing the results of univariate analysis for determinants of reduction in pulmonary hypertension.

Variables	Beta co-efficient	p-value	95% confidence interval
Age	-0.187	0.063	-0.569-0.015
Gender (female)	-0.017	0.863	-4.279-5.095
Body surface area (in m^2)	0.074	0.462	-17.96-8.228
Valve area (in cm)	0.100	0.324	-9.105-27.288
Valve area per unit body surface area	0.088	0.384	-12.833-33.067
Left atrial size (in mm)	-0.090	0.373	-0.537-0.203
Right ventricular size (in mm)	0.24	0.042	-.0910-0.830
Left atrial mean pressure in mmHg	0.315	0.001	0.202-0.820
Tricuspid regurgitation	.050	.033	-2.716-4.461

Table III: Results of multivariable analysis.

Variables	Beta co-efficient	p-value	95% confidence interval
Age (years)	-0.260	0.010	-0.677– -0.095
Precath left atrial mean pressure (mmHg)	4.059	0.000	0.311 – 0.907
Right ventricular size	0.216	0.038	0.025 – 0.871

DISCUSSION

Pulmonary hypertension frequently complicates mitral stenosis. PAH contributes to symptoms of dyspnea in patients with mitral stenosis. The mechanisms believed to contribute to the development of pulmonary hypertension in patients with mitral stenosis are multiple. There is a passive retrograde transmission of elevated left atrial and pulmonary venous pressures into pulmonary vasculature; pulmonary venous hypertension leads to reactive pulmonary vasoconstriction and morphologic changes are induced in the pulmonary vasculature.[2] Immediately following PTMC, pulmonary hypertension decreases slightly with further substantial regression occurring over time.[9] The persistence of some pulmonary hypertension after PTMC relates to the residual mitral stenosis as well as permanent morphologic changes in the pulmonary vasculature. In this study, the immediate decrease in PAH after PTMC and determinants of decrease in pressure were determined.

In this study, the Pulmonary Arterial Systolic Pressure (PASP) decreased by 29%, the mean left atrial pressure decreased by 48% and the left atrioventricular gradient by 77%. Right ventricular systolic pressure and pulmonary artery systolic pressure decreased by 29%. In a study by Fawzy *et al,* the PASP fell from 48.6±17.4 mmHg before PTMC to 31±10 mmHg.[14] Hannoush *et al.* reported 31% decrease in PASP immediately after PTMC.[15] Among these two studies, the patients were young as in the present study while Gomes *et al.* found no immediate decrease in PASP in older patients with a mean age of 52 years.[16]

Age, mean left atrial pressure, and right ventricular size were independent predictors of decrease in systolic pulmonary pressure postprocedure in the regression analysis. Association of increasing age with more severe PAH and less reversible changes in pulmonary circulation is known previously as well. In the study by Moaquin *et al,* older patients had more severe pulmonary pressure while Hannoush *et al.* observed less decrease in PASP in older age group, aged more than 35 years.[8,15] The present study showed that younger patients show more decrease in pressures post-procedure. With each one year decrease in age, the systolic pulmonary pressures decreased more by 0.26 mmHg. With increasing age, the pulmonary arteries are

stiffer and their compliance explaining the lesser decrease in pulmonary pressure after PTMC. In a study by Shaw *et al.* increasing age was found to lead to less favourable results.[17] In that series advancing age was associated with higher echocardiographic score, more incidence of postprocedure MR, and lesser increase in valve area. Fawzy *et al.* observed that their younger patients had lower echocardiographic scores, smaller valve areas, higher gradient across mitral valve and more mitral valve area.[18] These factors may be contributory to the lesser reduction in PAH with advancing age.

In this study, decrease in PAH was seen more in patients with increasing left atrial mean pressure. As a consequence of the stenosis, an increase in left atrial pressure is required to maintain cardiac output. Ali *et al.* found left atrial size as a predictor for improved leaflet excursion after PTMC.[19] The increase in left atrial pressure causes an increase pulmonary venous pressures. But after PTMC, there is a decrease in left atrial pressure and with more pressures, there was more decrease in pulmonary PASP. After the PTMC, the PASP decreased by 4.059 mmHg for each decrease of 1 mmHg in left atrial pressure.

Increase in pulmonary artery pressure leads to dilatation of right ventricular pressure and dilatation.[9] Right ventricular size was also an independent predictor of decrease in PASP (b=0.216; p=0.038: CI=0.25–0.871). Right ventricular enlargement is seen with worsening pulmonary hypertension. Right ventricular systolic and diastolic dysfunction has been described in patients with pure mitral stenosis and the diastolic dysfunction was found to be independent of pulmonary and left atrial pressures. This finding by Yildirim *et al.* suggests a possible rheumatological involvement of right ventricle as described for left ventricle.[21] The right ventricular size was only measured in parasternal long axis at the end of diastole and we think that this association should be looked further with right ventricular volumes and right ventricular functional assessment. These will give us new insight into pathophysiology of mitral stenosis and the hemodynamic improvement achieved with PTMC.

The current study gives a prognostic model of regression of pulmonary pressure after PTMC. This will help us risk-stratify patients and predict their post-procedure success rate. The authors feel that in future studies right ventricular and left atrial volumes should be correlated to pulmonary pressures.

CONCLUSION

The present study showed that younger age, higher mean, left atrial pressure and size of right ventricle were independent predictors of decrease in pulmonary artery pressures. The overall results show that PTMC can be done safely with acceptable complication rates.

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