

## RIGHT VENTRICULAR FAILURE IN SPITE OF SUCCESSFUL PERCUTANEOUS MITRAL COMMISSUROTOMY IN PATIENTS WITH SEVERE MITRAL STENOSIS

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### Contribution

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

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### ABSTRACT

**Objective:** To know the frequency of right ventricular failure inspite of successful percutaneous mitral commissurotomy (PTMC) for isolated severe mitral stenosis.

**Methodology:** This observational study was conducted from January 2011 to December 2014 in Cardiology Department of Lady Reading Hospital, Peshawar. Patients with severe isolated mitral stenosis after successful PTMC were followed for one year. Patients who develop symptoms of right ventricular failure were subjected to detailed transthoracic echocardiogram (TTE) including assessment of right ventricular function.

**Results:** A total of 307 patients with severe isolated mitral stenosis who had successful PTMC were studied. Females were 185(60.26%) and males were 122(39.74%). Mean age was  $26.44 \pm 7.26$  years. TTE performed before PTMC showing mean mitral valve area  $0.9 \text{ cm}^2 \pm 0.24 \text{ cm}^2$ . TTE 24 hours after PTMC showed mean left atrial diameter  $4.68 \pm 3.1 \text{ cm}$ , mean mitral valve area  $1.67 \pm 0.71 \text{ cm}^2$ , mean mitral valve gradient  $5.42 \pm 4.6 \text{ mm of Hg}$ , mean right ventricular systolic pressure (RVSP)  $43 \pm 18.41 \text{ mm of Hg}$ . After follow up for one year, 27(8.79%) patients developed signs and symptoms of congestive heart failure. Of these, 10(3.25%) patients were found to have right heart ventricular dysfunction with no previous echocardiographic documented right ventricular dysfunction. Their mean age was  $37.21 \pm 6.26$  years, of them, 6(60%) were males and 4(40%) females. Mean RVSP 24 hours post PTMC was  $63 \pm 10.21 \text{ mm of Hg}$ , mean LA diameter  $5.18 \pm 1.82 \text{ cm}$  and mean LVEF  $50.14\% \pm 5.82$ .

**Conclusion:** Patients with severe mitral stenosis who were older and who had higher right ventricular systolic pressure were more prone to develop right ventricular failure in spite of successful PTMC.

**Key Words:** Right Ventricular Dysfunction, Mitral Stenosis, PTMC

## INTRODUCTION

The mitral valve is the most frequently affected valve in rheumatic heart disease. It is solely affected in 25% and is affected with other valves in 40% of patients.<sup>1</sup>

Mitral stenosis can lead to enlargement of the left atrium leading to increased risk of thrombus formation.<sup>2</sup> In the last two decades; percutaneous transluminal mitral commissurotomy (PTMC) has become the treatment of choice for patients with symptomatic rheumatic mitral stenosis (MS). Since its introduction in 1984 by Inoue et al, PTMC by Inoue technique has been widely used in the treatment of mitral stenosis. Several studies have reported good immediate, short-term and long-term results.<sup>3,4</sup>

Left ventricular function in patients with mitral stenosis has been investigated during the last decades. First angiographic studies found higher left ventricular end-systolic volumes and lower ejection fraction in patients with mitral stenosis than in controls.<sup>5,6</sup> Ventriculography showed distorted contraction of the postero-basal segment and occasionally anterior hypokinesis, that was related to the rigidity and immobilization of mitral valve complex, proposed to be due to scarring of the mitral valve complex and fibrosis of the papillary muscle.<sup>5-8</sup> In some angiographic studies, generalized rather than regional LV dysfunction was found in patients with mitral stenosis that was explained by rheumatic myocarditis.<sup>9</sup> Low ejection performance indexes could be often found in mitral stenosis and were related to altered loading conditions.<sup>10</sup>

In patients with rheumatic mitral stenosis, right ventricular function is important in the development of patient symptoms, as well as it affects the prognosis. Right ventricular dysfunction in this category of patient may result from direct affection of the myocardium by the rheumatic process or secondary to hemodynamic alterations due to pulmonary vascular changes which lead to RV overload and failure.<sup>11,12</sup> A histo-morphological study discovered lesions in intramyocardial coronary branches in the form of active rheumatic vasculitis, and was supposed to be a possible cause of RV dysfunction.<sup>13</sup> The impaired RV function may improve to some extent over time after successful balloon mitral valvuloplasty.<sup>14,15</sup>

Rheumatic mitral stenosis is one of the commonest valvular heart lesions in developing countries. There is an observation that patients develop signs and symptoms of right ventricular failure in spite of successful PTMC. Since rheumatic heart affection is more severe and the degree of valvular damage is greater in developing countries than in industrialized Western communities, it seems appropriate to examine the frequency, extent and progression of right ventricular dysfunction in our patients.

## METHODOLOGY

This observational study was conducted from January 2011 to December 2014 in Cardiology Department of Lady Reading Hospital Peshawar. Patients with severe isolated mitral stenosis undergone successful percutaneous transluminal mitral commissurotomy (PTMC) were included by non probability consecutive technique and were evaluated first with transthoracic echocardiography (TTE) and then with transesophageal echocardiography (TEE) at echocardiography suite of Lady Reading Hospital Peshawar before PTMC and 24 hours after PTMC. Transthoracic Echocardiography had been used in this study for measurements of cardiac chamber dimensions and for the assessment of left ventricular performance. Severe mitral stenosis was defined by echocardiographic criteria as associated with mean transvalvular gradient of more than 10 mm of Hg, pulmonary artery pressures of more than 50 mm of Hg and a valve area of less than 1 cm<sup>2</sup>.

Transthoracic echocardiography was performed by a standard technique using Toshiba Xario 2100 and Philips D H 11 echocardiographic machines pre and 24 hour post PTMC. M-mode measurements were recorded according to American Society of Echocardiography criteria.<sup>16</sup> The mitral valve area was measured by continuous wave Doppler using the pressure half time method. The mean transmitral diastolic pressure was estimated from the maximal transmitral flow velocity using a modified Bernoulli equation. LA diameter was taken in the parasternal long axis view in M-mode at end systole. Measurements were taken in three beats in patients with normal sinus rhythm and in ten beats in atrial fibrillation and the mean values were taken for analysis. Assessment of left ventricular performance was performed using Simpson method. TTE was repeated 24 hours after PTMC to know about the successful PTMC.

All the patients with Diabetes, hypertension, suboptimal PTMC, mitral regurgitation more than grade 1, Aortic regurgitation more than grade 1, ECG evidence of Coronary artery disease or any echocardiographic evidence of ischemia / segmental wall motion abnormalities or Left Ventricle ejection fraction (LVEF) <50% were excluded from the study. Patients with suspected peripartum cardiomyopathy were also excluded from the study. The demographic, clinical and echocardiographic variables were entering through a specially designed proforma.

Optimal PTMC was defined as post PTMC mitral valve area of  $\geq 1.5\text{cm}^2$  or at least 25 % increase in valve area with no more than one grade increase in MR and with no major complication. All these patients were then followed for one year for any symptoms of right ventricular failure including easy fatigability, exercise intolerance, raised jugular venous pulsation (JVP), abdominal distension, hepatomegaly and pedal edema. These patients with right ventricular failure

signs and symptoms were then subjected to detailed transthoracic echocardiography including Right ventricular function assessment by TAPSE.

All the data were analyzed by SPSS (Statistical Package for Social Sciences) Version 19.0 for Windows. Categorical variables were expressed as numbers and percentages while continuous variables were expressed as mean  $\pm$  SD (Standard deviations).

## RESULTS

A total of 307 patients with severe isolated mitral stenosis who underwent successful PTMC were studied. Females were 185 (60.26%) and males 122 (39.74%). Their mean age was  $26.44 \pm 7.26$  years. Transthoracic Echocardiography (TTE) performed before PTMC showed mean mitral valve area  $0.9 \text{ cm}^2 \pm 0.24 \text{ cm}^2$ , mean mitral valve gradient  $22.1 \pm 16.8$  mm of Hg and mean left atrial diameter  $4.72 \pm 2.4$  cm. Atrial fibrillation was found in 119 (38.76%). Mean right ventricular systolic pressure (RVSP) was  $49.67 \pm 13.41$  mm of Hg. TTE 24 hours after PTMC shows mean left atrial diameter of  $4.68 \pm 3.1$  cm, mean mitral valve area of  $1.67 \pm 0.71 \text{ cm}^2$ , mean mitral valve gradient of  $5.42 \pm 4.6$  mm of Hg, mean RVSP  $43 \pm 18.41$  mm of Hg and mean LV ejection fraction was  $57.23 \pm 8.32\%$  as shown in table 1. After follow up for one year, 27 (8.79%) patients developed signs and symptoms of congestive heart failure including easy fatigability, exercise intolerance, raised JVP,

abdominal distension and bipedal edema. Of these 10 (3.25%) patients found to have right heart failure on detailed transthoracic echocardiography. Mean TAPSE among these 10 patient was  $11.56 \pm 3.2$  mm. The mean age of these 10 patients were  $37.21 \pm 6.26$  years. Of them, 6 (60%) were males and 4 (40%) females. Atrial fibrillation was found in 4 (40%). Pre PTMC TTE showed mean mitral valve area  $0.81 \pm 0.21 \text{ cm}^2$ , mean mitral valve gradient  $27.1 \pm 10.8$  mm of Hg, mean left atrial diameter  $5.18 \pm 1.82$  cm and mean RVSP  $65.27 \pm 10.46$  mm of Hg. TTE 24 hours post PTMC showed mean RVSP  $63 \pm 10.21$  mm of Hg, mean Left atrial diameter  $5.18 \pm 1.82$  cm, mean mitral valve area  $1.7 \pm 0.51 \text{ cm}^2$  and mean LVEF  $50.14 \pm 5.82\%$  as shown in table 2.

## DISCUSSION

We performed this observational study to know the true incidence of progressive right ventricular failure in spite of successful PTMC. All the patients were followed after successful PTMC for signs & symptoms of right ventricular failure for one year. Patients found to have congestive heart failure signs and symptoms were then subjected to detailed transthoracic echocardiography including right ventricular function assessment by TAPSE. About half of the patients with right ventricular failure signs and symptoms have true right ventricular failure by TAPSE i.e. 3.25% of all the patients who undergone successful PTMC. These 3.25% were having no residual mitral stenosis or mitral regurgitation. Their left ventricular functions were normal. They have no evidence of myocarditis or any evidence of pulmonary embolism. They have also no evidence of pulmonary pathologies leading to secondary right ventricular failure as

**Table 1: Baseline Characteristics of Study Population with Successful PTMC**

Characteristics	Numbers	Percentage (%)
Age	$26.44 \pm 7.26$ years	
Males	122	39.74%
Females	185	60.26%
Pre PTMC mitral valve area	$0.9 \text{ cm}^2 \pm 0.24 \text{ cm}^2$	
Post PTMC mitral valve area	$1.67 \pm 0.71 \text{ cm}^2$	
Pre PTMC RVSP	$49.67 \pm 13.41$ mm of Hg	
Post PTMC RVSP	$43 \pm 18.41$ mm of Hg	
Atrial fibrillation	119	38.76%
LV ejection fraction	$57.23 \pm 8.32\%$	
LA diameter	$4.72 \pm 2.4$ cm	
Pre PTMC mitral valve gradient	$22.1 \pm 16.8$ mm of Hg	
Post PTMC mitral valve gradient	$5.42 \pm 4.6$ mm of Hg	
Signs & symptoms of congestive heart failure	27	8.79%
Right ventricular failure by TAPSE	10	3.25%

**Table 2: Patients with Right Ventricular Dysfunction Baseline Characteristics**

Characteristics	Numbers	Percentage (%)
Age	$37.21 \pm 6.26$ years	
Males	6	60%
Females	4	40%
Mean TAPSE	$11.56 \pm 3.2$ mm	
Atrial fibrillation	4	40%
Pre PTMC Mean mitral valve area	$0.81 \pm 0.21 \text{ cm}^2$	
Pre PTMC Mean mitral valve gradient	$27.1 \pm 10.8$ mm of Hg	
Pre & post PTMC left atrial diameter	$5.18 \pm 1.82$ cm	
Pre PTMC mean RVSP	$65.27 \pm 10.46$ mm of Hg	
Post PTMC Mean mitral valve area	$1.7 \pm 0.51 \text{ cm}^2$	
Post PTMC Mean RVSP	$63 \pm 10.21$ mm of Hg	
LV ejection fraction	$50.14 \pm 5.82\%$	

the exclusion criteria were strictly followed. There is very scant DATA regarding right ventricular failure after successful PTMC. In agreement with the previous studies there were very fewer patients whose right ventricular function fall inspite of successful PTMC.<sup>17, 18</sup> Although most of these studies on RV function does not directly focus on worsening of right ventricular functions inspite of successful PTMC, but provides indirect clues, that in some of the patients RV functions either remain same or decline inspite of successful interventions. To our knowledge this is the first study of its kind which directly focuses on the frequency of right ventricular failure inspite of successful PTMC. Inspite of RV failure their left ventricular functions remained normal and also have no more than mild Mitral stenosis. The other observation was that these patients have significantly older age than overall study population i.e  $37.21 \pm 6.26$  years vs.  $26.44 \pm 7.26$  years and there were more males than females i.e. 60% vs. 40%, but these patients were only 10(3.25%), so we may not be able to generalize this observation. This study provides new insight for future researcher on this subject to study patients with progressive RV failure inspite of successful intervention and its demography. In a study by Hamdy up to 61.54% of patients normalized their RV systolic function after successful PTMC.<sup>17</sup> The rest of patients may have either static RV dysfunction or having progressive decline.<sup>17</sup> In the same direction of our results, Mohan et al, found that in spite of the significant drop of pulmonary pressure after successful valvuloplasty, the immediate improvement in RV systolic function was not clear, and about 65% of patients improved within one year duration and their RV systolic function returned to normal values.<sup>18</sup> So in these studies there was significant number of patients whose right ventricular function was not improved making ground for our observational study. In this study by Mohan et al, they studied 25 consecutive patients with isolated rheumatic mitral stenosis before, immediately after (mean,  $40 \pm 12$  h) and at a mean follow-up of 11.5 months after PTMC. Despite successful PTMC, right ventricular isovolumic indices remain abnormal during mid-term follow-up, although global function tends to normalize in two-thirds of the patients.<sup>18</sup>

Exercise intolerance and fatigue are common symptoms in mitral stenosis patients. Increased left atrium (LA) pressure and pulmonary venous hypertension are not the solely responsible factors for these symptoms.<sup>19</sup> Right ventricular (RV) function plays an important role in the development of clinical symptoms, exercise capacity, prognosis, and survival in patients having MS.<sup>20, 21</sup> Impaired Right ventricle function secondary to chronic pulmonary hypertension, is accepted as an undesired and important result of mitral stenosis. The effect of successful PTMC on global RV functions in patients with rheumatic MS has not been well defined. Echocardiography, radionuclide ventriculography, Tissue Doppler imaging (TDI) and magnetic resonance

imaging (MRI) are the methods that are used to evaluate RV functions. Conventional 2-D echocardiography and TDI are potentially appropriate non-invasive techniques and are also less expensive.<sup>22</sup> Because of the ventricle's complex trapezoidal anatomy, the quantitative echocardiographic assessment of RV function is difficult. Conventional M-mode, Doppler echocardiography evaluation, and TDI echocardiography, which is used to evaluate LV &RV functions, are preferred because they are less affected by physiologic changes in flow velocities and indicate subclinical functional effects. In the case of systolic dysfunction, isovolumetric contraction time increases, whereas ejection time decreases. MPI (Tei index), which is calculated using these three indices of time, is a reliable parameter evaluating both systolic and diastolic functions.<sup>23</sup> Despite of some limitations, TAPSE, which can be performed using echocardiography, can be readily used in daily practice. The comparative studies on the right ventricle have shown that TAPSE is correlated with MRI and radionuclide ventriculography.<sup>24-26</sup> Because of our limited resources and usefulness of TAPSE in literature; we used this technique to study right ventricular function in our patients. RV function is an important determinant of clinical signs & symptoms, exercise capacity, and survival in patients with MS. RV is sensitive to changes in afterload because of smaller mass and higher wall stress.<sup>27</sup> It was surprising to the researchers that the pulmonary artery pressure decreased after PTMC and this decrease reached the basal level at the 1-year follow-up.<sup>28</sup> So that is why we follow our study population for one year to see for any progression of RV failure inspite of successful PTMC. We have excluded all these confounders i.e. restenosis, new onset AF in patients with previous normal sinus rhythm and worsening Mitral regurgitation. It may be that the irreversible changes in the pulmonary vascular bed in the group with pulmonary hypertension presented a pseudo improvement for a given time due to the decreased post-PTMC after load.<sup>28</sup> The study by Mahfouz et al, analyzed the longterm effect of pulmonary artery stiffness on right ventricular functions and tricuspid regurgitation.<sup>29</sup> Based on the evaluations before, immediately after, and at 6 months and 12 months after the procedure, the investigator demonstrated that the pulmonary artery stiffness was significantly lower in the patients who had permanent improvement in right ventricular functions and regression in tricuspid regurgitation. The investigator argued that the tricuspid regurgitation and the continued right ventricular dysfunction in some patients, even though a sufficient mitral valve area opening could be ensured after PTMC, may be the increased pulmonary artery stiffness in this patient group, and highlighted the importance of early intervention. In the present study, the recovery of RV functions decreased in the mid-term, and disappeared at the end of the first year (an increase in the RV, Tei index, and pulmonary arterial pressure, and a reduction in TAPSE). Although similar

results were achieved in the group with pulmonary hypertension, the improved right ventricular functions occurred in the acute period in the group without pulmonary hypertension were maintained at 1 year. This is explained by myocardial dysfunction secondary to the rheumatic process, directly affecting RV myocardium or high wall stress due to ventricular dilatation.<sup>30</sup> Malhotra et al, in a histomorphological study of cases of rheumatic heart disease, found that intra myocardial branches of myocardial vessels were also involved in a form of active rheumatic vasculitis or inactive lesions characterized by medial hypertrophy and replacement fibrosis.<sup>13</sup> They speculated that these changes might affect myocardial function. It was shown by Drighil A et.al in their study that there was right ventricular fractional shortening and improvement in systolic functions, as assessed by the Tei index, after balloon valvuloplasty in the patients with mitral stenosis, whereas a decrease was observed in the right ventricular contraction, as assessed by IVA which is an advance and accurate measure of right ventricular function assessment.<sup>31</sup> No observed improvement in right ventricular function despite the improved hemodynamic status suggests irreversible myocardial damage due to rheumatic pathology or long-lasting hemodynamic burden in these patients which causes irreversible changes in pulmonary vasculatures or right ventricular myocardium. Arat et al, evaluated the RV functions in the early (first 48 hours) and mid-(3rd month) term after PTMC, and did not observe a significant difference in the Tei index.<sup>24</sup> The authors determined that the RV functions significantly increased in the early period in the group without pulmonary hypertension, and maintained its high level in the mid-term. Mahfouz et al, determined a significant decrease in the pulmonary arterial pressure and a significant increase in TAPSE in the post-PTMC evaluation.<sup>32</sup> Despite a sustained increase in mitral valve area, some patients showed no regression of TR, and progressive RV dysfunction suggests a significant role of PAS on RV function and the degree of TR regression in patients with MS suggests that PBMV must be performed early, utilizing PAS as a noninvasive parameter for proper timing for PBMV.<sup>32</sup> As demonstrated in these literature findings, during the acute phase and short-term, there is not clear data showing whether the effect of PTMC on RV functions and follow-up studies with larger numbers of patients are needed to assess whether this finding has any prognostic implications. However, same to our case, finding of a decrease in RV contractility, as assessed by IVA, by Drighil A et.al, May be clinically useful in prompting further diagnostic evaluation for patients with MS.<sup>31</sup> although echocardiography is a non-invasive and reproducible method to evaluate cardiac functions, it should be kept in mind that RV function parameters are also not fully independent parameters. Our observational study provides ground for further research on this subject especially in third world countries where rheumatic heart disease is still endemic and we can come

across these situations of unexplained RV failure. Furthermore large histo-pathological randomized control studies are warranted to fully elucidate this phenomenon of progressive right ventricular function decline despite of successful treatment. Detailed Echocardiography including Right ventricular function assessment, showed that frequency of right ventricular failure is 3.5% despite of successful PTMC in severe mitral stenosis patients. And pre PTMC RV functional assessment may be done to look for potential patients with RV dysfunction who may fail to responds to PTMC. Mitral valve surgery or balloon valvotomy should be performed before RV dysfunction, severe TR, or advanced heart failure has occurred.

## LIMITATIONS

One of the limitations of our study is that, this is single-center nonrandomized, and the study population is relatively small. The parameters used to predict RV dysfunction were not independent parameters. MRI and IVA (by echocardiography) which are the best tools for RV function assessment are not used. In the current study, invasive measurements were not made, and RV ejection fraction was not measured. TAPSE was performed in only symptomatic patients with congestive heart failure symptoms after PTMC. No RV functional assessments were done before undergoing PTMC or asymptomatic patients after PTMC. Further larger studies are warranted to see detailed right ventricular performance parameters in patients undergoing PTMC to stratify the patients at high risk of right ventricular failure.

## CONCLUSION

Patients with severe mitral stenosis who were Older and who had higher right ventricular systolic pressure were more prone to develop right ventricular failure in spite of successful PTMC.

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