Original Article

Safety and efficacy of percutaneous balloon mitral valvotomy in severe mitral stenosis with moderate mitral regurgitation – A prospective study

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Background: Percutaneous balloon mitral valvotomy (PBMV) is generally considered as a contraindication in patients with mitral stenosis (MS) associated with moderate to severe mitral regurgitation (MR). We sought to compare the safety and efficacy of PBMV in patients with severe MS and with moderate MR with those with less than moderate or no MR.

Materials and methods: Symptomatic patients of MS with mitral valve area \( \leq 1.5 \) \( \text{cm}^2 \) were screened into two groups: Group I with moderate MR and Group II with less than moderate or no MR. Clinical and echocardiographic assessments were done at 24 h, 1 month, and 6 months post-procedure. A treadmill testing was done prior to PBMV and at 6 months.

Primary safety outcome was a composite of cardiovascular death and development of severe MR with or without requirement for mitral valve replacement at 30 days of procedure. Efficacy of the procedure was measured as improvement in functional class, treadmill time, and mitral valve area (MVA) at 6 months.

Results: Seventeen patients with moderate MR and 208 patients with less than moderate MR underwent PBMV. Primary outcome showed no significant difference [RR = 4.87, 95% C.I. = 1.42–16.69]. In Group I patients, improvement in treadmill time was seen in 12 (70.59%), functional class in 13 (76.47%), and MVA in all patients.

Conclusion: In patients having severe MS associated with moderate MR, PBMV may be a safe option and provides sustained symptomatic benefit.

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1. Introduction

Rheumatic heart disease (RHD) remains a major public health problem in India. A survey of secondary care hospitals shows that nearly 30% of cardiac cases are related to RHD. As per WHO estimates, nearly 0.133 million deaths annually were attributable to RHD in the Southeast Asia region. Severe mitral stenosis (MS) is the major cause for hospital admissions and limitations in the functional capacity of patients with RHD. Percutaneous balloon mitral valvotomy (PBMV) is a safe and effective treatment for symptomatic severe MS [mitral valve area (MVA) <1.5 cm²] with favorable valve morphology. Presence of moderate mitral regurgitation (MR) is considered a contraindication to PBMV. It is estimated that around 40% of all patients with RHD have combined MS and MR. A significant proportion of patients with symptomatic severe MS have associated moderate MR. These patients are referred for mitral valve replacement (MVR), even though they otherwise have no indication for MVR, exposing them to surgical risk and long-term risks of anticoagulation and infective endocarditis. Preserving the native valve with relief of obstruction is an attractive option for this subset of patients.

2. Aims and objectives

We hypothesized that symptomatic patients with severe MS and associated moderate MR can be safely subjected to PBMV...
without increased mortality or need for urgent MVR and can have significant symptom alleviation.

The primary aim was to examine whether the composite of cardiovascular death and severe MR with or without requirement of MVR in patients undergoing PBMV for severe MS was significantly different in those having associated moderate MR as compared to those with mild or no MR. The secondary aim was to see whether patients undergoing PBMV for MS and associated moderate MR had improvement in their functional status and MVA after the procedure and had sustained symptomatic benefit at 6 months.

3. Patients and methods

Our study was a prospective cohort study approved by the Institutional Ethics Committee. Consecutive patients with symptomatic severe MS [2D-MVA < 1.5 cm²] were screened. These patients were evaluated clinically by transthoracic echocardiography [TTE] and transesophageal echocardiography [TEE] for the presence and severity of associated MR and suitability for PBMV. Patients with severe MR, valves with unsuitable morphology (patients with Wilkins score > 12 and those with heavy mitral valve calcification as judged by echocardiography and/or fluoroscopy), left atrial clot, requiring cardiac surgery for other indications, and those who refused to give consent were excluded. We divided patients with suitable morphology for PBMV into two groups depending on the severity of MR: Group I included patients with moderate MR and Group II included patients with less than moderate MR or no MR. Patients with moderate MR were given the option of either MVR or a high-risk PBMV under MVR backup. Patients opting for PBMV were enrolled in the study after informed consent.

We performed TTE and TEE reevaluations prior to PBMV in all patients. The following parameters were reassessed: 2D-MVA, mitral diastolic gradients, extent of mitral valve calcium, extent of subvalvular pathology, and MR jet characteristics – width of vena contracta (VC), effective regurgitant orifice area (EROA), regurgitant volume (R Vol.), and regurgitant fraction (RF). A treadmill testing (TMT) using Bruce protocol was done prior to PBMV for functional assessment of the patient.

We performed coronary angiogram just prior to PBMV. Left ventricular angiogram was done just prior to and immediately after PBMV to assess the degree of MR. Pulmonary artery (PA) pressures and pulmonary capillary wedge pressures were also taken prior to the procedure.

We did PBMV following standard technique.5 Pressure gradient across the mitral valve was measured by simultaneous pressure recordings in left atrium and left ventricle. Valvotomy was done using single balloon technique using PBMV balloon (PBMV balloon catheter set, Shenzhen Shineyard Medical Device Co Ltd., Shenzhen, China). Sizing of the balloon was done using Hung’s formula6 [patient’s height in cm is rounded to nearest zero and divided by 10, and 10 is added to the ratio to yield the reference size in mm]. Initial dilatation was done using a size 1 mm less than the calculated balloon size. The need for subsequent dilatation was assessed by the operator on the basis of echocardiography and clinical examination. The reason for repeat dilatation and size of balloon was noted. Pulmonary artery pressure was measured soon after the procedure in addition to valve gradient.

Clinical and echocardiographic assessment was done within 24 h, at 1 month, and at 6 months post-procedure in Group I. Symptom status (based on New York Heart Association (NYHA) functional class) was noted and TMT was done at 6 months post-procedure for objective assessment of functional status. The primary outcome measured was a composite of cardiovascular death within 30 days of procedure, MVR within 30 days for severe MR intractable to medical management, and development of severe MR [not undergoing urgent MVR]. The secondary outcome measured was the improvement in the treadmill time (in min), NYHA functional class, and in 2D-MVA at 6 months.

3.1. Definitions

We defined severe MS as MVA < 1.5 cm². Moderate MR described MR jet with any one of the following features: VC 0.3–0.69 cm, EROA 0.20–0.39 cm², R Vol. 30–59 > 0.70 cm, EROA > 0.40 cm², R Vol. > 60 ml/beat, and RF > 50% constituted severe MR. Satisfactory improvement in MVA was defined as more than 50% of baseline value or valve area greater than 1.5 cm².

3.2. Statistical analysis

We used IBM SPSS software (IBM SPSS Statistics for Windows, Version 20.0, Armonk, NY: IBM Corp. released 2011) for the statistical analysis. Baseline characteristics between the two groups were compared using Pearson chi-square test for significance. The composite of primary end points was calculated and compared between the two groups by Pearson chi-square test with Yates’s correction for significance. The relative risk for developing severe MR was also calculated. Secondary end points were measured in the group with preexisting moderate MR and compared using Student’s paired t test. The average improvement in the TMT time was noted. The average improvement in MVA of each patient was calculated and improvement in NYHA functional class noted. Also the degree of MR as assessed by the echocardiographic parameters [VC, EROA, R Vol., and RF] was compared between pre-BMV at 24 h after PBMV and at 6 months. A p-value of < 0.05 was taken to be significant.

4. Results

4.1. Baseline characteristics

The study period was between February 2012 and May 2013. Fig. 1 depicts the exclusions and the final sample. There were 17 patients in Group I and 208 in Group II. Both groups were comparable with respect to baseline characteristics, as shown in Table 1. The median Wilkins score of Group I was 7 (range 6–12).

4.2. Safety of PBMV in MS with moderate MR

All 17 patients in Group I underwent PBMV. The preprocedure and immediate post-procedure MVA were 0.886 (0.16) and 1.7 (0.28), respectively. The Mean (SD) PA systolic pressure soon after the procedure was 42.3 (12.5) mmHg. The primary outcomes at 1 month are as depicted in Table 2.

Overall, there were 2 instances of severe MR in Group I and 8 in Group II. Those in Group I who developed severe MR had Wilkins score of 12 and 11. There was one death at 30 days of PBMV, which occurred in Group II. This patient developed acute severe MR due to anterior mitral leaflet (AML) tear with severe hypotension and arterial oxygen desaturation, and died while being shifted for an emergency MVR. All patients who developed severe MR after BMV were counseled and posted for urgent or elective MVR. Three patients in Group II developed symptomatic severe MR, and underwent emergency MVR. Two patients in Group I and four patients of Group II who developed severe MR declined surgical correction and were medically managed. None of them died during the 30-day follow-up; one of these patients from Group I died after 3 months. The relative risk of developing severe MR was greater in patients with preexisting moderate MR [RR = 4.87, 95% CI = 1.42–16.69]. The composite of primary events was not statistically
Patients with severe MS and moderate MR during the period - 26

- Patients with Wilkins score >12 – 4
- Patients with score >12 and heavy calcification – 2
- Patients with heavy valve calcification - 1
  - Total - 7

Patients who refused to consent - 2

Excluded

Number of patients included in the study - 17

Fig. 1. Flow chart showing selection of patients in Group I.

Table 1
Baseline characteristics.

| Parameter                                      | Group I [n = 17] | Group II [n = 208] | p value  |
|------------------------------------------------|------------------|---------------------|----------|
| Age, years, mean (SD)                         | 46.2 (10.8)      | 41.0 (11.6)         | p = 0.076 |
| Women (%)                                      | 88.2%            | 75%                 | p = 0.498 |
| NYHA class (%)                                 |                  |                     |          |
| Class III                                      | 76.5             | 77.2                | p = 0.521 |
| Class IV                                       | 23.5             | 22.8                |          |
| Pulmonary artery systolic pressure, mmHg, mean (SD) | 47.7 (15.8)      | 42.5 (17.4)         | p = 0.345 |
| Presence of atrial fibrillation (%)            | 76%              | 71%                 | p = 0.323 |
| Mean mitral gradients by echo, mean (SD)       | 13.4 (2.3)       | 12.9 (2.5)          | p = 0.723 |
| 2-D MVA, cm², mean (SD)                       | 0.886 (0.16)     | 0.875 (0.18)        | p = 0.808 |
| Site of calcium, n (%)                         |                  |                     |          |
| Nil                                           | 10 (58.8%)       | 147 (70.7%)         | p = 0.099 |
| Unicommissural                                 | 2 (11.8%)        | 13 (6.2%)           |          |
| Bicommissural                                  | 1 (5.9%)         | 10 (4.8%)           |          |
| Leaflet                                       | 4 (23.5%)        | 38 (18.3%)          |          |
| Subvalvular pathology [as n (%)]               |                  |                     |          |
| Nil                                           | 0                | 43 (20.7%)          | p = 0.073 |
| Mild                                          | 11 (64.7%)       | 106 (51%)           |          |
| Moderate                                      | 5 (29.4%)        | 57 (27.4%)          |          |
| Severe                                        | 1 (5.9%)         | 2 (1%)              |          |

Table 2
Primary outcomes.

|                  | Group I [n = 17] | Group II [n = 208] | p value  |
|------------------|------------------|---------------------|----------|
| CV death within 30 days | 0                | 1 (0.48%)           | p = 0.1  |
| MVR for severe MR within 30 days | 0                | 3 (1.44%)           | p = 0.54 |
| Severe MR who did not undergo MVR          | 2 (11.76%)       | 4 (1.92%)           | RR = 5.87 (95% CI = 1.42–16.69) |
| Composite | 2 (11.76%)       | 8 (3.85%)           | p = 0.36 |

Different between the two groups [Group I – 2 (11.76%) and Group II – 8 (3.85%), p = 0.36].

4.3. Efficacy of PBMV in MS with moderate MR

Five patients in Group I could not undergo TMT due to musculoskeletal impairment. All other patients showed significant improvement in treadmill time after PBMV. Thirteen patients (76.47%) showed improvement in their NYHA functional class. Out of the 13 patients who were class III, 11 improved to class I and 2 patients with asthma remained class III. Out of the 4 patients who were class IV, 2 developed severe MR and remained class IV; 1 patient improved to class III and one to class II. All patients had significant improvement in their 2D-MVA with a percentage change of 86.5% in the valve area (Table 3).

In patients with Group I, the degree of mitral regurgitation was assessed via various echocardiographic criteria. There was a significant increase in moderate MR post-procedure in all patients, as shown in Table 4. Only two patients had values in the range of severe MR. There was no increase in values at 180 days compared to the immediate post-procedure values.

5. Discussion

Our study compared the safety and efficacy of performing PBMV in patients with severe MS associated with moderate MR.
with those having less than moderate MR or no MR. The study showed that the composite of CV death and occurrence of severe MR, with or without requirement of urgent MVR at 1 month, was not different from those with less than moderate MR. Significantly, higher proportion of patients developed severe MR in the group with moderate MR. None of the patients in the group with moderate MR had requirement for urgent MVR whereas 3 patients in the other group had the operation; the number of patients with moderate MR was not sufficient to make this comparison though. The efficacy of PBMV was assessed only in the group with moderate MR and no comparison with the other group was attempted. The efficacy parameters of treadmill time, functional class, and MVA showed improvement in this group at 6 months.

Development of severe MR is a well-recognized complication after PBMV. Previous studies have shown the occurrence of severe MR in patients with preexisting less than moderate or no MR to be in the range of 1.4–9.4%. Many of these cases do not require early MVR as the patients tolerate the complication reasonably well. Among the patients who undergo PBMV, only 1.3–3.2% required urgent MVR due to the development of severe MR. In some cases, the MR severity has shown improvement over time. While in our study the occurrence of severe MR was higher in the group with preexisting moderate MR, none of the patients required MVR during the 1-month follow-up. All these patients were considered for elective MVR, and due to performance of PBMV in these patients, operation could be avoided or at least could be postponed, thus obviating long-term anticoagulation and risk of prosthetic valve endocarditis.

There are only very few studies comparing PBMV in patients with MS and moderate MR with those with less than moderate MR. Zhang et al. performed double balloon mitral valvotomy in 25 patients having symptomatic mitral stenosis with moderate MR and showed that the possibility of developing moderate to severe (3+) MR after balloon dilatation was greater in patients with preexisting moderate MR as compared to 25 matched controls having mild or no MR. In this study, 40% of patients had no increase in MR and another 40% had an actual reduction in MR in the moderate MR group, but 20% developed severe MR. In our study, we found that all patients had an increase in MR but only two (11%) developed severe MR. Lau et al. performed PBMV in 21 patients with moderate MR as compared to 83 patients without moderate MR with Inoue balloon using serial dilation technique. The initial balloon size was much lower than that used in our study; each dilation was followed by hemodynamic and clinical evaluation and balloon size gradually uptitrated if required. The final balloon size was similar to that used in our study. With this technique, there was an increase in MR but no severe MR was reported in the study group. Even though the risk for developing severe MR was greater in the patients with preexisting moderate MR, no excess mortality in these patients was noted immediately after the procedure, which is also reflected in our study. Patients who did not develop severe MR after PBMV had significant symptomatic benefit at 6-month follow-up post-procedure. Even though patients have higher degrees of regurgitation than previously, they tend to tolerate MR better with the improvement in the MS, as evidenced by the higher NYHA functional class and improved treadmill time. All the patients with moderate MR had satisfactory improvement in MVA. Zhang et al. also showed that the improvements in hemodynamics and increases in mitral valve area can be equally achieved using balloon mitral valvotomy for treatment of mitral stenosis in patients with or without moderate MR. Similarly, Lau et al. showed that PBMV in patients with moderate MR produced symptomatic benefit in substantial majority of patients (>90%) even at a mean follow-up of 19–20 months.

It is worth noting that there was no patient with NYHA class II symptoms in Group I. Most of the patients were far advanced in symptoms as they constitute patients who either bear with symptoms for paucity of finances or fear of procedures. The logistic restrictions imposed by resources (the patients and the hospital) also lead to deferring procedures until patients are severely symptomatic. However, there was no difference between Groups I and II in terms of symptomatic status.

The most important limitation of the study was the large difference in the number of patients in the two groups, which made the statistical comparison between the groups less reliable. Although the baseline characteristics between the two groups did not show statistically significant difference, comparison would have been better if matched controls were used. Suitability of valve

### Table 3

Secondary outcomes in Group I.

| Parameter                                | Pre-PBMV [mean (SD)] | 6 months after PBMV | Difference | p value       |
|------------------------------------------|----------------------|---------------------|------------|---------------|
| Treadmill time, min, mean (SD)           | 3.1 (+0.66)          | 7.17 (+2.12)        | 4.07 (+1.61) | p < 0.001, 95% CI = 3.0–5.1 |
| MVA, cm², mean (SD)                      | 0.89 (+0.16)         | 1.62 (+0.31)        | 0.73 (0.28) | p < 0.05      |
| PA systolic pressure, mmHg, mean (SD)    | 47.7 (15.8)          | 37.4 (13.2)         | 10.3 (4.99) | p < 0.05      |
| NYHA class                               |                      |                     |            |               |
| I                                        | 12                   | 1                   |            |               |
| II                                       | 13                   | 4                   |            |               |
| III                                      | 4                    | 2                   |            |               |
| IV                                       | 2                    |                     |            |               |

### Table 4

Evaluation of mitral regurgitation pre- and post-BMV.

| MR parameters | Pre-PBMV [mean (SE)] | Post-PBMV [mean (SE)] | After 6 months [mean (SE)] | Significance |
|---------------|----------------------|-----------------------|-----------------------------|--------------|
| VC (cm)       | 0.376 (0.02)         | 0.567 (0.02)          | 0.557 (0.02)                | p1 < 0.001   |
| EROA (cm²)    | 0.271 (0.01)         | 0.345 (0.01)          | 0.344 (0.01)                | p2 = 0.248   |
| R Vol. (ml)   | 39.1 (1.0)           | 51.4 (1.69)           | 51.2 (1.78)                 | p1 = 0.001   |
| RF (%)        | 36.5 (0.83)          | 43.2 (0.67)           | 43 (0.70)                   | p1 = 0.001,  p2 = 0.90 |

* p1 = significance between pre-BMV and immediate post-BMV values; p2 = significance between immediate post-BMV and values at 6 months.
undergoing PBMV was operator-dependent and no definite scoring system was used to identify the valve most suitable in this subset of patients.

6. Conclusion

Our study is one of the few studies looking at the safety and efficacy of PBMV in patients with MS and moderate MR. It compared the safety outcomes in MS patients with or without moderate MR undergoing PBMV and showed that the composite of CV death and development of MR is not significantly higher in patients with moderate MR. Sustained symptomatic benefit [of up to 6 months] and an improved functional status can be achieved by PBMV in this subset of patients. Though MVR currently remains the treatment of choice in this subgroup of patients, our study shows that in suitably selected patients, PBMV with a MVR backup may be offered safely. However, being a small pilot study, it has some limitations and the conclusions should be viewed with caution. Larger methodologically sound studies enrolling more patients are needed to draw definitive conclusions.

Conflicts of interest

The authors have none to declare.

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