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Original Article

Predictors of the Development of Significant Mitral Regurgitation Following Repeated Percutaneous Balloon Mitral Valvuloplasty in Middle-Aged and Elderly Patients

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ABSTRACT

Background: We aimed to identify the predictor of developing significant mitral regurgitation (MR) after repeated percutaneous balloon mitral valvuloplasty (PBMV) via the Inoue Balloon Technique in middle-aged and elderly patients.

Methods: This prospective study was performed on 40 patients presenting to the cardiology department with severe symptomatic mitral restenosis following previous PBMV via the Inoue Balloon Technique. Informed written consent was obtained from all the patients. MR was evaluated before and after PBMV and subsequently at short-term follow-up.

Results: The study population was aged above 45 years. The 40 patients recruited were divided into 2 main groups: Group A comprised 28 patients who did not develop an increase in the grade of MR at follow-up and Group B consisted of 12 patients who developed at least a 1-grade increase in MR at follow-up. The results were compared before, after, and at short-term follow-up between the 2 study groups. The forward stepwise logistic regression analysis identified the presence of preprocedural Grade I MR as the most important independent predictor of the development of MR after PBMV (P = 0.01). No significant difference was observed between the study groups concerning symptomatic and hemodynamic improvements after PBMV.

Conclusions: The presence of preprocedural Grade I MR may be the most independent predictor of a rise in the MR grade following repeated PBMV in middle-aged and elderly patients.
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KEYWORDS: Mitral stenosis, Mitral commissurotomy, Mitral restenosis

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Rheumatic heart disease is endemic in developing countries, including Middle East countries. [1] There are more than 517 000 deaths each year due to severe Group A streptococcus diseases such as acute rheumatic fever, rheumatic heart disease, post-streptococcal glomerulonephritis, and invasive infections. The rate of severe Group A streptococcus disease prevalence is about 18 million cases, with about 2 million new cases every year. The prevalence of rheumatic heart disease is almost 15.6 million, with 282 000 new cases and about 233 000 mortalities every year. [1] The mitral valve is the structure most profoundly affected by fibrotic lesions, leading to mitral valve regurgitation (MR) and

mitral valve stenosis. Since Inoue et al [2] introduced percutaneous valvuloplasty in 1984, this procedure has become the management of choice in many patients with mitral stenosis. Many patients undergo percutaneous balloon mitral valvuloplasty (PBMV) for rheumatic mitral valve stenosis with favorable valvular morphology as an alternative to surgical treatment with a success rate of 93% and a low incidence rate of complications and postoperative infections by comparison with closed mitral commissurotomy. [3, 4] Despite the high technical expertise in PBMV, MR remains a major technical-related complication. [5] Many studies on the different techniques of PBMV have identified the mitral valve morphology as a predictive factor for the immediate outcome. Nonetheless, global echocardiographic anatomical classifications have some limitations. [6]

In the current study, we aimed to identify the most important predictors of the development of significant MR after repeated PBMV via the Inoue Balloon Technique in middle-aged and elderly patients.

METHODS

The present prospective study was conducted on 40 patients presenting to the Cardiology Department of Benisuef University Hospital with severe symptomatic mitral restenosis following previous PBMV via the Inoue Balloon Technique between April 2014 and May 2017. The study aimed to evaluate the degree of change in MR after PBMV via the Inoue Balloon Technique. The study protocol was approved by the Committee of Research and Medical Ethics of the Cardiology Department of Benisuef University in March 2013. Informed written consent was obtained from all the patients. Preprocedural assessments were carried out in the cardiology outpatient clinic. The inclusion criteria were comprised of symptomatic mitral restenosis following previous PBMV via the Inoue Balloon Technique, New York Heart Association functional classes (NYHA FC) of II/IV, a minimum age of 45 years, a mitral valve area (MVA) of 1.5 cm^2 or less, and a mitral valve echocardiographic score of 11 or less according to the scoring system described by Wilkins et al. [7]

Patients were excluded if they had left atrial (LA) thrombi in transesophageal echocardiography, severe MR or severe aortic regurgitation of Grade III or Grade IV, and a mitral valve echocardiographic score of greater than 11.

A comprehensive history was taken from all the patients with an emphasis on NYHA FC. Acute-phase reactants, including the erythrocyte sedimentation rate (ESR) and the total leucocyte count (TLC), were measured within 24 hours before the procedure. A 12-lead electrocardiogram was obtained from all the patients to detect the rhythm within 12 hours before the procedure. Transthoracic echocardiography was carried out for all the patients within a week before the intervention, 1 day after the procedure, and 3 months after the procedure. Additionally, transesophageal echocardiography was performed for all the patients within 24 hours before the intervention to exclude LA thrombi, to measure interatrial septal thickening, and to reassess the transthoracic echocardiographic data. An invasive hemodynamic study, consisting of pre-dilatation and early post-dilatation assessments of LA pressure, was also done. Further, detailed conventional M-mode and 2D transthoracic echocardiographic and Doppler studies were performed using standard views following the recommendations of the European Association of Cardiovascular Imaging [8] with a commercially available GE Vivid S5 imaging system, equipped with a 2-4 MHZ transducer and harmonic imaging to optimize endocardial border visualization. A single echocardiographer performed all the studies, and another expert echocardiographer

reassessed the patients. The severity of mitral stenosis was assessed through the measurement of MVA, the estimation of the mean transmitral pressure gradient, and the systolic pulmonary artery pressure. All the echo-Doppler studies were done while the heart rate was 60 to 70 beats per minute. MVA was measured by direct planimetry and the pressure half time method. The gradient was calculated by the software using the modified Bernoulli equation. [9] The systolic pulmonary artery pressure was measured when a tricuspid regurgitation signal was obtained. The severity of MR was determined before and after PBMV and subsequently at 3 months' follow-up through the calculation of the ratio of the maximal jet area to the left atrial area (LAA) using color flow mapping. The MR severity was graded from I to IV, as is shown in Table 1, according to the recommendations regarding echocardiography in Braunwald's Heart Disease, 7th edition. [10] The patients were divided into 2 groups according to the new appearance or the increase in MR severity after PBMV in the follow-up period: Group A was comprised of patients who did not develop an increase in the MR grade following PBMV and Group B consisted of patients who developed an increase in the grade of MR in comparison with its pre-PBMV grade.

The mitral valve morphology was studied using 2 different scoring systems. The first scoring system was the Massachusetts General Hospital score by Wilkins et al. [7] Four variables, namely leaflet thickness, leaflet calcification, leaflet mobility, and subvalvular apparatus involvement, were evaluated on a scale of 1 to 4 (maximum total score = 16). Patients with a Wilkins Score of greater than 11 were excluded. The second scoring system was the commissural score, introduced by Sutaria et al. [11] The extent of commissural calcification was quantified by giving each half commissure with such echoes a score of 1. Commissural calcification could, therefore, range from Grade 0 to Grade IV. Selected patients received diazepam (10 mg orally), an intravenous antihistaminic agent, and an intravenous antiemetic drug to stop anticoagulation (if present) 5 days before the procedure and bridge with low-molecular-weight heparin. For at least 8 hours before the procedure, the patients avoided eating or drinking. The appropriate balloon size was selected using the equation: balloon size = ([height in cm/10] +10). [12] A 6-F sheath was inserted in the right femoral vein for the trans-septal access. A pigtail (or multipurpose) catheter was advanced to the aortic valve, and the aortic pressure was monitored. The plane of the atrial septum runs from 1 to 7 o'clock as viewed from the feet with the patient lying supine. The fossa ovalis is posterior and caudal to the aortic root. Consequently, a pigtail (or multipurpose) catheter was advanced to the aortic valve to be a landmark for trans-septal catheterization. The Brockenbrough needle was advanced through the Mullins sheath and the dilator until its tip was near the distal aspect of the sheath. A pigtail catheter was employed in the ascending aorta for pressure monitoring and spatial orientation of the aorta. The needle was advanced to the tip of the catheter, and the whole system was then advanced. Successful entry into the LA was confirmed by both recording LA pressure waveforms and withdrawing oxygenated blood. The pre-dilatation mean LA pressure was measured at this stage in our study. Thereafter, the typical fluoroscopic appearance of the LA was visualized during contrast injection through the needle. Once the catheter was placed in the LA, heparin (5000 U) was administered. One of the Inoue balloon sizes of 24, 26, 28, or 30 mm was used. The balloon was flushed with saline and then inflated to the desired size, with every 1 mL in the syringe equaling a 1-mm increase in the balloon. (The balloon size was measured at its waist outside the patient's body using the ruler in the kit.) A stainless

steel guidewire was inserted into the catheter and advanced to form 2 or 3 loops in the LA, and the Mullins sheath was removed. The groin, the femoral vein, and the interatrial septum were dilated using a 14-F dilator. We dilated the Inoue Balloon on the wire and elongated it as much as it was elongated outside the body by advancing the gold hub to the plastic hub and then securing it. The balloon was advanced to the LA, and the guidewire and the inner elongator were removed. The silver and gold elongators were pulled back to the point where the gold elongator stopped the silver hub, and the Inoue Wire was pulled back. The stylet was then inserted. The balloon was maneuvered under fluoroscopic guidance. The stylet was pulled out as the balloon was advanced to the left ventricle across the mitral valve via counterclockwise rotation. The distal portion of the balloon was inflated, and then it was pulled back to ensure stabilization beneath the mitral valve annulus. Inflation occurred next at the level of the proximal part of the balloon, and finally in the central portion, with the disappearance of the central waist at full inflation, indicating that the balloon was anchored at the mitral orifice. The balloon was deflated and withdrawn into the LA. Following the initial inflation and deflation, the patients were examined clinically for auscultatory signs of a rise in MR. Next, echocardiographic measurements of MVA and the regurgitant jet area were repeated. If MR was not increased by more than 1 grade and MVA was less than 1 cm^2/m^2 of the body surface area, mitral valvuloplasty was repeated by increasing the balloon diameter by 1 mm. After the achievement of desirable results, the balloon was withdrawn into the LA, and the stylet was removed. The catheter was connected to measure the mean LA pressure at the end of the procedure. The balloon was then re-elongated in the LA by inserting the wire telescoped through the silver metal elongator to the gold hub. The procedure was ended when there was an adequate increase in the valve area, a decrease in the mitral valve gradient, or an increase in the degree of MR. The definition for good immediate results was a final MVA of larger than 1.5 cm^2 without MR greater than 2+, which we achieved in all our patients. The whole procedure was performed under echocardiographic guidance in all of its stages, and the regurgitant jet area was measured after every instance of balloon inflation.

Table 1: Severity of mitral regurgitation

Grade	Maximal Jet Area: LAA %
I	≤15%
II	15-35%
III	35-50%
IV	>50%

LAA, Left atrial area

Before hospital discharge, all the patients were examined clinically and echocardiographically with a particular emphasis on MVA and MR severity. The patients were asked to return for a follow-up 3 months after PBMV, with a particular emphasis on MVA, MR severity, NYHA FC, the pulmonary artery systolic pressure, the peak transmitral pressure gradient, and the mean transmitral pressure gradient.

The data were presented as numbers (%) or the median and the range (mean + SD), as indicated. The distribution of the qualitative variables was evaluated using the χ^2 test or the Fisher exact test, as appropriate. Clinical improvement was evaluated quantitatively by subtracting the postprocedural NYHA FC from the preprocedural NYHA FC, assigning the numbers 1, 2, 3, and 4 to classes I, II, III, and IV, respectively. The quantitative variables were correlated using the nonparametric Spearman correlation test. They were compared between the study groups with the aid of the nonparametric Mann–Whitney test, the Kruskal–Wallis distribution-free test, or the paired sign or Wilcoxon Signed-rank test, as appropriate.

The statistically significant variables according to the univariate analysis were introduced in a forward stepwise logistic regression model to detect the independent predictors of a postprocedural increase in the MR grade. The statistical analyses were conducted using the SPSS software, version 23. All the tests were bilateral, and the limit of statistical significance was 0.05.

RESULTS

The study population was comprised of 40 patients, 28 (70%) females and 12 (30%) males, aged from 46 to 65 years (mean age = 56.4 ± 9.56 y). Twenty-five patients were in sinus rhythm, and 15 patients had atrial fibrillation. All the patients had rheumatic mitral stenosis with a mean MVA of 0.95 ± 0.2 cm^2, a mean total Wilkins Score of 7.2 ± 1.24, and a mean commissural score of 1.85 ± 0.8. Based on Doppler color flow imaging before the procedure, 17 (42.5%) patients had no MR and 23 (57.5%) had Grades I/IV MR.

Table 2 presents the baseline clinical, laboratory, and echocardiographic data of the study population.

PBMV was completed successfully in all the 40 patients, resulting in a significant increase in MVA (from 0.95 ± 0.2 cm^2 to 2.41 ± 0.33 cm^2; P = 0.001) and a significant decrease in the mean LA pressure (from 27.58 ± 6.91 before PBMV to 15.38 ± 7.15 mm Hg immediately after PBMV; P = 0.001).

The mean LA pressure immediately after the procedure did not differ significantly between Group A and Group B (14.29 ± 7.44 mm Hg vs 17.9 ± 5.93 mm Hg; P = 0.122).

Of the 17 patients who had no MR before PBMV, 8 patients still had no MR, 6 patients developed Grade I MR, and the other 3 developed Grade II MR. From the 23 patients who had Grade I MR before PBMV, 19 patients still had Grade I MR, and the other 4 patients developed Grade II MR. Consequently, the incidence of the overall immediate postprocedural MR (increase or new appearance of MR) was 32.5% (13 patients): 25% (10 patients) had a 1-grade increase and 7.5% (3 patients) developed significant MR (≥ 2-grade increase in the preprocedural MR grade).

Table 2: Clinical, laboratory, and echocardiographic data of the study population

Variable		Value
Age (mean ±SD)		56.4±9.56 y
Gender	Males	12 (30%)
	Females	28 (70%)
NYHA FC	I	0
	II	18 (45%)
	III	21 (52.5%)
	IV	1 (2.5%)
Cardiac Rhythm	Sinus	25 (62.5%)
	AF	15 (37.5%)
		Mean ± SD
Acute-Phase Reactant and Echocardiographic data	ESR 1	24.65±15.47
	ESR 2	44.37±27.84
	TLC	10606±3523
	MVA	0.95±0.2 cm^2
	Wilkins Score	7.2 ±1.24
	Commissural score	1.85±0.8
	MR Grade 0 Grades I/IV	17 (42.5%) 23 (57.5%)
	Peak PG	28.47±6.88 mm Hg
	Mean TMG	17.34±6.23 mm Hg
	PASP	52.13±14.32 mm Hg

*MVA, Mitral valve area; NYHA FC, New York Heart Association functional class; AF, Atrial fibrillation; MR, Mitral regurgitation; Mean TMG, Mean transmitral pressure gradient; PASP, Pulmonary artery systolic pressure; Peak PG, Peak mitral pressure gradient

Table 3: Clinical characteristics of Group A and Group B

GROUP	Group A		Group B	*P*-value
Number	28		12	
Gender	male	8 (28.6%)	4 (33.3%)	0.763
	female	20 (71.4%)	8 (66.7%)	
Age (mean±SD)	56.8±9.7 y		57.9±9.5 y	0.760
Rhythm	sinus rhythm	19 (67.9%)	6 (50%)	0.285
	AF	9 (32.1%)	6 (50%)	
NYHA FC	II	13 (46.4%)	5 (41.7%)	0.302
	III	15 (53.6%)	6 (50%)	
	IV	0	1 (8.3%)	

NYHA FC, New York Heart Association functional class; AF, Atrial fibrillation

Table 4: Acute-phase reactants in Group A and Group B

	Group A	Group B	*P*-value
ESR 1	23.46±16.73	27.42±12.23	0.172
ESR 2	42.24±30.11	49.35±22.01	0.172
TLC	10230.36±3280.11	11482.5±4049.67	0.328

ESR, Erythrocyte sedimentation rate; TLC, Total leucocyte count

Our 40 patients were divided into 2 main groups according to the new appearance or increase in MR severity at 3 months' follow-up as compared with the pre-PBMV grade. Group A consisted of 28 patients who developed no increase in the grade of MR in comparison with the pre-PBMV grade and Group B comprised 12 patients who developed an increase in the grade of MR in comparison with the pre-PBMV grade. The study groups were followed for 3 months according to the following data to determine the predictors and outcomes of the development of or an increase in MR at follow-up: NYHA FC, ESR, TLC, MVA, the peak pressure gradient across the mitral valve, the mean pressure gradient across the mitral valve, the pulmonary artery systolic pressure, the mitral valve scores (the Wilkins scoring system and the commissural scoring system), and MR grades.

Table 3 shows that there were no significant differences between the study groups regarding their baseline clinical characteristics such as gender, age, cardiac rhythm, and NYHA FC.

Before PBMV, there were 18 patients (45% of the total) in NYHA FC II; at follow-up, 17 of them improved to NYHA FC I and only 1 of them remained in FC II. There were 21 patients in NYHA pre-FC III (52.5% of the total); at follow-up, 13 of them improved to NYHA FC I, 7 of them improved to NYHA FC II, and only 1 of them remained in NYHA FC III. Only 1 (2.5% of the total) patient in NYHA pre-FC IV improved to NYHA FC III. At the short-term follow-up, 30 (75%) patients were in NYHA FC I, 8 (20%) were in NYHA FC II, and only 2 (5%) were in NYHA FC III. In conclusion, there was a statistically significant improvement in NYHA FC with a mean improvement (1.275 ± 0.55) at the short-term follow-up in comparison with NYHA

pre-PBMV in the entire study population (P < 0.001). Group A showed NYHA FC improvements of 1.39 ± 0.5, as opposed to NYHA FC improvements of 1 ± 0.6 in Group B. There was no significant relationship in terms of NYHA FC improvements between the 2 groups (P = 0.108). Table 4 depicts comparisons between the study groups regarding acute-phase reactants. No statistically significant differences were detected between the study groups regarding ESR after the first hour, ESR after the second hour, or TLC. Neither ESR nor TLC could predict the development of MR after PBMV.

MVA was measured before and immediately after dilatation and subsequently at follow-up. Table 5 demonstrates MVA throughout 3 stages: Pre-PBMV (MVA1), immediately after PBMV (MVA2), and 3 months later (MVA3). The mean MVA1 was 0.95 ± 0.2 cm^2, which was increased significantly immediately after PBMV to (MVA2) 2.41 ± 0.33 cm^2 (P = 0.001). This significant increase in MVA immediately after PBMV continued at follow-up with a mean (MVA3) of 2.26 ± 0.32 cm^2 compared with the pre-PBMV MVA1 (P = 0.001). There was a slight nonsignificant reduction in MVA3 (2.26 ± 0.32 cm^2) at follow-up in comparison with the initial gain in MVA2 (2.41 ± 0.33 cm^2) immediately after PBMV (P = 0.1). Thus, there was an immediate 154% gain in the mean MVA, which decreased to a 138% gain at follow-up.

Table 5: Comparisons between MVA1, MVA2, and MVA3

	MVA1 Pre-PBMV	MVA 2 Post-PBMV	MVA 3 Follow-up
Mean	0.95	2.41	2.26
Median	0.90	2.40	2.25
SD	0.20	0.33	0.32
Minimum	0.60	1.90	1.80
Maximum	1.40	3.40	3.20

MVA, Mitral valve area; PBMV, percutaneous balloon mitral valvuloplasty

According to Figure 1, the patients in the study groups (Group A and Group B) showed a significant increase in MVA2 immediately after PBMV as compared with the preprocedural MVA1 (from 0.96 ± 0.21 cm^2 and 0.93 ± 0.2 cm^2 to 2.37 ± 0.26 cm^2 and 2.5 ± 0.47 cm^2, respectively). There was no statistically significant difference between the study groups regarding either pre-PBMV MVA1 or MVA2 immediately after PBMV or MVA3 at the end of the follow-up (P = 0.652, P = 0.550, and P = 0.827, respectively). At the end of the follow-up period, the peak transmitral pressure gradient dropped from (mean ± SD) 28.47 ± 6.88 mm Hg before PBMV to 12.35 ± 4.92 mm Hg, which was a statistically significant decrease for the whole study population (P = 0.001). At the end of the follow-up period, the mean transmitral pressure gradient dropped from (mean ± SD) 17.34 ± 6.23 mm Hg before PBMV to 6.38 ± 2.22 mm Hg, which was a statistically significant decrease for the entire study population (P = 0.001).

There was no statistically significant difference between the study groups regarding either the pre-PBMV peak pressure gradient or the peak pressure gradient at follow-up, as is shown in Table 6. There was also no statistically significant difference between the study groups regarding either the pre-PBMV mean pressure gradient or the mean pressure gradient at follow-up, as is demonstrated in Table 7.

Neither the peak transmitral pressure gradient nor the mean transmitral pressure gradient could predict the development of MR after PBMV.

There was a statistically significant decrease in the pulmonary artery systolic pressure from (mean ± SD) 52.13 ± 14.32 mm Hg pre-PBMV to (mean ± SD) 33.4 ± 7.83 mm Hg at the end of the follow-up period (P = 0.001). Before PBMV, the pulmonary artery systolic pressure was not significantly

different between Group A and Group B (52.04 ± 11.93 mm Hg vs 52.33 ± 19.42 mm Hg, respectively; *P* = 0.805). At follow-up, the pulmonary artery systolic pressure did not differ significantly between Group A and Group B (33.29 ± 5.66 mm Hg vs 33.67 ± 11.77 mm Hg, respectively). Thus, the pulmonary artery systolic pressure could not predict the development of MR after PBMV. Table 8 shows comparisons between the study groups regarding the mitral valve score via the Wilkins scoring system.

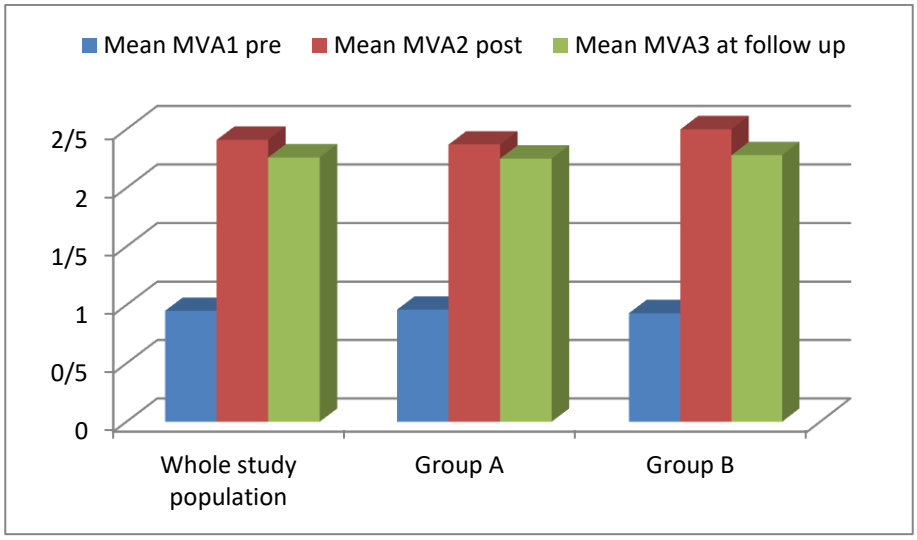

Figure 1: Comparisons are illustrated between mitral valve areas (pre-procedure, immediately after PBMV, and at follow-up).
PBMV, Percutaneous balloon mitral valvuloplasty; MVA, Mitral valve area

Table 6: Peak pressure gradient before PBMV and at follow-up in Group A and Group B

Variable		Group A	Group B	*P*-value
*PG Before PBMV	number	28	12	
	mean±SD	29.04±7.03	27.13±6.61	0.342
*PG at Follow-up	mean±SD	12.46±5.69	12.08±2.47	0.805

PBMV, Percutaneous balloon mitral valvuloplasty; PG, Pressure gradient

Table 7: MG before PBMV and at follow-up in Group A and Group B

Variable		Group A	Group B	*P*-value
*MG Before PBMV	number	28	12	
	mean±SD	17.57±6.68	16.78±5.27	0.827
*MG at Follow-up	mean±SD	6.11±1.71	7±3.1	0.738

MG, Mean pressure gradient; PBMV, Percutaneous balloon mitral valvuloplasty

Table 8: Wilkins Score of the mitral valve area in Group A and Group B

Variable	Group A (n=28)	Group B (n=12)	*P*-value
(i) Leaflet mobility	2.07±0.38	2.25± 0.45	0.405
(ii) Leaflet thickening	1.86±0.45	2± 0.43	0.531
(iii) Subvalvular apparatus	1.61±0.57	1.83±0.58	0.328
(iv) Calcification	1.5±0.69	1.5±0.52	0.805
(v) Total score	7.04±1.29	7.58±1.08	0.192

There was no statistically significant difference between the study groups regarding either each component of the Wilkins Score (leaflet mobility, leaflet thickening, and the involvement of the subvalvular apparatus and calcification) or the total score.

Group B showed insignificantly higher values of the mean (leaflet mobility, subvalvular apparatus involvement, and the total Wilkins Score) than Group A. There was no statistically significant difference between the study groups concerning the total commissural score (P = 0.439). Group B showed insignificantly higher values of the mean total commissural score (2 ± 0.74) than Group A. The mitral valve scoring systems failed to predict the development of MR after PBMV. MR was assessed on 3 occasions: before and immediately after PBMV and subsequently at follow-up. This assessment of the severity of MR was determined by calculating the ratio of the maximal jet area to LAA in the same view using color flow mapping and was graded from I to IV. This ratio was 15% or less in Grade I, from15% to 35% in Grade II, from 35% to 50% in Grade III, and more than 50% in Grade IV according to Braunwald's Heart Disease, 7th edition. [10] Thus, we measured the ratio of the maximal jet area to LAA in the same view to evaluate MR severity at each stage.

Table 9 shows that before the procedure, 17 (42.5%) patients had no MR and 23 (57.5%) had Grades I/IV MR. Immediately after the procedure, 8 (20%) patients still had no MR and 25 (62.5%) patients had Grades I/IV MR (6 patients had Grade 0 MR and 19 patients had Grade I MR before the procedure). Seven (17.5%) patients developed Grades II/IV MR (3 patients had Grade 0 MR and 4 patients had Grade I MR before the procedure). Three (7.5%) patients developed a 2-grade increase in MR (significant MR). At follow-up, the 8 (20%) patients who had no MR post-dilatation continued to have no MR. With respect to the 7 patients who had Grade II MR immediately after the procedure, 1 of them improved to Grade I, 2 of them worsened to Grade III, and the other 4 continued to remain in Grade II. Accordingly, 26 (65%) patients had Grade I MR, 4 (10%) Grade II MR, and 2 (5%) Grade III MR.

The incidence of the overall MR at follow-up (compared with pre-dilatation MR) was 30% (12 patients). Four (10%) patients developed significant MR. There was a statistically significant difference between the study groups regarding preprocedural MR grades (P = 0.006). Compared with Group A, Group B had a higher incidence rate of preprocedural MR (87% vs 47.1%). There was a statistically significant difference between the study groups vis-à-vis the mean MR jet area and the ratio of the MR jet area to LAA % (P = 0.033 and P = 0.049, respectively). There was no statistically meaningful difference between the study groups in terms of preprocedural LAA (P = 0.896).

Table 10 shows comparisons between the study groups regarding the mean preprocedural MR jet area, LAA, and the ratio of the MR jet area to LAA.

There was no statistically significant difference between the study groups regarding the postprocedural mean LAA (P = 0.896). There was no statistically significant difference between the study groups concerning the mean LAA at follow-up (P = 0.531). At follow-up, there was a statistically meaningful difference between the study groups regarding the mean MR jet area and the ratio of the MR jet area to LAA, which were significantly higher in Group B than in Group A (P = 0.001). Compared with Group A, Group B had a high incidence rate of preprocedural MR (87% vs 47.1%) (P = 0.006) and high values of the preprocedural MR jet area (P = 0.033), the ratio of the preprocedural MR jet area to LAA % (P = 0.049), the postprocedural MR jet area (P = 0.005), the ratio of the

postprocedural MR jet area to LAA % (P = 0.005), the follow-up MR jet area (P = 0.001), and the ratio of the follow-up MR jet area to LAA% (P = 0.001).

For the identification of the most independent predictor of the development of MR, the forward stepwise logistic regression analysis was repeated to detect independent predictors among the 3 statistically significant preprocedural variables only (Table 11). The results revealed that the preprocedural MR grade (0 vs I) was an independent predictor (P = 0.01). The odds ratio was 7.5, and its interval of confidence at 95% ranged from 1.5 to 35. The odds of the patients with Grade 1 MR to develop significant MR were 7.5 times those of the patients who were in Grade 0 MR. The wide interval of confidence of these odds (1.5–35) was due to the minimal sample size; however, it was statistically significant to the level of 0.1%.

DISCUSSION

The results of the present investigation showed that the incidence rate of an increase in MR following PBMV was 30% at 3 months' follow-up. This rate is comparable with that in most studies. In a study on 241 patients, Hernandez et al [13] reported that 31% of their patients had an increase in the MR grade, but only 16 (6.6%) patients developed severe MR (≥ Grades III/IV). Padial et al [14] studied 566 patients who underwent PBMV and reported that 37 (6.5%) patients developed severe MR after the procedure; in addition, 13 (1/3) of these patients underwent mitral valve surgery. Zaki et al [15] reported severe postprocedural MR in 9.8% of their study population (4 from 41 patients). Similarly, Kasem et al [16] reported that the incidence rate of severe MR after percutaneous mitral commissurotomy using via the Inoue Balloon Technique in their study population was 10%. In their investigation, Mezillis et al [17] reported the occurrence of severe post-PBMV MR in 2 (9%) patients. The mechanisms of new MR or increased MR grades after PBMV can be due to increased commissural splitting at the non-commissural part (mostly central jets), or a chordal rupture (mostly eccentric jets), or leaflet tear (mostly eccentric jets). In our study, only 1 patient improved from Grade II MR immediately after PBMV to Grade I MR at follow-up. This improvement in MR is in agreement with the findings reported by Krishnamoorthy et al, [18] who performed PBMV on 590 patients with severe mitral valve stenosis. They followed their patients for 1 year and reported that 21 (3.5%) patients developed moderate MR. Krishnamoorthy and colleagues also reported that at 3 months' follow-up, MR decreased in severity to the mild grade in 12 out of the 21 patients. In addition, at 1 year, MR was trivial in 5 patients, mild in 11, and remained moderate in 5. From their study, it may be concluded that PBMV can improve the MR grade in individual patients undergoing this procedure. The improvement in MR may be due to improved leaflet coaptation after a decrease in the mitral valve annulus, better valve closure during systole, and the fracture of calcium within the leaflet, making it more pliable. In contrast to the results of the present study, Hernandez et al [13] and Padial et al [14] reported that early mitral valve replacement was required in one-third of their patients who developed severe MR. Early mitral valve replacement may be due to higher grades of MR (III & IV) in their studies or may be due to the higher incidence of chordal rupture, which necessitates early surgical interventions.

Table 9: Changes in the severity of MR before/after PBMV and at follow-up

MR Grade	Before Dilatation	Immediately After Dilatation	At Follow-up
No MR	17 (42.5%)	8 (20%)	8 (20%)
Grade I MR	23 (57.5%)	25 (62.5%)	26 (65%)
Grade II MR		7 (17.5%)	4 (10%)
Grade III MR			2 (5%)
Grade IV MR			

MR, Mitral regurgitation; PBMV, Percutaneous balloon mitral valvuloplasty

Table 10: Preprocedural MR jet area, left atrial area, and the ratio of the MR Jet area to left atrial area

	Group A	Group B	*P*-value
MR Jet Area	1.89±1.55 cm^2	0.76±1.47cm^2	0.033
Left Atrial Area	39.79±3.97cm^2	38.83±4.71cm^2	0.896
Ratio of MR Jet Area to LAA %	4.77±3.93%	2.18±4.25%	0.049

N.B.: All the variables were measured before PBMV.
MR, Mitral regurgitation

Table 11: Forward stepwise logistic regression analysis

Variable in the Equation							
		B	SE	Wald	df	*P*-value	OR (95% CI)
Step 1a	Preprocedural MR Grade (I)	2.015	.787	6.554	1	.010	7.500 (1.5 to 35)
	Constant	-.118	.486	.059	1	.808	.889

MR, Mitral regurgitation

Our study showed no clinical, echocardiographic, procedural, or hemodynamic predictors (except for preprocedural MR grades) for the development of severe MR following BMV. In contrast to the results of the present study, many previous studies have identified mitral valve scoring systems to be the only predictor of the development of MR and outcome after PBMV. Indeed, Hernandez et al, [13] Feldman et al, [19] Essop et al, [20] Palacios et al, [21] Arora et al, [22] and Elasfar et al [23] all found that the total MR-echo score developed by Padial et al [14] was the only independent predictor of significant MR following percutaneous mitral commissurotomy via the Inoue Balloon Technique with a cutoff point of 7. Additionally, Nunes et al [24] found that the assessment of the mitral valve morphology by using both the Wilkins Score and the ratio between the commissural areas and the maximal excursion of the leaflets from the annulus in diastole could accurately predict the outcome following PBMV by comparison with the existing models. A smaller MVA, a higher mean pressure gradient, and a larger LA dimension were proposed by Mailer et al [25] to be the predictors of the development of MR following the Inoue PBMV. Cho et al [26] proposed the initial MVA as a determinant of increased MR following the Inoue Balloon Technique.

Limitations

The salient limitation to the current study is its small sample size; larger prospective studies are, therefore, needed to arrive at definite conclusions. In addition, we tested MR following repeated PBMV via only the Inoue Balloon Technique but not the other techniques such as the multi-track balloon technique. Another weakness of note is that we failed to evaluate other new mitral valve scoring systems such as the Cormier Score, [27] the grading of the mitral valve anatomy by Rifaie et al, [28] and the first scoring system

using real-time 3D transthoracic echocardiography by Anwar et al. [29]
We used 1 method to assess MR severity (the ratio of the maximal jet area to LAA); however, another expert echocardiographer reassessed all the echocardiographic studies. It is deserving of note that the long-term results of repeated PBMV in these patients and whether they will require further interventions in the future have yet to be determined by long-term follow-up studies in the future.

CONCLUSIONS

The presence of preprocedural Grade I MR may be one of the most independent predictors of a rise in the MR grade after repeated PBMV in middle-aged and elderly patients. Despite this increase in MR following PBMV, our results indicated sustained symptomatic benefits (up to 3 months). Functional status can be improved by PBMV in this subset of patients.

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