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Effect of Percutaneous Balloon Mitral Valvuloplasty on Six Minute Walk Test and Left Ventricular Performance by Speckle Tracking Chocardiography in Rheumatic Severe Mitral Stenosis

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Abstract
Background: *The effect of percutaneous balloon mitral valvuloplasty (PBMV) on left ventricular function in patients with rheumatic severe mitral stenosis (MS) has been controversial for decades. Our aim is to study the effect of PBMV on left ventricular (LV) performance by strain imaging*
Methods: *In this prospective study, we included 74 patients with rheumatic severe MS requiring PBMV. The echocardiographic parameters studied were left ventricular ejection fraction (LVEF), mitral annular systolic velocity (MASV), mitral annular early diastolic velocity (E'), mitral annular plane systolic excursion (MAPSE) and myocardial performance index (MPI). Strain parameters were studied by speckle tracking echocardiography. Six minute walk distance (6MWD) was measured.*
Results: *Out of the 74 patients, 48 were females, showing a female predominance. The mean age of the study population was 33.7±8.4 years.*
On comparing LV parameters before PBMV and at 48 hours after PBMV, MASV (cm/s) and E' showed a significant increase at 48hours after PBMV. No significant change was observed in MAPSE, MPI and LVEF either by Teicholz method or Simpson method. The global circumferential strain (GCS) (-21.1±2.8 vs -26.2±3.6; p = 0.02) and global circumferential strain rate (GCSR) (-1.1±0.2vs -1.3±0.2; p<0.01) showed significant improvement at 48 hours after PBMV. The global longitudinal strain (GLS) (%) (-17.8±3.2 vs -18.9±3.5; p = 0.18), global longitudinal strain rate (GLSR) (1/s) (-1.3±0.1 vs -1.3±0.2; p = 0.21), global radial strain (GRS) (40.1±8.5 vs 41.5±7.2; p = 0.32) and global radial strain rate (GRSR) (1.9±0.2 vs 1.9±0.3; p = 0.26) showed no significant change at 48 hours after PBMV. However, GLS (-17.8±3.2 vs -21.2±5.6; p = 0.03) and GLSR (-1.3±0.1 vs -1.5±0.2; p = 0.04) showed a significant improvement at 2 weeks after PBMV compared to the values before PBMV.
6MWD (m) increased significantly at 48hours after PBMV compared to pre-PBMV values (335.3±40.3 vs 394.3±52.2 ; p < 0.01). It also showed a significant improvement at 2 weeks after PBMV compared to values at 48 hours after PBMV (335.39±40.31 vs 434.3±58.6; p<0.01) .
On Pearson correlation, GLS and GCS showed a significant linear correlation with mitral valve area (MVA) before PBMV. On correlating the changes in the various parameters before PBMV and at 48 hours after PBMV, ∆GLS showed a significant linear correlation with ∆MVA and ∆6MWD. ∆GCS also showed a significant linear correlation with ∆MVA and ∆6MWD. ∆GRS did not show a significant correlation with either ∆MVA or ∆6MWD.
Conclusions: *GLS and GCS may be more sensitive than LVEF to detect changes in the LV performance after PBMV. Patients with higher improvement in GLS and GCS after PBMV had a higher increase in 6MWD suggesting that improvement in the strain parameters after PBMV actually translated into an improvement in the functional exercise capacity of these patients.*

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I. Introduction

Rheumatic heart disease (RHD) is the second most common cause of cardiovascular morbidity and mortality in developing countries next only to atherosclerotic vascular disease (1-3). Mitral stenosis (MS) is one of the key valvular pathologies seen in RHD.

One of the most important goals of echocardiography, performed for almost any indication, is to provide an estimate of left ventricular (LV) systolic function. A number of echocardiographic parameters have been developed over the years to accomplish this task. Among them, left ventricular ejection fraction (LVEF) appears to be the most widely used and clinically the most relevant parameter for this purpose. However LVEF has several limitations. It provides an indirect measure of the LV contractile function and does not measure it

directly. It is readily influenced by a number of factors including loading conditions, heart rate, etc. Most importantly, it is not sensitive enough to detect subtle changes in the contractile function and therefore not suitable for detecting subclinical myocardial damage which may have major therapeutic and prognostic implications in a variety of clinical conditions.

Strain imaging is a technological advancement that has been developed as a means to objectively quantify regional myocardial function (4). In echocardiography, the term "strain" is used to describe local shortening, thickening, and lengthening of the myocardium (5).

A complex deformation occurs in the LV myocardium during the cardiac cycle. The deformation is described in terms of three principle strains - longitudinal, radial and circumferential. Shortening of the LV along its long-axis is denoted by longitudinal strain. The circumferential strain denotes the decrease in the circumference of the LV cavity during the cardiac cycle whereas radial strain depicts the thickening of the LV wall along its radius. During each heart beat, the apex rotates in anticlockwise direction during systole whereas the base rotates in the clockwise direction. This twisting motion of LV during systole with the opposite rotation of the LV apex and base is important to the normal systolic functioning of the LV. The subsequent untwist generates a suction force during diastole that appears to be the key mechanism driving the early diastolic filling of the LV. This complex twisting and untwisting motion is brought about by an equally complex arrangement of the myofibres within the LV myocardium. These properties of the LV have important bearing on the effect of different cardiac pathologies on LV systolic and diastolic function.

Strain imaging offers a means to directly quantify the extent of myocardial contraction and promises to overcome many of the limitations of LVEF. Strain is the percentage change in the length of a myocardial segment during a given period of time and has a unit of %. Strain rate is the rate at which shortening or lengthening takes place and has a unit of 1/s. As the myocardium shortens during systole, the strain and strain rate have negative value but when there is stretch or lengthening of the myocardium, the strain and strain rate become positive.

Speckle tracking echocardiography (STE) is the most widely used technique to assess strain in a variety of clinical and research settings (6).

The current evidence on the LV performance in the setting of MS is highly controversial. Some studies showed no change in the LV function in patients with MS (7). Whereas, LV dysfunction has been reported in MS in some studies (8,9), which may be due to a change in the interaction of right and left ventricles, myocardial fibrosis or a chronic decrease in preload (7). Even with a normal LVEF, there can be an impairment in the long axis function of the LV in the early stages before the onset of LV dysfunction (10,11).

The increase in the mitral valve area (MVA) after percutaneous balloon mitral valvuloplasty (PBMV) can increase the preload to the LV and hence can affect the LV systolic function. Thus PBMV may alter the strain and strain rates of LV. But there is very little data available regarding the effect of PBMV on LV strain.

Apart from these investigations, there are simple tests of functional exercise capacity available to assess the response to therapeutic interventions like the six minute walk test (6MWT).

Six minute walk test:

Many different tests are available for objective evaluation of functional exercise capacity. The most popular clinical exercise tests are stair climbing, a 6MWT, a shuttle-walk test, detection of exercise-induced asthma, a cardiac stress test (e.g., Bruce protocol) and a cardio pulmonary exercise test(12,13).

The 6MWT requires no special exercise equipment or trained technicians. This test measures the distance that a person can quickly walk on a flat, hard surface in a period of 6 minutes. Most persons do not achieve maximal exercise capacity during the 6MWT; instead, they choose their own intensity of exercise and are allowed to stop and rest during the test. As many of the activities of daily living are performed at submaximal work levels, the six minute walk distance (6MWD) may better reflect the functional exercise level for daily physical activities. 6MWT provides an objective evaluation of the functional exercise capacity. It has been widely used to measure the response to therapeutic interventions for pulmonary and cardiac disease.

Very sparse published data is available regarding the effect of PBMV on LV performance in patients with severe MS and the data available on the effect of PBMV on LV strain parameters is even lesser. This prompted us to undertake the present study.

II. Material And Methods

Patients with severe MS who were planned PBMV in the cardiology department at Sri Venkateswara Institute of Medical Sciences (SVIMS), Tirupati, a tertiary care teaching hospital during the period April 2017 and October 2018 were included in the study.

Inclusion criteria:
(i) Patients with severe MS eligible for PBMV

Exclusion criteria:
i) Patients with more than mild organic disease (stenosis or regurgitation) of other valves
ii) Patients with diabetes mellitus
iii) Patients with hypertension
iv) Patients with evidence of coronary artery disease (symptomatic, electrocardiographic or angiographic)
v) Patients with any other heart disease likely to affect the LV function
vi) Patients with any medical condition likely to affect the LV function (thyroid disorders, chronic kidney disease, etc.,)
vii) Pregnant women
vii) Patients who are not willing to participate in the study

Regulatory clearances
The study was carried out after clearance by the Institutional Thesis Approval and Ethics Committees.

Informed consent
A written informed consent was obtained from all patients who participated in the study.

All the patients with moderate to severe MS who attend the cardiology out-patient department were treated as per the guidelines recommended by the American College of Cardiology/ American Heart Association (14). All the patients who were planned for PBMV were admitted in the cardiology department. Patients who satisfied the inclusion criterion and had no exclusion criteria were included in the study.

A careful detailed history was taken and complete physical examination was done. Electrocardiogram and chest xray postero-anterior view were obtained. Routine laboratory tests for haemoglobin, platelet count, renal function tests were carried out. The data was noted in a prefixed proforma. A detailed echocardiographic examination was done.

Echocardiography

Echocardiography was done by SIEMENS ACUSON SC2000 machine using probe frequency range of 2-5 Hz. A single experienced investigator did all the echocardiographic evaluation following the guidelines recommended by the American Society of Echocardiography (15). All echocardiographic measurements were taken as mean of 3 consecutive cycles in sinus rhythm.

LVEF was measured by M-mode and biplane Simpson method. MVA was calculated by planimetry. MVA was also measured by the pressure half time (PHT) method. PHT was obtained by tracing the deceleration slope of the E-wave on Doppler spectral display of transmitral flow. MVA was calculated by dividing 220 with PHT.

Maximum and mean trans-mitral pressure gradients were obtained by continuous wave Doppler across the MV in the apical four chamber (A4C) window. MAPSE was measured by M-mode echocardiography images obtained at the LV lateral, septal, anterior and posterior borders of the mitral ring in the A4C and apical 2-chamber (A2C) views and an average MAPSE value was calculated (16).

For pulsed wave tissue Doppler tracings, sweep speed of 100 mm/s was used. Mitral annular systolic velocity (MASV) and mitral annular early diastolic velocity (E') were measured.

MPI or Tei index is a pure number and was calculated from the ratio of time intervals (a-b/b) derived with the aid of pulsed Doppler echocardiography (17). The sample volume was located at the tips of the MV leaflets, in the A4C view, which enables the measurement of 'a', which is the time interval between the end and the start of transmitral flow (18). The sample volume is then located in the LV outflow tract, just below the aortic valve (apical 5-chamber view) for the measurement of b, the LV ejection time. Tei index or MPI can be calculated as MPI = a-b/b. Average value from four sites was obtained.

Speckle tracking echocardiography

Two-dimensional grey scale images were made in parasternal short axis (PSAX), A4C and A2C views. A sector scan angle of 30–60 degrees was chosen to obtain frame rates of 70–100 Hz. Probe was positioned and cine loops of three cardiac cycles triggered by the R wave of the QRS complex were digitally saved. Off-line analysis was performed using the software for echocardiographic quantification (EchoPAC 6.1.0, GE Medical Systems, Horten, Norway). Grey scale images of A4C, A2C and PSAX views were taken just as in the standard two dimensional echocardiography. Images of A4C view and A2C view were used to measure longitudinal strain, while those of PSAX view were acquired for radial and circumferential strain. The endomyocardial

borders were manually tracked at the end-systolic frame. The second epicardial tracing was automatically generated by the software. The software automatically divided the image into segments.

Myocardial segments were named and localized according to the statement of the Cardiac Imaging Committee of the Council on Clinical Cardiology of the American Heart Association (19). Quality of the tracking was verified for each segment and was adjusted when needed. Strain curves of three consecutive cardiac cycles and values of the manual timing were imported into a custom-made software package for further analysis. The average values of peak systolic longitudinal, radial and circumferential strain and strain rate of the three imported curves were calculated by the custom-made software. Global strain and strain rate were calculated by averaging all the segments. For calculating the global time to reach the peak systolic strain, we used the average of all the segments.

The parameters measured were global longitudinal strain (GLS), global longitudinal strain rate (GLSR), global circumferential strain (GCS), global circumferential strain rate (GCSR), global radial strain (GRS) and global radial strain rate (GRSR).

Six minute walk test

The 6MWT was done as per the guidelines recommended by the American Thoracic Society (20). It was conducted by a single investigator for all the patients on a 30 metre well marked flat surface and the 6MWD was noted. Patients were allowed for 6MWT only if the resting heart rate was less than 120 beats per minute, systolic blood pressure (BP) was less than 180 mm Hg and diastolic BP was less than 100 mm Hg. Patients who have any other medical problems like osteoarthritis, neuromuscular disorders etc., which will affect the 6MWD were also exempted from the 6MWT.

An experienced team performed PBMV in the catheterization laboratory. Balloon size was chosen according to height of the patient (21).

All the patients were followed up at 48 hours after PBMV and also 14 days after PBMV. Echocardiography for various indices of LV function and 6MWT were repeated as mentioned previously at 48 hours after PBMV and also 2 weeks after PBMV.

III. Statistical Analysis

For the categorical variables, descriptive statistics were performed by computing the frequencies (percentages) in each category. Approximate normality of the distribution was assessed for continuous variables. The variables that followed normal distribution were summarized by mean and standard deviation (SD); the remaining variables were summarized as median [interquartile range (IQR)].

Pearson correlation was used to correlate strain parameters with the MVA and 6MWD before PBMV. The change in strain parameters with PBMV i.e, change in global longitudinal strain (ΔGLS), change in global circumferential strain (ΔGCS), change in global radial strain (ΔGRS) were correlated with the change in mitral valve area (ΔMVA) and change in 6MWD (Δ6MWD) with PBMV. Qualitative variables, expressed as numbers and percentages were compared by the Chi-square test. Quantitative variables were compared by paired students t test and analysis of variance. p-value less than 0.05 was considered significant.

Statistical analysis was performed with SPSS software version 20 (SPSS Inc., Chicago, IL).

IV. Results

Out of the 102 patients who underwent PBMV during the study period, 28 patients were excluded due to various reasons like associated involvement of the other valves, atrial fibrillation, pregnancy, mitral regurgitation, diabetes mellitus and hypertension. The remaining 74 patients constitute our study population.

The mean age of the study population was 33.7±8.4 years and the age histogram is shown below in figure 1. Majority of the study population were in the age group of second to fourth decades. There was a atrong female predominance with the male to female ratio being 1:1.9.

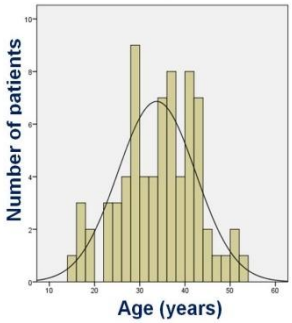

Figure 1: Age histogram showing the age distribution in the study population

The echocardiographic variables were compared before PBMV, at 48 hours after PBMV and 2 weeks after PBMV (Table 1). As one can expect, the peak and mean gradients across the mitral valve decreased at 48 hours after PBMV compared to the pre-PBMV values. MVA both by planimetry and PHT methods showed significant improvement at 48 hours after PBMV. MASV showed a significant improvement at 48 hours after PBMV compared to the pre-PBMV values. E′ also showed a significant improvement at 48 hours after PBMV compared to the pre-PBMV values. MAPSE did not show a significant improvement either at 48 hours or 2 weeks after PBMV. MPI did not a significant change after PBMV either at 48 hours or after 2 weeks. LVEF, either by Teicholz or Simpson methods, did not a statistically significant improvement either at 48 hours or after 2 weeks compared to the values before the procedure.

Table 1: Table showing the comparison of various echocardiographic parameters before PBMV (A), 48 hours after PBMV (B) and 2 weeks after PBMV (C)

VARIABLE (Mean)	BEFORE PBMV (A)	AT 48 HOURS OF PBMV (B)	2 WEEKS AFTER PBMV (C)	A vs B p-value	A vs C p-value	B vs C p-value
Peak gradient (mm Hg)	30.2±8.7	8.2±1.2	9.1±2.5	<0.001	<0.001	0.244
Mean gradient (mm Hg)	16.2±6.8	4.1±1.2	4.8±1.1	<0.001	<0.001	0.368
MVA by planimetry (cm^2)	0.92±0.12	2.01±0.34	2.00±0.78	<0.001	<0.001	0.188
MVA by PHT(cm^2)	0.87±0.23	1.98±0.32	1.97±0.46	<0.001	<0.001	0.212
MASV (cm/s)	7.3±2.3	9.8±3.2	9.7±3.3	0.043	0.026	0.453
E′ (cm/s)	10.4±2.61	13.8±4.5	14.0±3.6	0.033	0.021	0.120
MAPSE	13.2±0.9	13.8±1.2	13.8±1.1	0.091	0.126	0.244
MPI (LV)	0.5±0.2	0.8±0.1	0.4±0.1	0.072	0.061	0.316
LVEF by Teicholz (%)	57.2±10.2	58.3±11.7	58.7±14.2	0.245	0.212	0.455
LVEF by Simpson (%)	59.2±15.2	60.2±12.2	60.7±16.7	0.365	0.278	0.388

(MVA – Mitral valve area; E′ - Mitral annular early diastolic velocity; MAPSE – Mitral annular plane systolic excursion; MPI – Myocardial performance index; LVEF – Left ventricular ejection fraction)

Strain parameters:

The strain parameters studied were GLS, GLSR, GCS, GCSR, GRS and GRSR. The strain parameters were compared before PBMV, at 48 hours after PBMV and 2 weeks after PBMV as shown in table 2. GLS and GLSR did not show a significant improvement at 48 hours after PBMV. However they showed a significant increase at 2 weeks after PBMV compared to the values before PBMV or at 48 hours after PBMV. GCS and GCSR showed a significant improvement at 48 hours after PBMV compared to the pre-PBMV values. GRS and GRSR did not show a significant change either at 48 hours or 2 weeks after PBMV.

Table 2: Table showing the comparison of strain parameters before PBMV (A), 48 hours after PBMV (B) and 2 weeks after PBMV (C)

VARIABLE (Mean)	BEFORE PBMV (A)	AT 48 HOURS OF PBMV (B)	2 WEEKS AFTER PBMV (C)	A vs B p-value	A vs C p-value	B vs C p-value
GLS (%)	-17.81±3.20	-18.90±3.53	-21.26±5.65	0.182	0.031	0.048
GLSR (1/s)	1.30±0.18	1.31±0.21	1.51±0.24	0.214	0.042	0.045
GCS (%)	21.12±2.81	26.26±3.64	27.12±8.36	0.021	<0.001	0.124
GCSR (1/s)	1.17±0.26	1.34±0.29	1.36±0.33	<0.001	<0.001	0.082

GRS (%)	40.17±8.54	41.59±7.24	41.41±7.84	0.324	0.288	0.465
GRSR (1/s)	1.96±0.28	1.98±0.32	1.97±0.38	0.261	0.198	0.298

(PBMV – Percutaneous balloon mitral valvuloplasty; GLS – Global longitudinal strain; GLSR – Global longitudinal strain rate; GCS – Global circumferential strain; GCSR – Global circumferential strain rate; GRS – Global radial strain; GRSR – Global radial strain rate)

Correlation of strain parameters and MVA

Pearson correlation was used to study the correlation between the strain parameters and MVA. GLS and GLSR showed a significant linear correlation with MVA before PBMV suggesting that patients with higher MVA were having a higher GLS values. GCS and GCSR also correlated significantly with the MVA before PBMV suggesting patients with higher MVA were having a higher value of GCS. GRS and GRSR did not show a significant correlation with MVA before PBMV.

Table 3: Table showing the Pearson correlation of strain parameters with mitral valve area

VARIABLE	Mitral valve area (Pre-PBMV)	
	r	p-value
Global longitudinal strain	0.606	<0.001
Global circumferential strain	0.527	<0.001
Global radial strain	0.074	0.528

(PBMV – Percutaneous balloon mitral valvuloplasty; r – Correlation coefficient)

Six minute walk test:

The 6MWD was compared before PBMV, at 48 hours after PBMV and 2 weeks after PBMV as shown in table 4. 6MWD showed a significant improvement at 48 hours after PBMV compared to the pre-PBMV values. It also showed a significant improvement at 2 weeks after PBMV compared to the values at 48 hours after PBMV.

Table 4: Table showing the comparision of 6MWD before, at 48 hours and at 2 weeks after PBMV

VARIABLE (Mean)	**BEFORE PBMV (A)**	**AT 48 HOURS OF PBMV (B)**	**2 WEEKS AFTER PBMV (C)**	**A vs B p-value**	**A vs C p-value**	**B vs C p-value**
6MWD (metres)	335.39±40.31	394.32±52.28	434.36±58.64	<0.001	<0.001	<0.001

(PBMV – Percutaneous balloon mitral valvuloplasty; 6MWD – Six minute walk distance)

Correlation of strain parameters and 6MWD

The strain parameters were correlated with the 6MWD before PBMV by using Pearson correlation. GLS and GCS showed a significant linear correlation with the 6MWD suggesting that patients with higher GLS and GCS had a higher 6MWD. However, GRS did not show a significant correlation with 6MWD.

Table 5: Table showing correlation of strain parameters with six minute walk distance

VARIABLE	**Six minute walk distance (pre-PBMV)**	
	r	**p-value**
Global longitudinal strain	0.457	<0.001
Global circumferential strain	0.388	<0.001
Global radial strain	-0.195	0.096

(PBMV – Percutaneous balloon mitral valvuloplasty; r – Correlation coefficient)

Correlation between ΔMVA and strain parameters

We correlated the change in strain parameters after PBMV i.e, ΔGLS, ΔGCS and ΔGRS with the change in MVA i.e, ΔMVA. ΔGLS showed a significant linear correlation with ΔMVA. ΔGCS also showed a significant linear correlation with ΔMVA. But ΔGRS did not show a significant correlation with ΔMVA.

Table 6: Table showing correlation of delta strain parameters with delta mitral valve area

VARIABLE	ΔMVA	
	r	p-value
ΔGLS	0.819	<0.001
ΔGCS	0.634	<0.001
ΔGRS	0.058	0.624

(ΔMVA – Delta mitral valve area; ΔGLS – Delta global longitudinal strain; ΔGCS – Delta global circumferential strain; ΔGRS – Delta global radial strain)

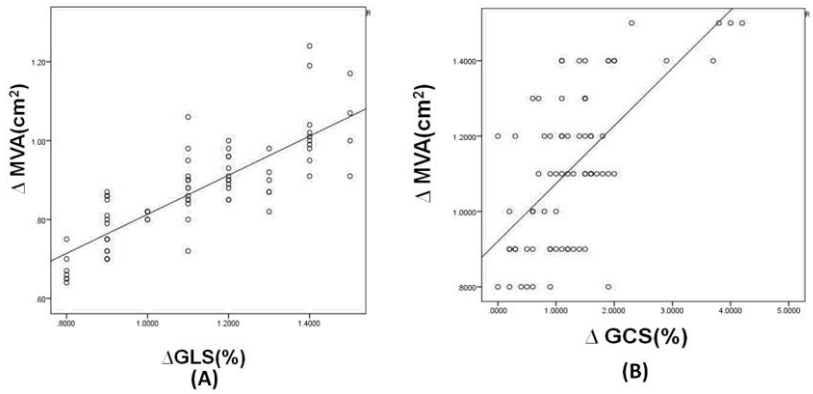

Figure 2: (A) Scatter plot showing the linear correlation of delta global longitudinal strain with delta mitral valve area; (B) Scatter plot showing the linear correlation of delta global circumferential strain with delta mitral valve area

Correlation of the change in 6MWD with delta strain parameters

Pearson correlation was done between 6MWD and various strain parameters. GLS showed a significant linear correlation with 6MWD. GCS also showed a significant linear correlation with 6MWD. However GRS did not show a significant correlation with 6MWD.

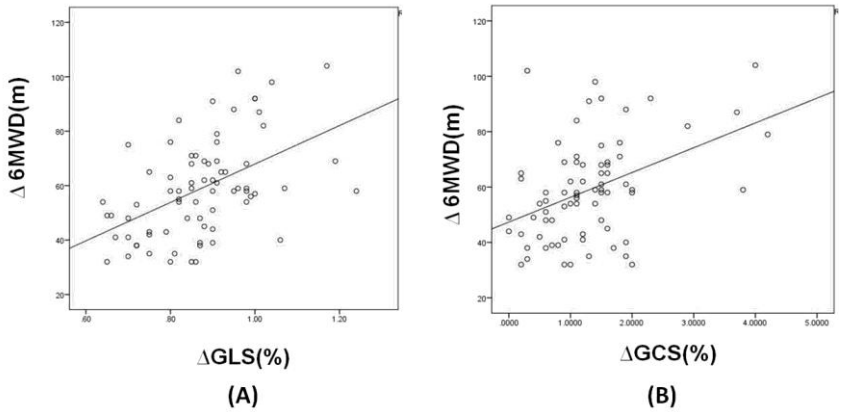

Figure 3: (A) Scatter plot showing the linear correlation of delta global longitudinal strain with delta six minute walk distance; (B) Scatter plot showing the linear correlation of delta global circumferential strain with delta six minute walk distance

Table 7: Table showing correlation of delta strain parameters with delta mitral valve area

VARIABLE	Δ6MWD	
	r	p-value
ΔGLS	0.495	<0.001
ΔGCS	0.430	<0.001
ΔGRS	0.040	0.737

(Δ6MWD – Delta six minute walk distance; ΔGLS – Delta global longitudinal strain; ΔGCS – Delta global circumferential strain; ΔGRS – Delta global radial strain)

Correlation of ΔMVA and Δ6MWD

We also correlated ΔMVA with Δ6MWD by using Pearson correlation. ΔMVA showed a significant linear correlation with Δ6MWD.

Table 8: Table showing correlation of delta six minute walk distance with delta mitral valve area

VARIABLE	ΔMVA	
	r	p-value
Δ6MWD	0.593	<0.001

(ΔMVA – Delta mitral valve area; Δ6MWD – Delta six minute walk distance)

V. Discussion

Rheumatic MS continues to be a major public health problem in the developing countries (2). In our study, there was a strong female preponderance of rheumatic MS, as was reported in many other studies on RHD. MASV and E′ showed a significant improvement after PBMV, but MAPSE and EF did not show a statistically significant improvement after PBMV, probably suggesting that the Doppler velocity paramaters are more sensitive than the M-mode parameters for detecting changes in LV function.

In patients with rheumatic MS, varying degrees of deterioration in LV function has been reported. The data available on the prevalence of longitudinal LV dysfunction in rheumatic MS is sparse. Our study focussed mainly on the strain parameters of LV before and after PBMV in these patients with rheumatic severe MS.

Comparision with other similar studies:

A few studies had been published on the LV function in patients with MS and the effect of PBMVon LV function in these patients. The comparision of our study with two other important studies on this topic is shown in the table 9.

The principal studies published on the effect of PBMV on LV strain parameters were done by Roushdy et al (22) and Sengupta et al (23), one from Egypt and another from Nagpur (India) respectively. Both the Egyptian and Nagpur studies were done during 2013-14. The present study was done during 2017-18. All were prospective studies. The sample size in the Egyptian study was 32, whereas it was 57, in the study by Sengupta et al. The sample size studied in the present study is larger than the other two studies.

The mean age of the study population was more or less similar in the Egyptian and the present studies, and it was slightly lower in the Sengupta et al study. There was a significant female predominance in all the three studies, but it was highest in the Nagpur study. Roushdy et al studied only the longitudinal strain and strain rates and did not study the other parameters of strain. All the longitudinal, circumferential and radial strain and strain rates were studied before and after PBMV in the two Indian studies.

The study by Roushdy et al concluded that PBMV resulted in a significant improvement in the LV longitudinal strain and strain rate in patients with rheumatic severe MS. Sengupta et al concluded that PBMV resulted in a significant improvement in the longitudinal and circumferential strain and strain rates, but did not show a significant influence on the global radial strain or strain rate.

Table 9: Table showing the comparision of our study with other similar studies

VARIABLE	Roushdy et al (22)	Sengupta et al (23)	Present study
Time period	2013-14	2013-14	2017-18
Place of study	Egypt	Nagpur (India)	Tirupati (India)
Type of study	Prospective study	Prospective study	Prospective study
Sample size	32	57	74
Mean age (years)	32.41±11.23	28.14±6.4 4	33.74±8.6 1
Male : female	1:1.6	1:2.5	1:1.9
Strain parameters studied	GLS	GLS GCS GRS	GLS, ΔGLS GCS, ΔGCS GRS, ΔGRS
Significant improvement after PBMV	GLS	GLS GLSR GCS GCSR	<u>At 48hr:</u> GCS GCSR MASV E' <u>Only after 2 weeks:</u> GLS GLSR

(PBMV – Percutaneous balloon mitral valvuloplasty; GLS – Global longitudinal strain; GLSR – Global longitudinal strain rate; GCS – Global circumferential strain; GCSR – Global circumferential strain rate; GRS – Global radial strain; GRSR – Global radial strain rate; MASV – Mitral annular systolic velocity; E' – Mitral annular early diastolic velocity)

The present study showed that PBMV resulted in a significant improvement in the global circumferential strain and strain rates at 48 hours after the procedure. The longitudinal and radial strain and strain rates did not show a significant improvement at 48 hours after PBMV. Global longitudinal strain and strain rate showed a significant improvement in these patients 2 weeks after PBMV compared to the values before PBMV and at 48 hours after PBMV. However, global radial strain and strain rate did not show a significant improvement with PBMV either at 48 hours or 2 weeks after PBMV. There was a significant improvement in 6MWD at 48 hours compared to pre-PBMV values. It is noteworthy that there was a significant improvement in 6MWD measured 2 weeks after PBMV compared to the values at 48 hours after PBMV.

Effect of PBMV on LV function

There have been many studies on the effect of PBMV on LV function, but still the topic remains controversial. Some studies reported an improvement in LV function after PBMV and the other studies reported no significant change in the LV function after PBMV. But the majority of the studies had LVEF as the parameter to assess LV function and the debate about the effect of PBMV on LV function has been controversial for decades. But with the introduction of STE, the strain parameters are also available for assessing the LV function.

In the present study, GCS and GCSR improved significantly at 48 hours after PBMV. However GLS and GLSR showed a significant improvement only 2 weeks after PBMV. GRS and GRSR did not show a significant change with PBMV. LVEF increased only slightly after PBMV and the increase was not statistically significant. This probably suggests that the strain parameters were more sensitive to detect changes in LV function than LVEF. There is a need for similar studies on the effect of PBMV on LV strain parameters than LVEF to put an end to the controversy on the effect of PBMV on LV function.

Correlation of strain parameters with MVA and 6MWD

GLS showed a significant linear correlation with MVA before PBMV, suggesting that patients with higher MVA were having a higher GLS. GCS also showed a significant linear correlation with MVA suggesting that patients with higher MVA were having a higher GCS. GRS had no significant correlation with MVA.

GLS showed a significant linear correlation with 6MWD before PBMV, suggesting that patients with higher GLS were having a higher 6MWD. GCS also showed a significant linear correlation with 6MWD suggesting that patients with higher GCS were having a higher 6MWD. GRS had no significant correlation with 6MWD.

ΔGLS had a significant linear correlation with ΔMVA, suggesting that patients with higher increase in MVA after PBMV were having a higher improvement in GLS after the procedure. ΔGLS also had a significant linear correlation with Δ6MWD, suggesting that patients with higher increase in GLS after PBMV were having a higher improvement in 6MWD after the procedure. ΔGCS correlated well with ΔMVA, suggesting that patients with higher increase in MVA after PBMV were having a higher improvement in GCS. ΔGCS also had a significant linear correlation with Δ6MWD, suggesting that patients with higher increase in GCS after PBMV were having a higher improvement in 6MWD after the procedure. ΔGRS did not correlate well with either ΔMVA or Δ6MWD.

Correlation of ΔMVA with Δ6MWD showed that patients with higher increase in MVA after PBMV had a higher improvement in 6MWD i.e, the functional exercise capacity of the patients.

Limitations of the present study

Firstly, India is a large country with wide regional variations in the patterns of RHD, mitral valve involvement and availability of health care facilities. The study sample might not reflect all the patients with rheumatic severe MS in India. So, there is a need for similar studies across the country.

Secondly, the study did not include patients with atrial fibrillation, and so the results of the present study could not be extended to those in atrial fibrillation.

VI. Conclusions

In patients with rheumatic severe MS, LVEF, either by Teicholz or modified Simpson methods, did not show a significant improvement either at 48 hours or at 2 weeks after the procedure.

PBMV resulted in significant improvement in LV GCS and GCSR at 48 hours after the procedure. There was no significant change in GLS and GLSR at 48 hours after PBMV. However, significant improvement in GLS and GLSR was observed 2 weeks after PBMV. GRS and GRSR did not show a significant change either at 48 hours or at 2 weeks after the procedure. This suggests that GLS and GCS may be more sensitive than LVEF to detect changes in LV performance after PBMV.

On correlating strain parameters with MVA and 6MWD by using Pearson correlation, GLS had a significant linear correlation with the baseline MVA and 6MWD in the patients with rheumatic severe MS, suggesting that patients with higher GLS were having a higher MVA and 6MWD before PBMV. Similarly, GCS had a significant linear correlation with the baseline MVA and 6MWD in the these patients, suggesting that patients with higher GCS were having a higher MVA and 6MWD before PBMV.

On correlating delta change in strain parameters before and after PBMV with ΔMVA and Δ6MWD by using Pearson correlation, ΔGLS had a significant linear correlation with ΔMVA suggesting that patients with a higher increase in MVA after PBMV were having a higher improvement in LV GLS.

ΔGCS also had a significant linear correlation with ΔMVA. Similarly, ΔGLS and ΔGCS also had a significant linear correlation with Δ6MWD suggesting that patients with a higher increase in GLS or GCS after PBMV were having a higher improvement in 6MWD.

So, the increase in MVA after PBMV had actually translated into an increase in GLS and GCS which inturn was associated with an increase in 6MWD. In other words, the increase in MVA after PBMV in patients with rheumatic severe MS had actually translated into an improvement in the LV performance (increase in LV strain parameters), which inturn was associated with an improvement in the functional exercise capacity of these patients.

There is a need to generate similar data on the effect of PBMV on LV strain parameters from other parts of the country and validate the prediction rule evolved in the present study, so that STE may be used to help in the evaluation of these patients before PBMV, assessment of the result of PBMV or estimating the prognosis after PBMV.

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